22-146

IN THE United States Court of Appeals for the Second Circuit

NICHOLE DANIELS-FEASEL, individually and as parent and natural guardian of C.F., JESSICA ANGLIN, individually and as parent and natural guardian of J.A., GINGER EUGLEY, individually and as parent and natural guardian of D.F., CHRIS HAYNER, individually and as parent and natural guardian of T.P, DEBORAH DIMEGLIO, individually and as parent and natural guardian of L.D., REBECCA WARBERG, as parent and natural guardian of B.W.,

Plaintiffs-Appellants,

LANA RUTHART, individually and as parent and natural guardian of L.M.,

Plaintiff,

v.

FOREST PHARMACEUTICALS, INC., FOREST LABORATORIES, LLC, FOREST LABORATORIES INC., ALLERGAN PLC,

Defendants-Appellees.

On Appeal from the U.S. District Court for the Southern District of New York
No. 17-cv-4188-LTS-JLC, Hon. Laura Taylor Swain

BRIEF OF WASHINGTON LEGAL FOUNDATION AS *AMICUS CURIAE* SUPPORTING APPELLEES AND AFFIRMANCE

Cory L. Andrews
John M. Masslon II
WASHINGTON LEGAL FOUNDATION
2009 Massachusetts Ave., NW
Washington, DC 20036
(202) 588-0302
jmasslon@wlf.org
Counsel for Amicus Curiae

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INTEREST OF *AMICUS CURIAE*[*]

Washington Legal Foundation is a nonprofit, public-interest law firm and policy center with supporters nationwide. WLF promotes free enterprise, individual rights, limited government, and the rule of law. It often appears as *amicus curiae* to urge the federal courts to exclude all scientifically unreliable expert evidence. *See In re Lipitor (Atorvastatin Calcium) Mktg., Sales Practices & Prods. Liab. Litig.*, 892 F.3d 624 (4th Cir. 2018); *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787 (3d Cir. 2017).

WLF's Legal Studies Division, the Foundation's publishing arm, regularly distributes articles by outside experts on the value of keeping unreliable expert testimony out of federal court. *See, e.g.*, Lee Mickus & Abigail Dodd, *Stop Calling Them "*Daubert *Motions": Federal Rule of Evidence 702 and Why Words Matter*, WLF Working Paper (Aug. 2021); Kirby T. Griffis, *The Role of Statistical Significance in* Daubert*/Rule 702 Hearings*, WLF Working Paper (Mar. 2017).

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[*] No party's counsel authored any part of this brief. No one, apart from Washington Legal Foundation and its counsel, contributed money intended to fund the brief's preparation or submission. All parties have consented to the filing of this brief.

Scientifically unreliable expert evidence hinders the pursuit of truth. The quality of decision-making in federal court thus hinges on the ability of district judges to stop unreliable expert testimony from ever becoming evidence. WLF fears that if the Court were to dilute the District Court's Rule 702 gatekeeping duty by, for example, deciding that methodological flaws in an expert's opinion bear upon the weight it should be given rather than its admissibility, then the judiciary's ability to produce a fair and just result will be severely eroded.

SUMMARY OF ARGUMENT

This appeal arises from a lawsuit against the designers, manufacturers, and marketers of the FDA-approved drug Lexapro®, an antidepressant therapy in the class of selective serotonin reuptake inhibitors (SSRIs). Plaintiffs are six women who allege that using Lexapro® while pregnant ultimately caused their minor children to develop autism spectrum disorder (ASD). Because Plaintiffs adduced no admissible, reliable evidence to prove general causation, the District Court granted Defendants summary judgment and dismissed Plaintiffs' claims. That judgment should be affirmed.

Rule 702 requires district courts to exclude all expert testimony lacking "sufficient facts or data" or "reliable principles and methods," or if the proposed witness has not "reliably applied the principles and methods to the facts of the case." Fed. R. Evid. 702. In excluding Plaintiffs' unreliable expert evidence, Judge Swain faithfully applied Rule 702's command. To prevail on appeal, Plaintiffs must show that the District Court's exercise of its gatekeeping duty was "manifestly erroneous." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 265 (2d Cir. 2002). Plaintiffs simply cannot meet that high bar.

Plaintiffs accuse the District Court of taking "too rigid an approach" to Rule 702's "reliability criteria" by "elevating" them "into a legal imperative." (Plaintiffs' Opening Br. 18) But the Federal Rules of Evidence are not mere "suggestions." (*Id.*) Rule 702 requires federal trial courts to "tak[e] a hard look at each expert's methodology." *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 982 F.3d 113, 123 (2d Cir. 2020) (per curiam). And that means "undertak[ing] a rigorous examination of . . . the method by which the expert draws an opinion from th[e] facts." *Amorgianos*, 303 F.3d at 267.

At bottom, Plaintiffs invite the Court to disregard Rule 702 by relaxing their burden to present scientifically reliable expert testimony derived from reliably applied methodologies. Yet doing so would not only discard Rule 702 and decades of Supreme Court precedent but—given the highly inconsistent and unreliable approach to causation employed by Plaintiffs' experts here—also inject harmful uncertainty well beyond this case.

Allowing a flimsy, unscientific "association" to serve as the basis for imposing massive tort liability on drug manufacturers would discourage the development of many beneficial drugs. Without enforced thresholds for the reliability of expert evidence on causation, drug manufacturers facing unwarranted liability would be forced either to raise prices significantly or to exit the market altogether—reducing access to important, even life-saving, therapies. Ultimately, patients and their physicians who rely on such therapies would suffer the most.

In sum, Plaintiffs' experts' "methods" are neither testable nor falsifiable. Allowing them into evidence would undermine the critical screening function district courts perform by preventing juries from being misled by speculation masquerading as scientific knowledge.

ARGUMENT

I. THE FLAWS IN PLAINTIFFS' EXPERTS' TESTIMONY GO TO RELIABILITY, NOT WEIGHT.

Plaintiffs contend (at 17) that the District Court "thwarted the adversarial process" and "took triable questions out of the jury's hands" by excluding their three causation experts under Rule 702. But the reliability of expert evidence is a threshold question for the court, not the jury. And here the District Court performed its gatekeeping duty both carefully and thoroughly.

A. None of Plaintiffs' experts applied reliable, objective standards.

Rule 702 demands that district courts reject expert testimony divorced from "sufficient facts or data," or that is not the product of "reliable principles and methods," or where the proposed witness has not "reliably applied the principles and methods to the facts of the case." Fed. R. Evid. 702. Here the District Court's criticisms of Plaintiffs' experts' opinions all went directly to those guideposts.

Start with Dr. Lemuel Moyé, who concluded that SSRI use "is a cause of autism separate and apart from any relationship between maternal depression and autism." (SPA-12) The District Court excluded

that opinion because his "weight-of-the-evidence" method lacked any objective standards. While Plaintiffs concede that Dr. Moyé never "tested his theory of general causation, submitted it for peer review or publication, or specified its error rate," they criticize the District Court's "hard look" at his methods. (Plaintiffs' Opening Br. 73) But this Court requires that "hard look," and has affirmed the exclusion of Dr. Moyé's unreliable opinion on similar grounds. *In re Mirena*, 982 F.3d at 123.

To pass muster, any weight-of-the-evidence method requires, above all, "some scientific method of weighting," lest it become a "mere conclusion-oriented selection process." *Zoloft*, 858 F.3d at 796. Because Dr. Moyé could not "explain the weights [he] place[d] on the various" Bradford Hill factors, *In re Mirena Ius Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 257 (S.D.N.Y. 2018), his weight-of-the-evidence analysis is no more than "subjective belief or unsupported speculation." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 590 (1993). Devoid of any objective standards, Dr. Moyé's analysis has no more evidentiary value than a Rorschach test.

Dr. Moyé also applied the Bradford Hill factors in a self-serving way that ignored studies contradicting his opinion. Given Dr. Moyé's

qualifications and decades of experience as an epidemiologist, he should have been able to account for the contrary peer-reviewed findings of other scientists. Yet he credited only "those studies that support his conclusions, such as Croen (2011) and Boukhris (2016)," while "disregard[ing] those studies that d[id] not support his opinions." (SPA-24) Rather than grapple with contrary opinions, Dr. Moyé simply dismissed them out of hand. That is not science; it is cherry-picking. The District Court properly excluded his opinion, and this Court should affirm.

Dr. Patricia Whitaker, who purportedly used the "face-validity" method to find a credible causal link between SSRIs and ASD, fares no better. As the District Court found, Dr. Whitaker could not "explain how she weighed any line of evidence" when "selecting the data she relie[d] on." (SPA-45) She also "deliberately disregarded those studies that showed no similarities" between animal models and humans by "only looking for those that supported her hypothesis." (*Id.*)

Not so, Plaintiffs insist. Dr. Whitaker "use[d] everything and interpret[ed] all the different findings and how they fit together." (Plaintiffs' Opening Br. 31) And besides, she consulted "several categories

of research" by "go[ing] back and forth" between them. (*Id.*) According to Plaintiffs, the District Court just wasn't entitled to a more "precise quantification" of Dr. Whitaker's weighing process. (*Id.* at 31-32) But Rule 702 says otherwise.

Merely consulting "several categories of research" and then "going back and forth" among them is *not* a weighted rubric capable of replication. At bottom, any methodology that Dr. Whitaker may wield however she pleases is no methodology at all. And in Dr. Whitaker's hands, "face validity" becomes a carnival game in which the outcome is already certain and the house always wins. The "Federal Rules of Evidence require a greater degree of discrimination than that." *Boucher v. U.S. Suzuki Motor Corp.*, 73 F.3d 18, 22 (2d Cir. 1996).

Lastly is Dr. Laura Plunkett, Plaintiffs' expert on "pharmacology and toxicology of SSRIs." On appeal, Plaintiffs emphasize (at 43) that Dr. Plunkett has appeared as an expert witness "over 170 times" and "roughly once a month" over "the past five years." But just as past performance is no guarantee of future results, every Rule 702 inquiry "is fact-intensive and case specific." *United States v. Mathis*, 264 F.3d 321, 341–42 (11th Cir. 2001).

That is good news for Dr. Plunkett, because this Court has already upheld her exclusion (along with Dr. Moyé's) as an unreliable causation expert. *In re Mirena,* 982 F.3d at 123. And an array of other federal courts has likewise excluded her proffered expert testimony. *See, e.g., Rodman v. Otsuka Am. Pharm., Inc.*, No. 18-cv-03732, 2020 WL 2525032, at *7 (N.D. Cal. May 18, 2020) ("extrapolat[ing] conclusions beyond the scope other sources"), *aff'd*, No. 20-166646, 2021 WL 5850914 (9th Cir. Dec. 9, 2021); *Terry v. McNeil-PPC, Inc. (In re Tylenol (Acetaminophen) Mktg., Sales Practices, & Prods. Liab. Litig.)*, MDL No. 2436, 2:12-cv-07263, 2016 WL 4039329, at *9 (E.D. Pa. July 28, 2016) (her opinion would "not be helpful to the jury and could lead to confusion about the legal duties of the defendant in this case"); *Tsao v. Ferring Pharm., Inc.*, No. 4:16-cv-1724, 2018 WL 3649714, at *10–13 (S.D. Tex. Apr. 19, 2018) (impermissible legal conclusions); *Newman v. McNeil Consumer Healthcare*, No. 10-cv-1541, 2013 WL 9936293, at *4 (N.D. Ill. Mar. 29, 2013) ("Dr. Plunkett is precluded from offering her opinion that acetaminophen is safer than ibuprofen with regard to the risk of SJS/TEN."); *Byrd v. Janssen Pharms., Inc.*, 333 F. Supp. 3d 111, 130 (N.D.N.Y. 2018) (Dr. Plunkett conceded she was not a causation expert,

and the bases for her opinion failed to acknowledge the distinction between association and causation). And no matter how seasoned a professional witness Dr. Plunkett may be, none of her prior testimony can salvage her unreliable opinion here.

In positing an amorphous "biologically plausible relationship" between SSRIs and ASD, Dr. Plunkett's heavy-handed approach to the data left much to be desired. She "misrepresented" underlying contradictory data as supporting her opinion. (SPA-38) For example, she misleadingly cited a study that found no association between in-utero SSRI exposure and ASD for the dubious proposition that "SSRIs as a class have been associated with adverse developmental effects." (*Id.*) And she "dissembled when confronted about her disregard of relevant evidence." (*Id.* at 39) Asked why she never addressed certain findings in regulatory materials and meta-analyses that contradicted her opinion, she claimed (under oath) that she had no occasion to review either of those categories of data. Yet she affirmatively relied on sources from both regulatory materials and meta-analyses in other parts of her report.

Worst of all, Dr. Plunkett's analysis of the Bradford Hill factors was "incomplete, selective, misleading, and ultimately unreliable." (SPA-40)

She selectively addressed only four of the nine factors. Even if she did not undertake a "full" general causation analysis, Dr. Plunkett's "malleable and vague approach," *Mirena*, 341 F. Supp. 3d at 268, cannot satisfy Rule 702's minimal reliability threshold.

As this Court has insisted, an expert's conclusions must be "supported by good grounds for each step in the analysis." *Amorgianos*, 303 F.3d at 267. This "reliability analysis applies to all aspects of an expert's testimony, the facts underlying the expert's opinion, the link between the facts, and the conclusion." *Id.* (quoting *Heller v. Shaw Indus.*, 167 F.3d 146, 155 (3d Cir. 1999)). Every link in the chain of reliability must be strong.

None of Plaintiffs' experts cleared this hurdle. And no court may "admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997). Such evidence "contributes nothing to a 'legally sufficient evidentiary basis'" for a verdict. *Weisgram v. Marley Co.*, 528 U.S. 440, 454 (2000) (internal citation omitted).

B. Because Plaintiffs' unreliable expert evidence is inadmissible, it cannot reach the jury.

Because unreliable expert evidence is entitled to no weight, it is inadmissible. So it makes little sense here to invoke the "tools" of our "adversary system" (Plaintiffs' Opening Br. 21) by leaving any dispute about reliability to the "weight" a jury may give disputed expert testimony. While cross-examination has its benefits, it is no panacea; it cannot readily distinguish valid expert opinions from junk science. And it is no substitute for the court's gatekeeping role in determining an expert's reliability in the first instance.

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 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). In other words, the mere "fact that an expert witness was 'subject to a thorough and extensive examination' does not ensure the reliability of the expert's testimony; such testimony must still be assessed *before* it is presented to the jury." *Nease v. Ford Motor Co.*, 848 F.3d 219, 231 (4th Cir. 2017) (emphasis added) (citation omitted).

It's no surprise, then, that 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). On the contrary, studies have revealed jurors' common assumption that, because the trial judge admitted the expert evidence, it must have passed at least some degree of scientific 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).

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). Thus, any doubts 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* admitting it. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 149 (1999) (emphasis added). The District Court did not abuse its discretion by carefully performing that gatekeeping role here.

II. RELAXING THE RELIABILITY THRESHOLD FOR EXPERT EVIDENCE OF CAUSATION IN PHARMACEUTICAL-LIABILITY LITIGATION WOULD SIGNIFICANTLY HARM PUBLIC HEALTH.

This Court should not relax Rule 702's demanding standard for yet another important reason: doing so would severely chill the development and marketing of many beneficial medicines.

According to a recent Stanford University study, a pregnant mother's risk of depression has "nearly doubled" in the COVID-19 era. *See* Lucy S. Kind et al., *Pregnancy during the pandemic: the impact of COIVD-19-related stress on risk for prenatal depression*, Psychological

Med. (Mar. 30, 2021) <https://bit.ly/3znYPm1>. Physicians routinely rely on SSRIs like Lexapro® as the frontline therapy for maternal depression during pregnancy. In fact, "untreated mental illness itself poses risks to a developing fetus." Lauren M. Osborne, Johns Hopkins Medicine, *Antidepressants and Pregnancy: Tips from an Expert* <https://bit.ly/3aSiZex>. "Babies of depressed moms" have a higher risk of developing "depression, anxiety, and behavioral disorders later in life." *Id.*

Since first securing FDA approval in the 1980s, SSRIs have received countless bench studies, clinical trials, animal experiments, observational studies, and meta-analyses. As the record shows—and the District Court painstakingly confirmed—the cumulative body of scientific evidence reveals no causal association between using SSRIs like Lexapro® during pregnancy and neurodevelopmental disorders in children.

From a public-health vantage, then, vindicating the District Court's broad discretion in exercising its gatekeeping duty to exclude Plaintiffs' unreliable expert evidence is crucial. As Justice Breyer has 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 [Rule

> 702] 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").

"[S]imply because a person takes drugs and then suffers an injury does not show causation." *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1243 (11th Cir. 2005). Many assumptions about risks of harm from taking certain drugs have been exaggerated and are overwhelmingly wrong. And yet, there are countless product-liability suits pending throughout the country—in both state and federal courts—against the manufacturers of beneficial pharmaceutical therapies.

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 if manufacturer liability can stand on a "scientific" expert's say-so. *See Black v. Food Lion, Inc.*, 171 F.3d 308, 313 (5th Cir. 1999). Given the

sheer pace and frequency of such litigation, rigorous gatekeeping is vital 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).

Without rigorous thresholds for the reliability of expert evidence on causation, drug manufacturers will have little guidance about how to structure their conduct to avoid debilitating liability. Permitting flimsy, unscientific "expert" opinions to serve as the basis for vexatious litigation against drug manufacturers would create a strong disincentive for the continued development of 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."); 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.").

For many drug companies, the easiest way to avoid frivolous litigation and unwarranted liability may be to exit the market altogether. Indeed, leading scientific organizations—such as the National Academy of Sciences and the American Association for the Advancement of Science—have warned that permitting experts to present novel causation theories to juries "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)." Br. for the Am. Ass'n for the Advancement of Science & the Nat'l Academy of Sciences 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.

Drug manufacturers who opt to remain in the market may still be forced 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' urge here, liability may be imposed even where the data shows no reliable causal link between Lexapro® and ASD, 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). Not only would that be unfair to manufacturers, but it would prove disastrous for the millions of expectant mothers each year who rely on SSRI therapies like Lexapro® in their battle against depression.

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

If "[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 a worthy task. Indeed, the parallels between this lawsuit and the Supreme Court's watershed case *Daubert v. Merrell Dow Pharmaceuticals, Inc.* are both striking and instructive. *Daubert*'s backstory is a concrete reminder that a seemingly obvious "link" between a drug taken by millions of pregnant women and tragic disorders suffered by a fraction of children born to those women must be carefully proven, not presumed.

In *Daubert*, the plaintiff sued the manufacturer of the anti-morning-sickness drug Bendectin on the theory that his mother's use of the drug while pregnant caused him to suffer severe birth defects. *Daubert*, 509 U.S. at 582. At that time, Bendectin was the only FDA-approved medicine for treating morning sickness. Sold in 22 countries, American doctors had prescribed Bendectin to more than 35 million women since 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, some studies appeared in the medical literature suggesting a possible association between Bendectin use and certain

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.

Although the mainstream scientific community—including an expert panel of the FDA—found *no* causal link between Bendectin and birth defects, plaintiffs' lawyers across the country brought more than a thousand lawsuits against Bendectin's manufacturer, Merrell Dow Pharmaceuticals, between 1977 and 1986. *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 (not unlike the standard urged here by Plaintiffs). As a result, hundreds of Bendectin lawsuits were bolstered by testimony from experts with "impressive credentials," but whose opinions on general causation were based on 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 did not reflect the consensus of the scientific community, many Bendectin

plaintiffs secured lucrative jury awards, including one for $95 million. *See, e.g.*, *Ealy v. Richardson-Merrell, Inc.*, 1987 WL 18743, *1 (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, many of these outsized jury 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) (summarizing state and federal Bendectin litigation); *see also* Lasagna & Shulman, *supra*, at 113-15 (same). Even so, given the enormous litigation costs incurred, Merrell Dow's liability-insurance premiums for Bendectin soon approached its gross sales on the drug: "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 1983. Lasagna & Shulman, *supra*, at 141.

In 2013, doxlamine-pyridozine, the same chemical compound in Bendectin, was remarketed as Diclegis®. *See* The Associated Press, *Morning Sickness Drug Returns*, N.Y. Times (Apr. 8, 2013) <https://nyti.ms/3oh1Y0C> ("That long-ago safety scare, prompted by hundreds of lawsuits claiming birth defects, proved to be a false alarm."). Unsurprisingly, FDA rated Diclegis® as Pregnancy Category A, the best rating available. That rating is authorized only when well-controlled studies in pregnant women fail to show any risk to the fetus. *See* Jennifer Levin, FIERCE Biotech, *FDA approves Diclegis for pregnant women experiencing nausea and vomiting* (April 8, 2013) <https://bit.ly/3cpBQ0F>.

For the intervening three decades in which the drug was unavailable, the Bendectin litigation frenzy produced a genuine public health tragedy. Millions of pregnant women suffered needlessly. According to the American College of Obstetrics and Gynecology, the manufacturer's business decision to halt production of Bendectin created "a significant therapeutic gap." Jane E. Brody, *Shadow Of Doubt Wipes Out Bendectin*, N.Y. Times (June 19, 1983) <https://nyti.ms/3yZPTSr>. Because nausea and vomiting in pregnancy can lead to serious maternal

nutritional deficiencies, the lack of any viable therapy jeopardized untold mothers' and babies' well-being. *Id.*

Desperate for relief, many pregnant women resorted to homeopathic or other unregulated 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's market exit in 1983, hospitalizations for severe cases of nausea and vomiting during pregnancy had doubled. A. Skolnick, *Key Witness Against Morning Sickness Drug Faces Scientific Fraud Charges*, 263 J. Am. Med. Ass'n 1468, 1473 (1990). JAMA 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. *Id.*

It is now well settled that Bendectin's exit 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). On the contrary, a 2003 study concluded that the

constant rate of birth defects during the three decades that Bendectin was unavailable "is not consistent with the hypothesis that Bendectin is a teratogen." *Id.* (citing Jeffrey S. Kutcher et al., *Bendectin and Birth Defects II: Ecological Analyses*, 2 Birth Defects Research 67, 88 (2003)).

As this historical example shows, caving in to Plaintiffs' demands to advance to trial based merely on a hypothetical connection between Lexapro® and ASD would have far-reaching public-health ramifications well beyond this case. Of course, the notoriously unreliable evidence of the Bendectin litigation led directly to the Supreme Court's landmark ruling in *Daubert* and Rule 702, which imposes a vital gatekeeping duty on all district court judges. Here the designers, manufacturers, and marketers of Lexapro® stand accused of causing neurodevelopmental disorders in children whose mothers took the drug during pregnancy. Because Plaintiffs' experts' causation opinions are *at least* as unreliable as those rejected in *Daubert*, this Court should affirm the District Court's well-reasoned decision.

CONCLUSION

The judgment should be affirmed.

September 14, 2022

Respectfully submitted,

/s/ John M. Masslon II

Cory L. Andrews
John M. Masslon II
WASHINGTON LEGAL FOUNDATION
2009 Massachusetts Ave., NW
Washington, DC 20036
(202) 588-0302
candrews@wlf.org
Counsel for Amicus Curiae

CERTIFICATE OF COMPLIANCE

I certify:

This brief complies with the type-volume limits of Fed. R. App. P. 29(a)(5) and Local Rule 29.1(c) because it contains 4,784 words, excluding the parts exempted by Fed. R. App. P. 32(f).

This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type-style requirements of Fed. R. App. P. 32(a)(6) because it has been prepared in a proportionally spaced serif typeface in 14-point font, using Microsoft Office Word 2010

September 14, 2022

/s/ John M. Masslon II
JOHN M. MASSLON II

CERTIFICATE OF SERVICE

I certify that on this 14th day of September, 2022, a copy of this brief was filed and served on all registered counsel through the Court's CM/ECF system.

/s/ Cory L. Andrews
CORY L. ANDREWS