No. 16-2247

IN THE
United States Court of Appeals
FOR THE THIRD CIRCUIT

In re Zoloft (Sertraline Hydrochloride) Products Liability Litigation

JENNIFER ADAMS, *et al.*,

Plaintiffs-Appellants,

v.

WOLTERS KLUWER HEALTH INC., *et al.*,

Defendants-Appellees.

On Appeal from the United States District Court
for the Eastern District of Pennsylvania
Case No. 12-cv-02342 (Hon. Cynthia M. Rufe)

BRIEF OF WASHINGTON LEGAL FOUNDATION AS *AMICUS CURIAE* IN SUPPORT OF DEFENDANTS-APPELLEES, URGING AFFIRMANCE

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES:

Page(s)

RULES:

LEGISLATIVE SOURCES:

OTHER SOURCES:

Page(s)

Page(s)

IDENTITY AND INTEREST OF *AMICUS CURIAE*[1]

Washington Legal Foundation (WLF) is a non-profit, public-interest law firm and policy center with supporters in all 50 States. WLF devotes a substantial portion of its resources to defending and promoting free enterprise, individual rights, a limited, accountable government, and the rule of law. WLF regularly calls on courts to prevent "junk science" from ever reaching the jury by faithfully applying the rules governing the admissibility of expert testimony. To that end, WLF has long appeared as *amicus curiae* in cases in support of the principle that trial courts must exclude expert testimony that lacks sufficient indicia of reliability. *See, e.g.*, *Kumho Tire Co. v. Carmichael*, 526 U.S. 137 (1999); *Gen. Elec. Co. v. Joiner*, 522 U.S. 136 (1997); *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579 (1993).

In addition, WLF's Legal Studies Division, the publishing arm of WLF, regularly publishes articles on evidentiary issues, including the proper reliability threshold for expert testimony. *See, e.g.*, Victor E. Schwartz, In re Zoloft *MDL Judge's Rejection of Causation Testimony Provides Helpful Lessons for Bench and Bar*, WLF Legal Backgrounder (May 13, 2016); Evan M. Tager & Carl J.

[1] Pursuant to Federal Rule of Appellate Procedure 29(c), *amicus* WLF states that no counsel for any party authored this brief in whole or in part, and that no person or entity, other than WLF and its counsel, made a monetary contribution intended to fund the preparation and submission of this brief. All parties have consented to the filing of this brief.

Summers, *Ninth Circuit Expands* Daubert *Gatekeeping Role for Both Trial and Appellate Courts*, WLF Counsel's Advisory (March 28, 2014).

WLF believes that the quality of decision-making in the federal courts largely depends on the willingness of federal judges to take seriously their responsibility as gatekeepers, to ensure that unsound "scientific" expert evidence is not presented to the finder of fact. When judges disregard that obligation by, for example, deciding that reliability goes to weight rather than admissibility, they undermine the justice system's ability to produce a fair and just result.

In this case, after extensive briefing and an exhaustive, three-day *Daubert* hearing, the district court found that Dr. Jewell's opinion that Zoloft is a cause of cardiac birth defects was inconsistent with well-accepted epidemiological standards. Because Judge Rufe carefully and responsibly applied the correct legal standard under *Daubert*, the Court should affirm her decision to exclude Dr. Jewell's testimony as unreliable and therefore inadmissible.

STATEMENT OF THE CASE

Zoloft is a leading prescription antidepressant used to treat depression, anxiety, and other mental health conditions. This appeal arises from a Multi-District Litigation (MDL) consolidating more than 300 lawsuits alleging that maternal exposure to Zoloft caused cardiac birth defects in Plaintiffs' children. Although the "gold standard" for establishing epidemiological causation is a

double-blind, randomized, controlled trial study, generally such studies are not ethically permissible on pregnant women. Rather, epidemiologists seeking to establish general causation for birth defects must resort to estimating odds ratios from observational evidence, which is often attributable to random chance, bias, or confounding variables—rather than a true association.

Under reliable scientific methods, epidemiological studies generally cannot be used to establish that certain drugs are "associated" with birth defects in the absence of replicated, statistically significant epidemiological findings that adequately control for confounding factors and biases. Even when established, mere "association" is necessary but not sufficient to prove causation. Once a true association has been clearly established, scientists must then seek to infer a causal relationship from that association by consulting various factors commonly known as the Bradford Hill criteria.

At the initial MDL proceedings in this case, Plaintiffs' counsel offered the opinion of epidemiologist Dr. Anick Bérard to establish general causation, *i.e.*, that the use of Zoloft during pregnancy can cause a wide range of birth defects. Following a full *Daubert* hearing, Judge Rufe excluded Dr. Bérard's proffered testimony because she employed a "methodology [that] is not reliable or scientifically sound" by engaging in "cherry-picking" of studies and "failing to account adequately for contrary evidence." JA4283, JA4291.

Subsequently, Judge Rufe also excluded the opinions of Plaintiffs' other general-causation experts, explaining that Drs. Robert Cabrera, T.W. Sadler, and Michael Levin were "premature to draw conclusions about human causation from the evidence [they] relied upon" and that their "opinions about human causation require speculative leaps which are unacceptable in science and in the courthouse." JA120.[2] Lacking any admissible expert evidence of general causation, Plaintiffs sought and obtained leave to replace Dr. Bérard with Dr. Nicholas Jewell, a biostatistician purporting to rely on recently published studies and newly analyzed data to conclude "that maternal use of Zoloft during pregnancy is capable of causing, or contributing to cause, cardiovascular birth defects." JA51.

Following a comprehensive review of the scientific literature and a thorough, three-day *Daubert* hearing, Judge Rufe excluded Dr. Jewell's proffered opinion as scientifically unreliable. JA82. She found that "before concluding that there is a 'true' association between maternal medication use and birth defects," the scientific community generally requires "repeated, consistent, statistically significant human epidemiological findings, and studies which address suspected

[2] Judge Rufe allowed the experts' proffered testimony on biological plausibility, which simply concluded that plausible biological mechanisms exist by which altered concentrations of Zoloft might cause birth defects in humans. JA120. Because the experts had conducted and reviewed both *in vitro* and *in vivo* research to reach their conclusions, the district court found their methodology on biological plausibility to be "generally reliable." *Ibid.*

confounders and biases." JA55, JA60. She further explained that Dr. Jewell cited "no replicated statistically significant findings from non-overlapping data," JA60, but relied instead on studies derived from overlapping data on the Danish population. JA62.

Nor could Dr. Jewell adequately account for the cumulative evidence indicating that *no* association exists between Zoloft and birth defects. JA69. For example, a large 2015 study by Dr. Kari Furu could not replicate the Danish findings, suggesting instead "that there is no association between Zoloft use and cardiac birth defects." JA63. Although Dr. Jewell testified at the *Daubert* hearing that he was familiar with Furu's 2015 study, he could not explain why Dr. Furu's findings should be discounted in favor of earlier studies derived from overlapping, non-independent data. *Ibid.*

In the absence of *any* replicated statistically significant data showing a true association between Zoloft and cardiac birth defects, JA67, Judge Rufe had no need to fully address Dr. Jewell's analysis under the Bradford Hill factors. Concluding that Dr. Jewell's proffered opinion on general causation "failed to consistently apply scientific methods," "deviated from or downplayed certain well-established principles of his field," and "inconsistently applied methods and standards to the data so as to support his *a priori* opinion," Judge Rufe excluded his testimony under *Daubert* as "likely to confuse or mislead the jury." JA82.

Without the testimony of Dr. Jewell or any other epidemiological expert, Plaintiffs could not possibly satisfy their threshold burden of establishing general causation. After more than three years of proceedings, including two *Daubert* hearings on five experts, the district court granted summary judgment in favor of Defendants. *See* JA48, JA50. Plaintiffs appeal only from the district court's exclusion of Dr. Jewell's opinion (and the resulting grant of summary judgment).

SUMMARY OF ARGUMENT

Consistent with *Daubert* and Rule 702, this Court uniformly requires the proponent of an expert to establish (through independent proof) that the basis for that expert's causation opinion—*i.e.*, either the principle of general causation itself or each step in any proposed causal theory—is scientifically reliable. As the district court found in carefully exercising its gatekeeping responsibility in this case, Dr. Jewell's opinion that Zoloft causes birth defects simply cannot meet that basic test. Not only did Dr. Jewell fail to rely on replicated, statistically significant data showing a true association between Zoloft and cardiac birth defects, but he also failed to account for the cumulative evidence in the scientific community indicating that *no* association exists between Zoloft and birth defects. Because the district court acted well within its discretion in rejecting Dr. Jewell's opinion as unreliable, this Court should affirm.

Affirmance is also required to ensure that reliability remains a threshold

question for the court, not the jury. It is not enough for Plaintiffs to invoke the "cross-examination" as a cure-all while leaving any dispute about reliability to the "weight" a jury decides to give that testimony. Although cross-examination has its benefits, it cannot help jurors readily distinguish valid expert conclusions from junk science, nor can it supplant the court's duty to determine the reliability of an expert's testimony in the first instance. That rarified task must fall only on the court's shoulders, and in this case Judge Rufe performed her role as gatekeeper with painstaking care.

In seeking an abuse-of-discretion reversal, Plaintiffs invite the Court to disregard *Daubert* by significantly relaxing a product-liability plaintiff's burden to establish reliability. But doing so would not only sweep aside more than two decades of Supreme Court precedent, it would also produce detrimental consequences that would reverberate well beyond this case. Permitting a flimsy, unscientific "association" to serve as the basis for imposing massive tort liability on drug manufacturers would undoubtedly disincentivize the continued development of lifesaving drugs. Absent clearly enforced thresholds for the reliability of expert evidence on general causation, drug manufacturers facing unwarranted liability would be forced either to raise prices significantly or to exit the market altogether—reducing access to an important mental health therapy. In such a litigious climate, physicians and their patients who rely on such drugs

would suffer the most.

If such a scenario seems improbable, one need only consult recent history. Indeed, this case is not the first time that a widely prescribed medication has been wrongly accused of causing birth defects. Thirty years ago, Bendectin, a popular drug prescribed to pregnant women to alleviate morning sickness, was also suspected of causing a variety of birth defects—despite the consensus of the FDA and the scientific community to the contrary. An avalanche of lawsuits—made possible by "expert" testimony purporting to "reinterpret" existing epidemiological data—ultimately prompted Bendectin's manufacturer to remove the drug from the market. As a result, hospitalizations for severe cases of nausea and vomiting during pregnancy more than doubled, while the incidence of birth defects (once alleged to be caused by Bendectin) never decreased.

Fortunately, the same chemical compound found in Bendectin has recently been reintroduced to the market. But the notoriously unreliable evidence employed in the Bendectin litigation led directly to the Supreme Court's landmark ruling in *Daubert*, which imposes a vital gatekeeping duty on all district courts. As this historic example makes clear, caving in to Plaintiffs' demands to proceed based on nothing more than a hypothetical connection between Zoloft and birth defects would have far-reaching ramifications on public health.

ARGUMENT

I. THE DISTRICT COURT ACTED WELL WITHIN ITS DISCRETION IN REJECTING DR. JEWELL'S UNRELIABLE EXPERT OPINION

Judge Rufe's decision to exclude Dr. Jewell's opinion is entitled to review under an abuse-of-discretion standard, which "grants the trial judge broad latitude" and "applies as much to the trial court's decisions about how to determine reliability as to its ultimate conclusions." *Kumho Tire Co.*, 526 U.S. at 152-53. Discretion is abused "when the judicial action is arbitrary, fanciful or unreasonable, which is another way of saying that discretion is abused only where no reasonable man would take the view adopted by the trial court." *Zavala v. Wal-Mart Stores Inc.*, 691 F.3d 527, 534 (3d Cir. 2012) (citations omitted). Plaintiffs cannot possibly meet that high burden.

On appeal, Plaintiffs complain that "where the challenge is to an expert's application of an accepted methodology, that challenge is 'not the proper subject of a Rule 702-based exclusion, but is rather the subject of cross-examination of the expert and resolution by the jury.'" Plaintiffs' Brief at 43-44 (quoting *In re Paoli R.R. Yard PCB Litig. ("Paoli I")*, 916 F.2d 829, 858 (3d Cir. 1990)). But that is simply no longer the law.

After *Daubert*, reliability is a threshold question for the court, not for the jury, and Rule 702 now demands that district courts reject expert testimony that is not based on "sufficient facts or data," or is not the product of "reliable principles

and methods," or where the proffered witness has not "reliably applied the principles and methods to the facts of the case." Fed. R. Evid. 702. The Plaintiffs' dismissive approach to reliability thus obscures the fact that Judge Rufe's criticisms of Dr. Jewell's methodology went directly to the guideposts established by *Daubert* and Rule 702: whether Jewell's opinion was based on sufficient facts, whether Jewell reliably applied principles and methods to the facts of the case, and whether Jewell accounted for alternative explanations in reaching his conclusion. *See Daubert*, 502 U.S. at 593-94; Fed. R. Evid. 702.

Since *Daubert*, this Court has emphasized that "*any* step that renders the analysis unreliable under the *Daubert* factors renders the expert's testimony inadmissible." *In re Paoli R.R. Yard PCB Litig. ("Paoli II")*, 35 F.3d 717, 745 (3d Cir. 1994). "This is true whether the step completely changes a reliable methodology or merely misapplies that methodology." *Ibid.* Indeed, "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." *Joiner*, 522 U.S. at 146.

That is precisely what happened in this case, where Dr. Jewell betrayed an insurmountable analytical gap between the available scientific evidence and his opinion. As for how much "weight" a jury should give such evidence, there is only

one acceptable answer: *none*. Such "[i]nadmissible evidence contributes nothing to a 'legally sufficient evidentiary basis'" for a jury verdict. *Weisgram v. Marley Co.*, 528 U.S. 440, 454 (2000). Accordingly, Judge Rufe did not abuse her broad discretion by wisely rejecting Plaintiffs' "standard of meaninglessly high generality" and instead "boring in on the precise state of scientific knowledge in this case." *Black v. Food Lion, Inc.*, 171 F.3d 308, 314 (5th Cir. 1999); *Rodriguez v. Striker Corp.*, 680 F.3d 568, 572 (6th Cir. 2012) ("[C]ourts have a duty to inspect the reasoning of qualified experts … including whether an expert's sources support his conclusions.") (quotation and citation omitted).

Nor is it enough to invoke the "cross-examination" of expert testimony while leaving any dispute about reliability to the "weight" a jury decides to give that testimony. While cross-examination has its benefits, it is no panacea; it cannot readily distinguish valid expert conclusions from junk science, and thus it cannot take the court's place in determining an expert's reliability in the first instance. As Professor Jules Epstein has explained:

> This treatment of cross-examination as the palliative of choice has its flaws, not merely in its expectation that cross-examination without other resources can fairly respond to an expert witness. The mythic status of cross-examination in this regard actually impedes accurate fact-finding because leading questions are not always an appropriate or sufficient tool for truth finding. Courts have not acknowledged these limitations.

Jules Epstein, *Cross-Examination: Seemingly Ubiquitous, Purportedly Omnipotent, and "At Risk,"* 14 Widener L. Rev. 427, 437 (2009) (internal citations omitted).

Indeed, legal scholars have long insisted that "cross-examination does little to affect jury appraisals of expert testimony." Christopher B. Mueller, Daubert *Asks the Right Questions: Now Appellate Courts Should Help Find the Right Answers*, 33 Seton Hall L. Rev. 987, 993 (2003). To the contrary, studies have revealed jurors' commonly held assumption that, because the trial judge admitted the expert evidence, it must have passed at least some minimal level of scrutiny. *See, e.g.*, N.J. Schweitzer & Michael J. Saks, *The Gatekeeper Effect: The Impact of Judges' Admissibility Decisions on the Persuasiveness of Expert Testimony*, 15 Psychol. Pub. Pol'y & L. 1, 7 (2009).

Urging the Court to admit Dr. Jewell's unreliable expert testimony, Plaintiffs contend that a jury can somehow muddle through the relevant science with the aid of competing expert evidence and cross-examination. But dismissing key, demonstrable, and objective flaws in expert evidence as going to the "weight" of that evidence inevitably leaves jurors with the rarified task of resolving the basic *reliability* of a given expert's testimony. Jurors cannot and should not be expected to make those sorts of reliability determinations.

As both *Daubert* and Rule 702 make clear, the only way to ensure that a jury does not give too much weight to unreliable evidence is not to admit it in the first place. "The basic calipers that jurors use to evaluate testimony—their own life experience—are of little value when jurors evaluate whether an expert is telling the truth." Victor E. Schwartz & Cary Silverman, *The Draining of* Daubert *and the Recidivism of Junk Science in Federal and State Courts*, 35 Hofstra L. Rev. 217, 220 (2006). For that reason, any questions about the "factual basis, data, principles, [or] methods" of expert testimony—or "their *application*"—require the trial judge to determine whether that testimony is reliable *before* sending it to the jury. *Kumho Tire Co.*, 526 U.S. at 149 (emphasis added). That is precisely what Judge Rufe did in this case, and she did not abuse her broad discretion in doing so.

II. RELAXING THE RELIABILITY THRESHOLD FOR EXPERT OPINION ON GENERAL CAUSATION WOULD CREATE PERVERSE INCENTIVES FOR DRUG MANUFACTURERS, SIGNIFICANTLY HARMING PUBLIC HEALTH.

As the record demonstrates, physicians and patients routinely rely on Zoloft as a first-line therapy for women with depression during pregnancy. At the same time, the cumulative body of scientific evidence shows *no* association between Zoloft and cardiac birth defects. From a public health perspective, therefore, vindicating the district court's broad discretion in exercising its gatekeeping duty to exclude Dr. Jewell's testimony is especially important. As Justice Breyer has astutely recognized:

> [M]odern life, including good health as well as economic well-being, depends upon the use of artificial or manufactured substances, such as chemicals. And it may, therefore, prove particularly important to see that judges fulfill their *Daubert* gatekeeping function, so that they help assure that the powerful engine of tort liability, which can generate strong financial incentives to reduce, or to eliminate, production, points toward the right substances and does not destroy the wrong ones.

Joiner, 522 U.S. at 148-49 (Breyer, J. concurring); *see also Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 678 (6th Cir. 2010) (explaining that "allowing the law to get ahead of science" would "stifle innovation unnecessarily").

Many assumptions about risks of harm from prenatal exposure to certain drugs have been exaggerated and are overwhelmingly wrong. And yet, there are literally thousands of product-liability suits pending throughout the country—in both state and federal court—against the manufacturers of pharmaceutical products. Lay juries are naturally sympathetic to plaintiffs who appear to have suffered harm while using prescription drugs, and the temptation is great to indulge the *post hoc ergo propter hoc* fallacy, especially when manufacturer liability can be imposed on the basis of a "scientific" expert's say-so. Given the sheer number of such cases, rigorous gatekeeping is essential to ensure that "the powerful engine of tort liability" does not do more harm than good. *Joiner*, 522 U.S. at 149 (Breyer, J. concurring).

Absent clearly enforced thresholds for the reliability of expert evidence on general causation, drug manufacturers will be left with little guidance about how to

structure their conduct to avoid liability. Permitting a flimsy scientific "association" to serve as the basis for imposing massive tort liability on drug manufacturers would undoubtedly disincentivize the development of lifesaving, innovative drugs. *See, e.g., Browning Ferris Indus. of Vt., Inc. v. Kelco Disposal, Inc.*, 492 U.S. 257, 282 (1989) (O'Connor, J., concurring in part and dissenting in part) (observing that "the threat of … enormous awards" has convinced prescription drug manufacturers "that it is better to avoid uncertain liability than to introduce a new pill"); *Carlin v. Superior Court*, 920 P.2d 1347, 1361 (Cal. 1996) ("[T]he imposition of excessive liability on prescription drug manufacturers may discourage the development and availability of life-sustaining and lifesaving drugs.").

For many manufacturers, the easiest way to prevent unwarranted litigation may be to avoid market participation altogether. Indeed, leading scientific organizations—such as the National Academy of Science (NAS) and the American Association for the Advancement of Science (AAAS)—have warned that permitting experts to present novel theories in a court of law "can unwittingly inject bad science into broader decisions affecting society (for example, by encouraging meritless litigation against the producers of products that in fact are safe, or, even worse, by causing the abandonment of products that might prevent injuries)." Brief for the Am. Ass'n for the Advancement of Science and the Nat'l

Academy of Science as *Amici Curiae* in Support of Respondent, *Daubert v. Merrell Dow Pharms.*, 509 U.S. 579 (1993) (No. 92-102), *available at* 1993 WL 13006381, at *23; *see also* Margaret Gilhooley, *Innovative Drugs, Products Liability, Regulatory Compliance, and Patient Choice*, 24 Seton Hall L. Rev. 1481, 1483 (1994) ("[M]edical experts have expressed concern that uncertain liability standards, coupled with litigation costs, may discourage useful drug innovation.").

Another unpalatable alternative is for drug manufacturers to pass ever-increasing operating costs along to consumers in the form of significantly higher prices. *See, e.g., Brown v. Superior Court*, 751 P.2d 470, 478 (Cal. 1988) (warning that "the consuming public … will pay a higher price for the product to reflect the increased expense of insurance to the manufacturer resulting from its greater exposure to liability"); S. Rep. No. 105-32, at 3 (1997) ("Increased product liability costs are reflected in dramatic increases in liability insurance costs. Over the last forty years, general liability insurance costs have increased at over four times the rate of growth of the national economy."). If, as Plaintiffs here urge, liability could be imposed in the absence of *any* replicated, statistically significant data showing that Zoloft causes cardiac birth defects, the resulting "product price may reflect external costs not associated with the risks of the medication [and] distort the cost-benefit calculus faced by each consumer." Note, *A Question of Competence: The Judicial Role in the Regulation of Pharmaceuticals*, 103 Harv. L.

Rev. 773, 781 (1990). That would not only be fundamentally unfair to manufacturers, but it would prove disastrous for the public health.

III. THE FACTS UNDERLYING THE SUPREME COURT'S LANDMARK *DAUBERT* DECISION PROVIDE A CAUTIONARY TALE FOR THIS CASE.

If it is true that "[t]hose who cannot remember the past are condemned to repeat it," George Santayana, *The Life of Reason* 284 (Archibald Constable & Co. Ltd. 1906), then revisiting the recent history—still in living memory—of the disastrous legacy of junk science in American courtrooms is highly appropriate in this case. Indeed, the parallels between the Supreme Court's watershed case *Daubert v. Merrell Dow Pharmaceuticals, Inc*. and this case are both striking and instructive. The facts underlying the *Daubert* litigation provide a concrete reminder that a seemingly obvious "link" can never be assumed between a drug taken by millions of pregnant women and tragic defects suffered by a percentage of children born to those women.

In *Daubert*, the plaintiff sued the manufacturer of the anti-morning-sickness drug Bendectin, claiming that his mother's use of the medicine during pregnancy caused him to suffer severe birth defects. *Daubert*, 509 U.S. at 582. Bendectin was the only medicine ever approved in the United States for treatment of morning sickness. Sold in 22 countries, Bendectin had been prescribed to more than 35 million American women since it entered the U.S. market in 1956. *See* Louis Lasagna & Sheila R. Shulman, "Bendectin and the Language of Causation," in

Phantom Risk: Scientific Inference and the Law 101 (Kenneth R. Foster *et al.* eds., 1993). In the mid-1970s, a number of case studies appeared in the medical literature suggesting a possible association between Bendectin use and a variety of congenital anomalies. After exhaustive research, however, "[n]o study had found Bendectin to be a human teratogen (*i.e.*, a substance capable of causing malformations in fetuses)." *Daubert*, 509 U.S. at 582.

Notwithstanding that the mainstream scientific community—including an expert panel of the FDA—found *no* causal link between Bendectin and birth defects, more than a thousand lawsuits were filed between 1977 and 1986 against Bendectin's manufacturer, Merrell Dow Pharmaceuticals. *See* Lasagna & Shulman, *supra*, at 102-10. Before *Daubert* raised the reliability threshold for the admission of expert testimony, many state and federal courts applied a relaxed standard for the admissibility of such testimony (similar to the standard urged by Plaintiffs here). As a result, hundreds of Bendectin lawsuits were bolstered by testimony from experts with "impressive credentials," but whose opinions on general causation were "based upon 'in vitro' (test tube) and 'in vivo' (live) animal studies; pharmacological studies … that purported to show similarities between the structure of the drug and that of other substances known to cause birth defects; and the 'reanalysis' of previously published epidemiological (human statistical) studies." *Daubert*, 509 U.S. at 583. Although those "expert" opinions clearly did

not reflect the consensus of the scientific community, many juries awarded plaintiffs in Bendectin cases huge monetary awards, including one for $95 million. *See Ealy v. Richardson-Merrell, Inc.*, Civ. A. No. 83-3504, 1987 WL 18743, at *6 (D.D.C. Oct. 1, 1987), *rev'd*, 897 F.2d 1159 (D.C. Cir. 1990).

After decades of litigation in state and federal courts, most of those egregious monetary awards were either set aside by the trial judge or reversed on appeal. *See Merrell Dow Pharms., Inc. v. Havner*, 953 S.W.2d 706, 709-11 (Tex. 1997) (chronicling state and federal Bendectin litigation); *see also* Lasagna & Shulman, *supra*, at 113-15 (same). Nonetheless, due to the enormous litigation costs incurred, Merrell Dow's liability insurance premiums for Bendectin quickly approached its gross sales of Bendectin: "Despite two substantial price increases in 1982 and 1983, Merrell [Dow] anticipated that it would lose money on Bendectin in 1983." Michael D. Green, *Bendectin and Birth Defects: The Challenges of Mass Toxic Substances Litigation* 180 (1996). After spending more than $100 million defending itself in court—despite the scientific community's consensus that Bendectin did not cause birth defects—Merrell Dow ultimately withdrew Bendectin from the market in June of 1983. Lasagna & Shulman, *supra*, at 141.

In 2013, doxlamine-pyridozine, the same chemical compound contained in Bendectin, was reintroduced to the market as Diclegis. *See* The Associated Press, *Morning Sickness Drug Returns*, N.Y. Times (Apr. 8, 2013) ("That long-ago safety

scare, prompted by hundreds of lawsuits claiming birth defects, proved to be a false alarm."). Unsurprisingly, Diclegis received FDA Pregnancy Category A, the best rating available, which is authorized only when well-controlled studies in pregnant women fail to show any risk to the fetus. *See* Press Release, FDA, FDA approves Diclegis for pregnant women experiencing nausea and vomiting (April 8, 2013).

Yet for the intervening 30 years that the drug was unavailable, unfounded Bendectin litigation produced a genuine public health tragedy, as millions of pregnant women suffered needlessly. According to the American College of Obstetrics and Gynecology, the manufacturer's business decision to discontinue the production of Bendectin "create[d] a significant therapeutic gap," as "[n]asuea and vomiting in pregnancy cannot always be treated by symptomatic means, and in the past years severe cases have led to serious maternal nutritional as well as other deficiencies." Bd. of Trustees of the Am. Med. Ass'n, Impact of Product Liability on the Development of New Medical Technologies, Proceedings House of Delegates, 137th Annual Meeting, 18-22 June 1988, Chicago, IL, at 10.

Desperate for relief, many pregnant women resorted to homeopathic and other alternative remedies that notoriously provide "little, if any, safety information." Thomas H. Strong, Jr., *Alternative Therapies of Morning Sickness*, 44 Clinical Obstetrics & Gynecology 653, 656 (2001). By 1990, the Journal of the

American Medical Association reported that, since Bendectin exited the market in 1983, hospitalizations had doubled for severe cases of nausea and vomiting during pregnancy. A. Skolnick, *Key Witness Against Morning Sickness Drug Faces Scientific Fraud Charges*, 263 J. Am. Med. Ass'n 1468, 1473 (1990). The report cautioned that severe nausea and vomiting can lead to dehydration and acidosis, which threaten the health of both mother and fetus and, ironically, can lead to an *increased* incidence of birth defects. *Ibid.*

Moreover, it is now well settled that the removal of Bendectin from the market "did not lead to a reduction in *any* category of birth defects." David E. Bernstein, *Learning the Wrong Lessons from 'An American Tragedy': A Critique of the Berger-Twerski Informed Choice Proposal*, 104 Mich L. Rev. 1961, 1966 (2005-06) (emphasis added). Indeed, a "2003 study concluded that the fact that the rate of birth defects remained constant after Merrell Dow withdrew Bendectin from the market is not consistent with the hypothesis that Bendectin is a teratogen." *Ibid.* (citing Jeffrey S. Kutcher *et al*., *Bendectin and Birth Defects II: Ecological Analyses*, 2 Birth Defects Research 67, 88 (2003)).

The notoriously unreliable evidence employed in the Bendectin litigation led directly to the Supreme Court's landmark ruling in *Daubert*, which imposes a vital gatekeeping duty on all district court judges. Here, Zoloft's manufacturer stands accused of causing birth defects based on purported scientific evidence that is

every bit as unreliable as the opinions that were used to impose liability on the manufacturer of Bendectin. As this historic example makes clear, caving in to Plaintiffs' demands to proceed based on nothing more than a hypothetical connection between Zoloft and birth defects would have far-reaching ramifications on public health well beyond this case. Because Dr. Jewell's causation opinion is *at least* as unreliable as those rejected in *Daubert*, this Court should affirm the district court's well-reasoned decision.

CONCLUSION

For the foregoing reasons, *amicus* Washington Legal Foundation respectfully requests that the Court affirm the well-reasoned judgment below.

Respectfully submitted,

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COMBINED CERTIFICATIONS

I hereby certify that:

1. This brief complies with the type-volume limitations of Fed. R. App. P. 32(a)(7)(B) because this brief contains 4,947 words, excluding those parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii).

2. This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the typestyle requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced serif typeface using Microsoft Office Word 2010 in 14-point Times New Roman font.

3. Pursuant to Local Rule 46.1, Cory L. Andrews is a member in good standing of the bar for the United States Court of Appeals for the Third Circuit.

4. The text of the electronically filed brief is identical to the text in the paper copies.

5. A virus detection program (VIPRE Business, Version 5.0.4464) has scanned the electronic file and no virus was detected.

Dated: October 18, 2016

/s/ Cory L. Andrews
Cory L. Andrews

CERTIFICATE OF SERVICE

Pursuant to Fed. R. App. P. 25(d), I hereby certify that on October 18, 2016, the foregoing *amicus curiae* brief was filed electronically with the Clerk of the Court for the United States Court of Appeals for the Third Circuit using the appellate CM/ECF system. To the best of my knowledge, all parties to this case are represented by counsel who are registered CM/ECF users and will be served electronically by the appellate CM/ECF system.

/s/ Cory L. Andrews
Cory L. Andrews