APPENDIX

TABLE OF APPENDICES

Appendix A

SUPREME COURT OF PENNSYLVANIA
EASTERN DISTRICT

No. 95 EAL 2020

A.Y. AND BILLIE ANN YOUNT,

Respondent,

v.

JANSSEN PHARMACEUTICALS INC., JOHNSON & JOHNSON, JANSSEN RESEARCH & DEVELOPMENT, LLC; EXCERPTA MEDICA, INC., and ELSEVIER INC.,

Petitioner.

Filed: Sept. 1, 2020

ORDER

PER CURIAM

AND NOW, this 1st day of September, 2020, the Petition for Allowance of Appeal is **DENIED**.

Appendix B

SUPERIOR COURT OF PENNSYLVANIA

No. 3058 EDA 2016

A.Y. AND BILLIE ANN YOUNT,

Appellants,

v.

JANSSEN PHARMACEUTICALS INC., JOHNSON & JOHNSON, JANSSEN RESEARCH & DEVELOPMENT, LLC; EXCERPTA MEDICA, INC., and ELSEVIER INC.,

Appellees.

No. 3059 EDA 2016

A.Y. AND BILLIE ANN YOUNT,

Appellants,

v.

JANSSEN PHARMACEUTICALS INC., JOHNSON & JOHNSON, JANSSEN RESEARCH & DEVELOPMENT, LLC; EXCERPTA MEDICA, INC., and ELSEVIER INC.,

Appellees.

Filed: Nov. 26, 2019

Before: PANELLA, P.J., KUNSELMAN, J., and STEVENS*, P.J.E.

OPINION

Janssen Pharmaceuticals, Inc., Janssen Research & Development, LLC, and Johnson & Johnson Company (collectively, "Defendants/Appellants" or "Janssen") appeal from the judgment of $70 million entered on September 8, 2016, after a jury found in favor of A.Y. and his mother, B.A.Y. (collectively, "Plaintiffs/Appellees") and against Janssen in this pharmaceutical failure to warn case. In addition, Plaintiffs/Appellees have filed a cross-appeal from the June 10, 2016 order granting partial summary judgment in favor of Defendants/Appellants on Plaintiffs/Appellees' punitive damages claim.

On Defendants/Appellants' appeal, we affirm. On Plaintiffs/Appellees' cross-appeal, we reverse and remand for the trial court to consider conflict-of-law principles with respect to New Jersey and Appellees' home state of Tennessee in a manner consistent with this decision.

The trial court opinion aptly sets forth the record-based procedural history and relevant facts, as follows:

* Former Justice specially assigned to the Superior Court.

PROCEDURAL HISTORY

On April 15, 2013, Plaintiffs A.Y. and [B.A.Y., "Mother,"] filed a Complaint against Defendants Janssen Pharmaceuticals Inc., Johnson & Johnson, Janssen Research & Development, LLC, Elsevier, Inc., and Excerpta Medica Inc. Appellees' Complaint alleged the following thirteen causes of action: (1) negligence, (2) negligent-design defect, (3) fraud, (4) strict product liability—failure to warn, (5) strict product liability—design defect, (6) breach of express warranty, (7) breach of implied warranty, (8) violation of Pennsylvania Unfair Trade Practices and Consumer Protection Law, 73 P.S. § 201-1 et seq., (9) unfair and deceptive trade practices, (10) conspiracy, (11) punitive damages, (12) medical expenses incurred by parent, and (13) loss of consortium.

By Order dated May 2, 2014, the Honorable Arnold L. New ruled that New Jersey Law applied to the issue of punitive damages and that New Jersey law barred the award of punitive damages. On June 2, 2014, Plaintiffs filed a Motion for Reconsideration of the Honorable Arnold New's May 2, 2014 Order barring the award of punitive damages. On June 9, 2014, Defendants filed an Answer to Plaintiff's Motion for Reconsideration. On July 18, 2014, Plaintiff's Motion for Reconsideration was denied.

On November 4, 2015, the Honorable Arnold New approved a stipulation dismissing the

action as to Defendants Excerpta Medica, Inc., and Elsevier Inc. On April 14, 2016, remaining Defendants, Janssen Pharmaceuticals, Inc., Johnson & Johnson, and Janssen Research & Development, LLC, filed a motion for summary judgment.

On May 5, 2016, Plaintiffs filed an Answer to Defendant's Motion for Summary Judgment. On May 11, 2016, Defendants filed a Reply.

On June 10, 2016, the Honorable Arnold New ruled that Tennessee Law applies to Plaintiffs' substantive claims [because Plaintiffs live in Tennessee and allege causes of action arising in Tennessee]. Plaintiffs' claims for: negligence, negligent design defect, strict liability—failure to warn, strict liability—design defect, breach of express warranty, breach of implied warranty [were deemed] subsumed into two claims: (a) Product Liability action because Risperdal was defective and (b) Product Liability action because Risperdal was unreasonably dangerous.

The Honorable Arnold New further ruled that Defendants' Summary Judgment [motion] was granted as to the following causes of action: (A) product liability action because Risperdal was defective, (B) fraud, (C) Pennsylvania's Unfair Trade Practices and Consumer Protection Law, (D) unfair and deceptive trade practices (under the Tennessee Consumer Protection Act), (E) conspiracy, and (F) loss of consortium.

Defendant's Motion for Summary Judgment was denied as to all other causes of action.

On June 16, 2016, a jury trial commenced in this matter; the Honorable Paula A. Patrick presided. On July 1, 2016, the jury returned a verdict in favor of the Plaintiffs. The jury found that Defendants negligently failed to adequately warn Plaintiffs of the risk of gynecomastia associated with Risperdal™ use and Defendants' negligence was a cause in bringing about A.Y.'s gynecomastia. The jury awarded Plaintiffs compensatory damages in the amount of $70,000,000.00 (seventy million dollars). On July 5, 2016, the jury's verdict was entered.

On July 8, 2016, Plaintiffs filed a Post-Trial Motion for Delay Damages. On August 10, 2016, Plaintiffs' Motion for Delay Damages was granted. Plaintiffs were awarded $6,661,027.40 in Delay Damages. The jury verdict of $70,000,000.00 was molded to add Delay Damages of $6,661.027.40 for a total verdict of $76,661,027.40. On September 7, 2016, judgment was entered in this matter.

On September 9, 2016, Defendants filed an Appeal to the Superior Court from decisions dated July 1, 2016, July 5, 2016, July 25, 2016, and August 10, 2016. On September 13, 2016, Plaintiffs filed a cross-appeal to the Superior Court from decisions dated May 2, 2014, July 18, 2014, and July 25, 2016. On September 22, 2016, Plaintiffs filed a Statement of Errors Complained of on Appeal

pursuant to Pa.R.A.P. 1925(b). On October 12, 2016, Defendants filed a Statement of Errors Complained of on Appeal pursuant to Pa.R.A.P. 1925(b).

FACTUAL BACKGROUND

Risperdal (risperdone) is an antipsychotic medication belonging to a class of drugs which [has] become known as "atypical" or "second generation" ("SGA") antipsychotics. Risperdal was originally developed and approved for use in the treatment of symptoms associated with schizophrenia. The adverse effects associated with Risperdal are: rapid weight gain, hyperprolactinemia, gynecomastia (abnormal development of breasts in males), galactorrhea (lactation), pituitary tumors, microadenomas of the pituitary gland, breast cancer, osteoporosis, decreased bone mineral density, metabolic syndrome, dyslipidemia, hypertension, diabetes mellitus, diabetic ketoacidosis (DKA), hyperosmolar coma, hyperglycemia, glucose dysregulation, insulin insufficiency, insulin resistance, pancreatitis, tardive dyskinesia, extrapyramidal symptoms, involuntary movement disorders, dyskinesia, dystonia, akatisia, parkinsonism, neuroleptic malignant syndrome (NMS) and/or other related conditions. Risperdal is designed, developed, tested, labeled, packaged, distributed, marketed, and sold throughout the United States by the Janssen Defendants.

On December 29, 1993, Janssen obtained approval from the Food and Drug Administration ("FDA") to market Risperdal oral tablets for the treatment of "manifestations of psychotic disorders" (schizophrenia) in adults. In September 2000, the FDA requested that the label be changed to more clearly indicate that Risperdal was only approved for use in treating schizophrenia in adults. In October 2006, Risperdal was approved for the treatment of irritability associated with autistic disorder in children and adolescents (between the ages of 5 and 16), including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums and quickly changing moods. Risperdal has not been approved for children younger than 5 or those older than 16 years old for irritability associated with autistic disorder.

The prescribing of drugs "off-label" occurs when a drug is prescribed by a medical professional for use beyond those contained in the drug's FDA-approved uses. This includes prescribing a drug for a condition not indicated on the label, treating the indicated condition at a different dose or frequency than specified in the label, or treating a different patient population. An example of off-label use is the treatment of a child with the drug when the drug is approved to treat adults.

Plaintiff A.Y. was born in 1999. [A.Y.] was diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD). In August of 2003, when A.Y. was four and a half years old, he was prescribed Risperdal by Dr. Deniz Eker, a pediatric psychiatrist. Eker Dep. 2/8/16, at 31-32. At the time Dr. Eker prescribed Risperdal to A.Y., she did not warn A.Y.'s mother about the risk of gynecomastia. Dr. Eker stated that she would have warned A.Y.'s mother, but Dr. Eker did not know at the time that there was such a significant risk of gynecomastia from elevated prolactin. *Id.* at 56, 61.

In January 2004, four months after [A.Y.] began taking Risperdal, A.Y.'s mother went to Doctor Eker and expressed concern that A.Y's breasts were enlarging. *Id.* at 65. Dr. Eker then began tapering the Risperdal because she was concerned about gynecomastia. *Id.* at 66.

In February 2005, after the initial tapering, Dr. Eker noted that A.Y.'s breasts were getting big and that she was discontinuing Risperdal because A.Y. had gynecomastia. *Id.* Dr. Eker testified that when she first noticed gynecomastia, she began tapering off from the Risperdal but would have stopped it immediately if she had been properly informed about the risk of gynecomastia from Risperdal. *Id.* Dr. Eker believed gynecomastia was much less frequent and

that A.Y.'s development of female breasts (at five years old) was a rare occurrence. When Dr. Eker believed the gynecomastia had gone down, she put A.Y. back on Risperdal. *Id*. at 76-77.

Dr. Eker transferred A.Y.'s psychiatric care to Dr. Michael Hughes in the first half of 2005. *Id*. at 78. Dr. Hughes testified that the idea to put A.Y. on Risperdal originated with Dr. Eker, and he was simply continuing the treatment. *Id*. at 279-80.

Dr. Hughes could not say that he would have put A.Y. on Risperdal at all if Dr. Eker had not prescribed it first. *Id*. Dr. Hughes testified that if he had known that there was a statistically significant association between prolactin elevation from Risperdal use and gynecomastia this information would have had a significant impact in his thinking with regard to prescribing Risperdal. *Id*. at 266-267. Dr. Hughes stated that he would have pushed against Risperdal use if he had known of the additional significant concerns. *Id*. at 83-84. Dr. Hughes treated A.Y. from May 2005 through May 2011. *Id*. at 228-29. Dr. Hughes discontinued Risperdal at the request of A.Y.'s mother because A.Y. was gaining so much weight. *Id*. at 161-62.

Dr. Brian Bonfardin, a psychiatrist, began treating A.Y. in June 2011. *Id*. at 16. In June of 2012, A.Y. was struggling, and A.Y.'s mother suggested trying Risperdal again to Dr. Bonfardin. At that time, Dr. Bonfardin's

> prescription of Risperdal had already plummeted because he had learned prior to 2012 that Risperdal increased prolactin levels more than other antipsychotics. *Id*. at 48-49.
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> Dr. Bonfardin testified that he did not know of [Janssen's own clinical] studies showing a 5.5% and 12.5% frequency of gynecomastia among children who used Risperdal. If he had such information, he would have warned A.Y.'s mother about this significant risk. Bonfardin Dep., 2/11/16, at 16.
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> A.Y.'s care was transferred to Dr. Gordon Greeson in October of 2012. Dr. Greeson took A.Y. off Risperdal once he took over care because A.Y. gained quite a bit of weight and had hypertension in the short period he had been put back on Risperdal. A.Y.'s mother requested he be put back on Risperdal [the] next month.
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> In 2013, A.Y.'s mother saw an advertisement discussing gynecomastia from Risperdal use. A.Y. Mother Dep., 12/14/15, at 6-8. She got in contact with an attorney and then went to talk to A.Y.'s treating physicians about the problem. *Id*. Dr. Greeson learned of the gynecomastia from A.Y.'s mother in March 2013. Dr. Greeson immediately decided he needed to stop Risperdal because he feared making the problem worse.

Trial Court Opinion, 6/20/18, at 1-7.

Appellants raise the following questions for our consideration:

1. Were Defendants/Appellants entitled to JNOV because federal law preempts Plaintiffs'/Appellees state-law failure-to-warn claim?
2. Were Defendants/Appellants entitled to JNOV because Plaintiffs/Appellees failed to establish any inadequate warning was the proximate cause of A.Y.'s Risperdal use and gynecomastia?
3. Is a new trial required because the trial court erroneously excluded: (1) testimony of a treating doctor who continued to prescribe Risperdal for A.Y. at his mother's request and after she filed this lawsuit, which called into question whether a different warning would have changed the prescribing decision; and (2) testimony and evidence establishing A.Y.'s serious mental illness and the significant benefit of Risperdal therapy for him, which was relevant to the benefit/risk analysis made by A.Y.'s prescribers?
4. Is a new trial required because the trial court did not instruct the jury that under Tennessee's "learned intermediary" rule, the jury had to assess whether the warnings were adequate to warn A.Y.'s doctors, to whom Janssen owed a duty to warn?
5. Is a new trial or remittitur required because the trial court failed to apply Tennessee's $750,000.00 cap for non-economic damages?
6. Is a new trial or remittitur required because the jury's $70,000,000.00 compensatory-damages award was excessive?

Appellants' brief, at 6-7.

In their first two issues, Appellants contend they were entitled to judgment *non obstante veredicto* ("JNOV") because federal law preempts Plaintiffs/Appellees' state failure-to-warn claim that Tennessee law required Janssen to change labeling to reflect juvenile Risperdal users' heightened risk of gynecomastia. We set forth our standard of review from the denial of a motion for judgment n.o.v.:

> A motion for judgment n.o.v. is a post-trial motion which requests the court to enter judgment in favor of the moving party. There are two bases on which the court can grant judgment n.o.v.:
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> > [O]ne, the movant is entitled to judgment as a matter of law and/or two, the evidence is such that no two reasonable minds could disagree that the outcome should have been rendered in favor of the movant. With the first, the court reviews the record and concludes that even with all factual inferences decided adverse to the movant the law nonetheless requires a verdict in his favor, whereas with the second, the court reviews the evidentiary record and concludes that the evidence was such that a verdict for the movant was beyond peradventure.
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> *Polett v. Public Communications, Inc.*, 83 A.3d 205, 212 (Pa.Super. 2013), *reversed on other grounds*, 633 Pa. 445, 126 A.3d 895 (Pa.

2015). In an appeal from the trial court's decision to deny judgment n.o.v.,

> we must consider the evidence, together with all favorable inferences drawn therefrom, in a light most favorable to the verdict winner. Our standard of review when considering motions for a directed verdict and judgment notwithstanding the verdict are identical. We will reverse a trial court's grant or denial of a judgment notwithstanding the verdict only when we find an abuse of discretion or an error of law that controlled the outcome of the case. Further, the standard of review for an appellate court is the same as that for a trial court.

Id. at 211.

Drake Mfg. Co., Inc. v. Polyflow, Inc., 109 A.3d 250, 258-259 (Pa.Super. 2015).

> "Concerning any questions of law, our scope of review is plenary. Concerning questions of credibility and weight accorded the evidence at trial, we will not substitute our judgment for that of the finder of fact. . . . A JNOV should be entered only in a clear case." [*Advanced Telephone Systems, Inc. v. Com-Net Professional Mobile Radio, LLC*, 846 A.2d 1264, 1279 (Pa.Super. 2004), *appeal denied*, 580 Pa. 687, 859 A.2d

> 767 (2004) (citation omitted)]. "[T]he entry of a judgment notwithstanding the verdict … is a drastic remedy. A court cannot lightly ignore the findings of a duly selected jury." *Education Resources Institute, Inc. v. Cole*, 827 A.2d 493, 497 (Pa.Super. 2003), *appeal denied*, 577 Pa. 721, 847 A.2d 1286 (2004) (citation omitted).
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> *Growall v. Maietta*, 931 A.2d 667, 670 (Pa.Super. 2007), *appeal denied*, 597 Pa. 717, 951 A.2d 1164 (2008). Rule 702 of the Pennsylvania Rules of Evidence.

Stange v. Janssen Pharmaceuticals, Inc., 179 A.3d 45, 52-53 (Pa. Super. 2018).

"Federal 'preemption is an affirmative defense on which [the] defendant bears the burden of proof.'" *Aaron v. Wyeth*, 2010 WL 653984, at *3 (W.D. Pa. Feb. 19, 2010) (quoting *Cambridge Literary Props., Ltd. v. W. Goebel Porzellanfabrik G.m.b.H. & Co. KG.*, 510 F.3d 77, 102 (1st Cir. 2007), *cert. denied*, 555 U.S. 815, 129 S.Ct. 58, 172 L.Ed.2d 25 (2008); citing *Wyeth v. Levine*, 555 U.S. 555, ----, 129 S.Ct. 1187, 1193, 173 L.Ed.2d 51 (2009) (characterizing a manufacturer's argument that federal drug law preempted the plaintiff's claims as a defense)) (hereinafter "*Wyeth*"). Our courts acknowledge a presumption against such a defense:

> We recognize a presumption against federal pre-emption of state law. *Dooner v. DiDonato*, 601 Pa. 209, 971 A.2d 1187 (2009) (citing *Altria Group, Inc. v. Good*, 555 U.S. 70, 129

S.Ct. 538, 172 L.Ed.2d 398 (2008)). In *Kiak v. Crown Equipment Corp.*, 989 A.2d 385, 390 (Pa.Super. 2010), this Court attributed that presumption to the "dual jurisdiction" which "results from reasons of comity and mutual respect between the two judicial systems that form the framework of our democracy." *Fetterman v. Green*, 455 Pa.Super. 639, 689 A.2d 289, 292 (1997); *see also Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992). As the United States Supreme Court noted in *Altria Group, Inc.*, *supra*: When addressing questions of express or implied preemption, we begin our analysis "with the assumption that the historic police powers of the States [are] not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress." *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230, 67 S.Ct. 1146, 91 L.Ed. 1447 (1947). That assumption applies with particular force when Congress has legislated in a field traditionally occupied by the States. [*Medtronic Inc. v.*] *Lohr*, 518 U.S. at 485, 116 S.Ct. 2240, 135 L.Ed.2d 700; *see also* [*Lorillard Tobacco Co. v.*] *Reilly*, 533 U.S. at 541-542, 121 S.Ct. 2404, 150 L.Ed.2d 532 [(2001)] ("Because 'federal law is said to bar state action in a field of traditional state regulation,' namely, advertising, we 'work on the assumption that the historic police powers of the States are not to be superseded by the Federal Act unless that is the clear and manifest purpose of Congress'" (citation

> omitted)). Thus, when the text of a pre-emption clause is susceptible of more than one plausible reading, courts ordinarily "accept the reading that disfavors pre-emption." *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005). *Altria Group, Inc.*, 555 U.S. at 77, 129 S.Ct. 538.

Hassett v. Dafoe, 74 A.3d 202, 210 (Pa.Super. 2013). *Accord*, *Lake v. Memphis Landsmen*, LLC, 405 S.W.3d 47, 56 (Tenn. 2013)

In their preemption argument, Appellants insist Janssen's labeling at all relevant times was adequate as a matter of Tennessee law. Nevertheless, they posit that even if Tennessee law required Janssen to change labeling as Appellees propose, the federal law doctrine of "impossibility preemption" applies to Plaintiffs/Appellees' state-law negligent failure-to-warn claim, because it was "impossible for Janssen simultaneously to comply with its federal and state-law obligations" regarding Risperdal labeling of pediatric gynecomastia risks. *See* Appellants' brief, at 27 (quoting *Strayhorn v. Wyeth Pharm., Inc.*, 887 F.Supp. 2d 799, 809-10 (W.D. Tenn. 2012) ("Impossibility preemption is a type of implied conflict preemption which occurs when 'state and federal law conflict [and] it is impossible for a private party to comply with both state and federal requirements.'"), *aff'd*, 737 F.3d 378 (6th Cir. 2013) (quoting *PLIVA, Inc. v. Messing*, 564 U.S. 604, 618 (2011)).

We have previously discussed controlling decisional law characterizing impossibility pre-emption as "a demanding defense." *Hasset*, 74 A.3d at

210 (quoting *Wyeth*, 129 S.Ct. at 1199). Similarly, Tennessee has observed:

> The United States Supreme Court has identified two fundamental principles that must guide any preemption analysis. First, no matter what type of preemption is at issue, "the purpose of Congress is the ultimate touchstone." *Wyeth*, 555 U.S. 555, 565, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009) (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996)). Second, in conducting any preemption inquiry, courts must "start with the assumption that the historic police powers of the States were not to be superseded by [federal law] unless that was the clear and manifest purpose of Congress"—particularly when the federal law in question pertains to "a field which the States have traditionally occupied." *Id*. (quoting *Medtronic*, 518 U.S. at 485, 116 S.Ct. 2240) (internal quotation marks omitted); *see also Leggett*, 308 S.W.3d at 854; *Morgan v. Ford Motor Co.*, 224 W.Va. 62, 680 S.E.2d 77, 83 (2009) ("Preemption of topics traditionally regulated by states—like health and safety—is greatly disfavored in the absence of convincing evidence that Congress intended for a federal law to displace a state law.").

Lake, 405 S.W.3d at 56.

In *Wyeth*, the United States Supreme Court held that impossibility preemption did not apply to state claims based on a failure to warn of the risk of

gangrene from Phenergan delivered by an IV-push method, where it was within the power of the defendant manufacturer, Wyeth, to comply with both state and federal law by unilaterally strengthening the label's warning. In so holding, the Court explained that the Federal Food, Drug and Cosmetic Act ["Act"] is premised upon the expectation that manufacturers are primarily responsible for drug safety through proper labeling. The presumption follows, the Court continued, that compliance with both state and federal labeling requirements is possible unless there exists clear evidence that the FDA would block a proposed change to the label.

With regard to *Wyeth*, it has been observed:

> In holding that the FDA's approval of Wyeth's label did not provide a complete defense to the plaintiff's failure to warn claim under a federal preemption theory, the *Wyeth* Court emphasized that it was Congress' intent that state law act as a "complimentary form of drug regulation" because "manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge." *Wyeth* at 1202. The Court further emphasized:
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> > State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. Failure-to-warn actions, in particular, lend force

> to the [Federal Food, Drug and Cosmetic Act's] premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times. Thus, the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation.
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> *Id.*
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> Moreover, the Court found no Congressional intent to vest the FDA with the sole authority to ensure drug safety and effectiveness, as would result from the preemption of state tort actions. *Id*. at 1200. *Wyeth*, however, does not render state law failure-to-warn claims immune to preemption in every case. The Supreme Court recognized that "some state-law claims might well frustrate the achievement of congressional objectives" in the federal regulation of drug labeling. *Wyeth*, 129 S.Ct. at 1204. To prevail here, Wyeth "faces an exacting burden to establish preemption of state law claims because compliance with both state and federal requirements for drug labeling is not impossible 'absent clear evidence that the FDA would not have approved a change' in the drug's labeling." *Forst v. Smithkline Beecham Corp.*, 639 F.Supp.2d 948, 953-954 (E.D.Wis.2009) (quoting *Wyeth*, 129 S.Ct. at 1198).

Aaron, 2010 WL 653984, at *5.

According to Appellants, however, federal law set forth in the Act at 21 C.F.R. §§ 201.57(e) and 312.32 provides that only the Food and Drug Administration ("FDA") may require a warning concerning a risk of an off-label or non-approved use, and even then only in the case of a "serious" risk, namely, one that threatens life or normal life functions, or requires hospitalization. Appellants acknowledge the regulations provide an exception to this general restriction, the "changes being effected," or "CBE" exception articulated at 21 C.F.R. §§ 314.70(c)(6)(iii)(A), but they maintain the facts do not bring the present case within the bounds of the exception.

Specifically, the CBE exception permits a manufacturer to change labeling without prior FDA approval only if (1) the manufacturer had newly acquired information about the drug (2) that showed a causal association (3) between the drug and an effect that warranted a new or stronger warning. 21 C.F.R. §§ 314.70(c)(6)(iii)(A). "[N]ewly acquired information is data, analyses, or other information not previously submitted to the [FDA that] reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 314.3; *see also Wyeth*, 129 S.Ct. 1197 (quoting 73 Fed.Reg. 49607).

Appellees argue that Janssen's extensive clinical studies culminating with data compiled in its "Table 21,"[1] discussed at length in the testimony of expert

[1] Expert witness Dr. David Kessler, FDA commissioner from 1991-1997, testified that by the year 2000 or 2001, Janssen had collected data at Table 21 showing a statistically significant

witness David Kessler, M.D., *see infra*, brought them within the contours of the CBE regulations, as the studies supplied the manufacturer with newly acquired information showing a causal association between Risperdal and more frequent and severe gynecomastia in juvenile boys than had been observed in the adult male population.

Appellants, however, dispute that Janssen had the authority to change labeling to inform that: Risperdal is associated with higher prolactin levels than other antipsychotic medications; elevated prolactin "causes" gynecomastia in the pediatric population; and clinical studies show sufficiently higher rates of gynecomastia in the pediatric population to qualify the condition as "frequent" in that population, as differentiated from the "rare" occurrence reported in adults. This is so, they claim, because Risperdal was not approved for pediatric use—it was an "off-label" use—and only the FDA had the authority to warn about off-label uses.

Plaintiffs/Appellees assail Appellants' "off-label use" defense as also being inconsistent with governing statutory law as it existed at the time A.Y. began taking Risperdal. Specifically, Appellees accurately point out that 21 C.F.R. § 201.57(f)(9)(i), which pertained to "pediatric care," was in effect in 2003 and provided that any "specific hazard" associated with an

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increase in both prolactin levels in children taking Risperdal for at least 8 to 12 weeks and in prolactin-related gynecomastia in children. Janssen, however, never shared this information. In his expert opinion, by the year 2000 or 2001, Janssen was marketing Risperdal for children and adolescents, and was, thus, obligated to share their studies at this time. N.T. 5/19/2015, at 88-127.

unapproved pediatric use "shall be described in this subsection of the labeling . . . ." *Id.*

Appellants' position is out of step with controlling jurisprudence on drug manufacturers' responsibilities to act on their unique access to product information by adequately warning consumers of newly discovered heightened risks of injury associated with the drug. Indeed, as the United States Supreme Court has recently reiterated, the CBE regulation contemplates that drug manufacturers bear ultimate responsibility to provide adequate descriptions of a drug's newly discovered risks to ensure consumer safety.[2] This was particularly so prior to 2007—the relevant period in the case *sub judice*—when the FDA lacked authority to order manufacturers to revise their labels:

> We also observed that "through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." *Wyeth*, at 570-571, 129 S.Ct. 1187. A drug manufacturer "is charged both with crafting an adequate label and with ensuring that its

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[2] While the *Wyeth* Court acknowledged FDA regulations generally provide that a manufacturer may change a drug label only after FDA approval of a change application, as we note *supra*, it interpreted the misbranding provision of the regulations as proscribing not labels that enhance warnings but, instead, those that fail to include adequate warnings. Indeed, on this point, the High Court stated frankly, "And the very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning … is difficult to accept." *Wyeth*, 129 S.Ct. at 1197.

> warnings remain adequate as long as the drug is on the market." *Id.*, at 571, 129 S.Ct. 1187. Thus, when the risks of a particular drug become apparent, the manufacturer has "a duty to provide a warning that adequately describe[s] that risk." *Ibid.* "Indeed," we noted, "prior to 2007, the FDA lacked the authority to order manufacturers to revise their labels." *Ibid.* And even when "Congress granted the FDA this authority," in the 2007 Amendments to the FDCA, Congress simultaneously "reaffirmed the manufacturer's obligations and referred specifically to the CBE regulation, which both reflects the manufacturer's ultimate responsibility for its label and provides a mechanism for adding safety information to the label prior to FDA approval." *Ibid.*

Merck Sharp & Dohme Corp. v. Albrecht, 139 S. Ct. 1668, 1677, 203 L. Ed. 2d 822 (2019).

Moreover, the High Court emphasized that impossibility preemption under the relevant regulatory scheme requires the manufacturer to have fully disclosed the need for the additional warning, only to be met with FDA refusal:

> The underlying question for this type of impossibility pre-emption defense is whether federal law (including appropriate FDA actions) prohibited the drug manufacturer from adding any and all warnings to the drug label that would satisfy state law. And, of course, in order to succeed with that defense the manufacturer must show that the answer

> to this question is yes. But in *Wyeth*, we confronted that question in the context of a particular set of circumstances. Accordingly, for purposes of this case, we assume—but do not decide—that, as was true of the warning at issue in *Wyeth*, there is sufficient evidence to find that Merck violated state law by failing to add a warning about atypical femoral fractures to the Fosamax label. In a case like *Wyeth*, showing that federal law prohibited the drug manufacturer from adding a warning that would satisfy state law requires the drug manufacturer to show that it fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning.

Merck Sharp & Dohme Corp., 139 S. Ct. at 1678. In the present matter, Janssen did not make such a showing of full disclosure to the FDA during the relevant time.

The FDA surely possesses the authority under the statutory scheme to reject a revised label submitted by Janssen or any other manufacturer. This fact, alone, however, does not insulate a manufacturer from state failure to warn claims where the CBE scheme is available to enable compliance with state law:

> Of course, the FDA reviews CBE submissions and can reject label changes even after the manufacturer has made them. *See* §§ 314.70(c)(6), (7). And manufacturers

> cannot propose a change that is not based on reasonable evidence. § 314.70(c)(6)(iii)(A). But in the interim, the CBE regulation permits changes, so a drug manufacturer will not ordinarily be able to show that there is an actual conflict between state and federal law such that it was impossible to comply with both.

Id., 139 S. Ct. at 1679.

As such, viewing Appellants' defense in light of the above authority, we disagree that the regulatory scheme would have "clearly" prevented it from warning about the statistically significant increase in frequency and severity of gynecomastia in boys taking Risperdal. In fact, we view Appellants' "misbranding avoidance" argument offered to justify Janssen's withholding of additional warnings to be of the type effectively rejected in *Wyeth* and its progeny. Because Appellants, therefore, have not carried their burden of proof applicable to their preemption defense, we find that federal drug labeling laws did not preempt Appellees' Tennessee tort law claim.

In Appellants' next issue, they contend JNOV was required because Plaintiffs/Appellees failed to establish that the lack of a gynecomastia warning specific to juvenile risk was the proximate cause of A.Y.'s harm.[3] According to Appellants, even if the

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[3] Proximate causation was but one of two forms of causation—cause-in-fact being the other—Plaintiffs/Appellees bore the burden of establishing at trial. *See infra*. The Tennessee Supreme Court has explained the distinction between the two causations, as follows:

Risperdal warnings were inadequate—a supposition they deny—the evidence showed that the label Plaintiffs/Appellees' advocated at trial would not have prevented A.Y. from taking Risperdal and developing gynecomastia.

A.Y.'s physicians were aware of a potential risk of gynecomastia when they decided to prescribe Risperdal for A.Y., Appellants maintain, and his parents either continued with or returned to Risperdal despite having learned of its causative role in A.Y.'s gynecomastia diagnosis. Moreover, Appellant posits that a plaintiff cannot prove the causation element when he or she elects to continue a medication after

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> The distinction between cause in fact and proximate, or legal, cause is not merely an exercise in semantics. The terms are not interchangeable. Although both cause in fact and proximate, or legal, cause are elements of negligence that the plaintiff must prove, they are very different concepts. Cause in fact refers to the cause and effect relationship between the defendant's tortious conduct and the plaintiff's injury or loss. Thus, cause in fact deals with the "but for" consequences of an act. The defendant's conduct is a cause of the event if the event would not have occurred but for that conduct. In contrast, proximate cause, or legal cause, concerns a determination of whether legal liability should be imposed where cause in fact has been established. Proximate or legal cause is a policy decision made by the legislature or the courts to deny liability for otherwise actionable conduct based on considerations of logic, common sense, policy, precedent and "our more or less inadequately expressed ideas of what justice demands or of what is administratively possible and convenient."

White v. Lawrence, 975 S.W.2d 525, 529 (Tenn. 1998) (quoting *Snyder v. Ltg. Lufttechnische GmbH*, 955 S.W.2d 252, 256 n. 6 (Tenn.1997) (citations omitted)). Appellants, however, challenge only Appellees' proximate causation proffer at trial.

raising a failure-to-warn claim. It is undisputed that A.Y. continued to take Risperdal after filing the present action.

To establish proximate causation in a pharmaceutical failure-to-warn case, under Tennessee law, a plaintiff must show that "had additional warnings been given, the plaintiff[] would not have sustained [his] injuries.' *King v. Danek Med., Inc.*, 37 S.W.3d 429, 453 (Tenn.Ct.App. 2000). Because the flow of information in this context, however, runs through the treating physician, the law applies a "learned intermediary" doctrine, whereby the plaintiff must show that the absent warning, if given, would have altered the prescribing physician's actions and, thereby, averted the patient's injury. The purpose of the learned intermediary doctrine is to ensure that makers of "unavoidably unsafe products" with a duty to give warnings may "reasonably rely on intermediaries [often physicians] to transmit their warnings and instructions." *Pittman v. Upjohn Co.*, 890 S.W. 2d 425, 429 (Tenn. 1994).

With respect to a plaintiff's burden to prove causation under the learned intermediary doctrine, the Tennessee Court of Appeals has held:

> In order to recover for failure to warn under the learned intermediary doctrine, a plaintiff must show: (1) that the defendant failed to warn the physician of a risk associated with the use of the product not otherwise known to the physician; and (2) that the failure to warn the physician was both a cause in fact and proximate cause of the plaintiff's injury.

Harden v. Danek Med., Inc., 985 S.W.2d 449, 451 (Tenn. Ct. App. 1998).

Appellants' learned intermediary argument asserts that Appellees presented insufficient evidence that A.Y.'s treating physicians would have refrained from using Risperdal had Janssen issued a different warning. To support this position, Appellants provide numerous citations to the record, albeit it without any accompanying explanation of the testimony involved.

Our review of this record, however, brings us in accord with the trial court and its determination that Appellant's physicians amply testified they would have chosen a different course of treatment had Janssen disclosed on the Risperdal label the significantly heightened risk of prolactin-related gynecomastia that existed for juvenile boys. To that end, we adopt the trial court opinion's salient discussion of how Dr. Eker's and Dr. Hughes' respective reliance on inadequate Risperdal information supplied by Janssen, coupled with their lack of independent knowledge about juvenile, prolactin-related gynecomastia, defeated Janssen's learned intermediary defense. Additionally, the extensive videotaped deposition testimony of Dr. Kessler regarding Janssen's breach of duty to inform physicians under the learned intermediary rubric also supports the trial court's conclusion on proximate causation. *See* N.T., 5/19/15, at 15-317; N.T., 5/20/15, at 333-656.

Nevertheless, we discuss briefly the testimony pertinent to the issue of proximate causation. To carry its evidentiary burden with respect to causation, Plaintiffs/Appellees presented the testimony of, *inter*

alia, A.Y.'s treating physician, pediatric psychiatrist Dr. Deniz Eker, treating phyisican, pediatric psychiatrist Dr. Michael Hughes, M.D., and expert David Kessler, M.D., who, as mentioned *supra*, served as Commissioner of the FDA between 1990 and 1997.

Specifically, Dr. Eker testified that she first prescribed Risperdal to A.Y. in August of 2003 to treat A.Y.'s ADHD and oppositional defiant disorder. She maintained she did not warn A.Y.'s mother about the risk of gynecomastia at the time because she was unaware there was such a significant risk from elevated prolactin. Eker Dep. 2/8/16, at 56, 61. Though Dr. Eker could not remember whether she had consulted the Risperdal label thirteen years ago, she testified that she would have checked the Physician's Desk Reference (PDR), which relies in part on drug labeling, for potential side effects associated with Risperdal. *Id*. at 100.

Had Dr. Eker known of the risk, she testified, she would have warned A.Y.'s mother. *Id*. at 61. A.Y.'s parents confirmed Dr. Eker did not discuss gynecomastia with them, and they testified they never would have agreed to the use of Risperdal if they had known the true risk of gynecomastia. N.T., 6/29/16, at 238-40,317; N.T., 6/24/16, at 23-24, 48. Dr. Hughes, who assumed care of A.Y. starting in 2005, also expressed in his deposition testimony the importance of knowing the actual risk of juvenile gynecomastia stemming from hyperprolactinemia in his making his prescription decision. Hughes Dep. 3/10/16, at 66-69. Furthermore, both doctors denied having meaningful training or experience with, or independent

knowledge of, gynecomastia. N.T., 2/8/16, at 126-28; N.T., 3/10/16, at 91, 122-24.

At the time Dr. Eker first prescribed Risperdal to A.Y., according to the testimony of Dr. Kessler, Janssen already knew that Risperdal posed an increased risk of gynecomastia to juveniles. *See* fn. 1, *supra*. Yet, the Risperdal label failed to warn of this increased risk.

Specifically, Dr. Kessler testified in his video deposition that in August of 2003, the Risperdal label indicated the drug's effect on prolactin levels was consistent with other drugs in its class, that hyperprolactinemia had unknown clinical significance, and that gynecomastia was a "rare" occurrence associated with Risperdal use, occurring in fewer than 1 in 1000 patients, compared to a "frequent" occurrence, defined as more than 1 in 100 patients. Kessler Tr. Dep., 5/19/2015, at 13-29.

Yet, Dr. Kessler explained, Janssen knew of Risperdal's increased risk from eighteen clinical studies it had conducted through the 1990's and into the 2000's to overcome its prior failed efforts to obtain FDA approval to introduce pediatric dosing information on the label. Two of the studies of boys ranging from 5 to 18 years old, in particular, showed a frequent occurrence of gynecomastia. The first was a long-term clinical study in which patients underwent a 48-week observation while taking Risperdal. An interim analysis in 2000 showed a gynecomastia incidence rate of 3.7% (13 cases/266 boys). The 2002 final analysis for the clinical study revealed an incidence rate of 5.5% (23 cases/419 boys).

The second study represented a one-year extension of the first study, by recording the incidence of new and continuing gynecomastia in boys who had participated in the first study and continued to take Risperdal for a second year. The study found an incident rate of gynecomastia at 12.5%. Dr. Kessler testified the rate was "frequent." *Id*. at 46-72.

By Janssen's own 2002 internal analysis of its studies, there was a statistically significant correlation between Risperdal and prolactin-related gynecomastia in children. Dr. Kessler testified Janssen was obligated to warn about the risks at this time by submitting the results of its studies to the FDA as an "important finding," but it did not do so. *Id*. at 143-77. Instead, in December 2003, Janssen sought FDA approval of Risperdal for pediatric use without submitting the new data on gynecomastia risk. When the FDA denied Janssen's application for safety concerns regarding prolactin elevation, Janssen responded, "A review of the safety information did not show a correlation between prolactin levels and adverse events that are potentially attributable to prolactin." Dr. Kessler characterized Janssen's response as misleading. *Id*. at 177-84.

Accordingly, we agree with the trial court that the record belies Appellant's "learned intermediary" defense that A.Y.'s physicians prescribed Risperdal with knowledge of the heightened pediatric gynecomastia risks associated with the drug. *See Pittman*, *supra* at 29 (indicating that an adequate warning to learned intermediaries must convey, *inter alia*, a warning with the degree of intensity required by the nature of the risk). *See also Proctor v. Davis*,

291 Ill.App.3d 265, 682 N.E.2d 1203, 1214. (Ill.App. 1997) (holding drug manufacturer Upjohn could not rely on prescribing physicians as "learned intermediaries" when their off-label use occurred without knowledge of dangerous side effects and was promoted through misleading information at time Upjohn possessed undisclosed, adverse information about drug).

Here, evidence showed that the label not only failed to state with the correct degree of intensity the nature of the risk, it failed altogether to state the heightened risk that Janssen, through administration of its own clinical trials, knew applied to juvenile boys.

Appellants also posit, however, that Appellees were precluded from establishing proximate cause because A.Y.'s mother elected to continue with Risperdal even after knowing about the gynecomastia risk. Our review of Appellants' court-ordered Pa.R.A.P. 1925(b) statement, however, reveals that Appellants did not raise this issue sufficiently to preserve this alternate argument against Appellees' proximate causation proffer at trial.

Specifically, Appellants' statement does reference that A.Y.'s mother acknowledged Dr. Eker told her that breast enlargement was a possible side effect of Risperdal, and she still requested that A.Y. stay on Risperdal, even after filing the present lawsuit. *See* Appellants' Concise Statement of Matters Complained of on Appeal, Paragraph 5. However, this reference is contained within a larger passage focused exclusively on the treating physicians' independent knowledge of Risperdal's risks, and as such appears to be offered as

part and parcel of the argument that Dr. Eker knew of Risperdal's risks and conveyed them to A.Y.'s mother.

Indeed, the sentence immediately following the reference to A.Y.'s mother brings the issue to its conclusion by stating, "Where, as here, the prescribing physicians testified that they understood the risks of a medication at the time they prescribed it to their patient, they conveyed that risk to the patient (here the patient's mother), and there is no evidence that either prescribing physician even read the product label, any alleged deficiency in the label could not be the proximate cause of A.Y.'s injury. Judgment as a matter of law therefore should have been granted." Pa.R.A.P. 1925(b) Statement, at Issue 5.

Despite having conducted an exhaustive review of Appellants' Concise Statement, the trial court did not perceive in Issue 5 the question of whether Plaintiffs/Appellees were precluded by law from meeting their their proximate causation burden once A.Y.'s mother decided to continue with Risperdal even after she filed suit against Janssen. This was due not to the trial court's oversight but, instead, to Appellants' vague-at-best drafting of Issue 5, which appears dedicated solely to the issue of the physicians' knowledge. It is well-settled that a vague Rule 1925(b) statement fails to preserve a purported issue contained therein. *See M.G. v. L.D.*, 155 A.3d 1083, 1099 (Pa.Super. 2017) (citing *Reinert v. Reinert*, 926 A.2d 539 (Pa.Super. 2007) (issue raised on appeal waived where Rule 1925(b) statement was too vague for trial court review)). Therefore, we conclude Appellants have waived their claim as presented in this context.

Nevertheless, Appellants have preserved what amounts to essentially the same issue in its next Question Presented, where they ask whether a new trial is required for what they view as the trial court's erroneous evidentiary ruling excluding the testimony of one of A.Y.'s treating physicians, Gordon Greeson, M.D., who prescribed Risperdal to A.Y. in 2012. According to Appellants, Dr. Greeson's testimony was "uniquely important to rebut Plaintiffs/Appellees' theory that [A.Y.'s mother] would have refused Risperdal treatment for A.Y. if she had known it could cause gynecomastia." Appellant's brief, at 41. In that respect, Appellants maintain, the testimony would have shown the failure to warn was not the proximate cause of A.Y.'s gynecomastia, for Mother would have continued with Risperdal even had it contained an accurate statement of risk. We disagree.

With respect to the grant or refusal to grant a new trial upon allegations of error in the admissibility of evidence we have stated:

> Decisions regarding the admissibility of evidence are within the discretion of the trial court and will be reversed on appeal only if the trial court abused its discretion or committed an error of law . . . . We will grant a request for a new trial based upon a trial court's evidentiary rulings only if those rulings not only are erroneous, but also are harmful to the complaining party . . . . Evidence is relevant if it logically tends to establish a material fact in the case, tends to make the fact at issue more or less probable, or supports a reasonable inference

> or presumption about the existence of a material fact.

Phatak v. United Chair Co., 756 A.2d 690, 691 (Pa.Super. 2000) (citation omitted).

Dr. Greeson provided deposition testimony that A.Y.'s mother asked to restart Risperdal in June 2012—more than nine years after A.Y. first developed gynecomastia and more than one year after A.Y. had discontinued the medication in large part because of the gynecomastia effect. By March 2013, Dr. Greeson recommended that A.Y. switch from Risperdal to another antipsychotic, but Mother declined to follow the doctor's advice, even though she indicated she was prompted to file the present lawsuit against the manufacturer of Risperdal by advertisements pertaining to Risperdal/juvenile gynecomastia causes of action. At this point, Dr. Greeson testified in his deposition that he believed there was "no doubt" Mother was aware of the risk of gynecomastia from Risperdal at the time she asked him to restart A.Y. on the medication.

Appellants argue, "The only rational inference from Dr. Greeson's testimony is that a risk of gynecomastia would not cause Mother to refuse Risperdal—because A.Y.'s actual gynecomastia did not cause her to do so." They posit the doctor's testimony would have contradicted Mother's testimony that she resumed Risperdal only because A.Y.'s gynecomastia would not have resolved even if she discontinued the medication permanently.

Dr. Greeson explained in his deposition that his advisement to Mother included his concern that resuming Risperdal could make A.Y.'s gynecomastia

worse. Mother's willingness to continue Risperdal in the face of this warning was thus relevant to the proximate cause element to the failure to warn case at bar, Appellants conclude, for it shows Mother would likely have disregarded any risk-of-gynecomastia warning to obtain the antipsychotic benefits of Risperdal.

The trial court responds that Dr. Greeson's testimony was irrelevant to Plaintiffs' failure to warn claim, as Mother's willingness to resume Risperdal in 2013, after A.Y. had developed irreversible gynecomastia over the previous 10 years, did not have the tendency to make it more or less likely that Janssen's failure to warn proximately caused Mother to agree to Risperdal therapy for her then four-and-one-half year-old son. *See* Pa.R.E., Rule 401 ("Relevant evidence" means evidence having any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence."); *Hennessey v. Moyer*, No. 905 EDA 2019, 2019 WL 4862183, at *6 (Pa. Super. Ct. Oct. 2, 2019) ("Relevant evidence is admissible if its probative value outweighs its prejudicial impact."). *Accord* Tenn. R. Evid. 401 ("'Relevant evidence' means evidence having any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence."); Tenn. R. Evid. 402 ("Evidence which is not relevant is not admissible."). The court further notes that the jury heard other evidence pertaining to Mother's request to resume Risperdal despite obviously knowing that her son had likely developed gynecomastia because of the medication.

We agree with the trial court's assessment. The proximate cause inference Appellants seek to make is simply too attenuated given the significant passage of time and change in circumstances from when A.Y. began Risperdal treatment in 2003 to when he came under the care of Dr. Greeson in 2012-2013. Contrary to Appellants' contention, the proposed testimony would not have shed light on Mother's state of mind at the outset of A.Y.'s treatment, nor would it have "contradicted" Mother's statement that she requested continuation of the medication because A.Y. already had severe, irreversible gynecomastia by 2013. Under our standard of review, we cannot conclude that the ruling in question was both erroneous and harmful to the Appellants. Accordingly, we view this claim as meritless.

Appellants next challenge the court's evidentiary ruling excluding specific act evidence of A.Y.'s "biting, hitting, smashing windows out with his fist, persistent fighting with other children, refusal to follow instructions at school or at home, and on one occasion breaking a chicken's back." Appellant's brief, at 44. Appellants also contest the court's ruling limiting the testimony of expert medical witness, child psychiatrist Nadine Schwartz, M.D., whom Appellants had offered to speak on the Risperdal risk/benefit analysis conducted by psychiatrists, on her opinions regarding whether A.Y.'s treatment records reflected any evidence of significant emotional distress from gynecomastia.

> "The admission of expert testimony is a matter of discretion [for] the trial court and will not be remanded, overruled or disturbed

> unless there was a clear abuse of discretion." *Blicha v. Jacks*, 864 A.2d 1214, 1218 (Pa.Super.2004). Indeed, admission of the disputed testimony "must be shown to have been not only erroneous but also harmful . . . . Evidentiary rulings which did not affect the verdict will not provide a basis for disturbing the jury's judgment." *Detterline v. D'Ambrosio's Dodge, Inc.*, 763 A.2d 935, 940 (Pa.Super. 2000) (quoting *Ratti v. Wheeling Pittsburgh Steel Corp.*, 758 A.2d 695, 707 (Pa.Super.2000)).

Helpin v. Trustees of Univ. of Pennsylvania, 969 A.2d 601, 617 (Pa.Super. 2009), *aff'd*, 10 A.3d 267 (Pa. 2010).

According to the trial court, it committed no error in its evidentiary rulings excluding specific act evidence, as it did not preclude Dr. Schwartz from "testifying about Risperdal generally, the patients for whom Risperdal is appropriate, and the analysis a prescriber engages in when determining whether to prescribe Risperdal, including consideration of the risks and benefits. As the transcript demonstrates, Dr. Schwartz testified regarding these matters and more at trial." Trial Court Opinion, at 59-61.

The transcript shows the court permitted Dr. Schwartz to testify not only generally about Risperdal use in child psychiatry but also specifically about the risk/benefit assessment relevant in A.Y.'s case given his medical and behavioral history. For example, Dr. Schwartz discussed how a psychiatrist would approach a risk/benefit analysis, and she applied the approach to examine A.Y.'s particular case. She

explained he had been diagnosed with ADHD, oppositional defiant disorder, and mood disorder (either depressed or bipolar) at various points, and offered her opinion that A.Y. exhibited "very serious symptoms." She confirmed that the severity of the condition is the most essential piece to the risk/benefit analysis. *Id*.

Dr. Schwartz went on to discuss how Risperdal would have benefitted A.Y. given his diagnoses. She primarily emphasized the drug's mood stabilization properties as a way of helping such a patient with aggressive, explosive, violent, or impulsive outbursts, which, she opined, can be very quick and severe. Dr. Schwartz was permitted to restate these behaviors and the drug's corresponding benefits several times without objection or interruption by either opposing counsel or the court. N.T. 6/24/16 at 21-26, 54-56.

The trial court concludes:

> The above-referenced testimony belies Defendants' claim that this court limited Dr. Schwartz to only discussing the general benefits of Risperdal. As the transcript demonstrates, Dr. Schwartz testified about Risperdal as a treatment for certain mood disorders, the patients for whom Risperdal is appropriate, and the factors to be considered when prescribing such a medication. Dr. Schwartz also discussed A.Y.'s medical conditions, the seriousness of his symptoms, and why the severity of the conditions is relevant to a psychiatrist's risk/benefit analysis.

Trial Court Opinion, at 62.

We agree with the trial court and discern no error with its evidentiary rulings precluding specific act evidence, as Appellants still informed the jury, through expert testimony, that A.Y. demonstrated "very serious symptoms" and that Risperdal for juveniles with his diagnoses has been shown to help with highly aggressive, impulsive, explosive, and violent outbursts. This expert proffer, therefore, fairly characterized A.Y.'s condition and enabled Appellants to frame its theory of the case that Mother faced a dilemma between risking a relapse in A.Y.'s very serious mood disorder from Risperdal cessation and exacerbating A.Y.'s gynecomastia from Risperdal continuation. As such, we discern neither error with, nor prejudice stemming from, the court's ruling precluding testimony regarding A.Y.'s specific acts manifesting his mood disorder.

Similarly, we reach the same conclusion with respect to the trial court's ruling precluding Dr. Schwartz from inferring from the record whether Appellant exhibited any evidence of significant emotional distress from his gynecomastia. Dr. Schwartz never met or treated A.Y. and, therefore, had no first-hand knowledge of how his gynecomastia affected him emotionally, psychologically, or socially, leaving her to speculate from records about such matters.

Appellants cite to *McClain v. Welker*, 761 A.2d 155, 156 (Pa.Super. 2000) as supporting its position, but *McClain* is inapposite, as it addressed whether the trial court erred when it refused to qualify Dr. Theodore Lidsky, a neuroscientist, as an expert on plaintiff children's cognitive defects from ingesting

lead paint because he lacked a medical degree. In reversing and remanding, the panel ordered, "Accordingly, on remand, Dr. Lidsky should be permitted to render an expert opinion within the guise of Pa.R.E. 702 as to the causation of cognitive disorders." *Id*. at 158.

The expert in *McClain*, therefore, was permitted to clarify how ingesting lead can cause the particular cognitive defects exhibited by the plaintiff children. Such a scientific subject was clearly within the neuroscientist's scope of expertise. Appellants, in contrast, failed to establish that Dr. Schwartz's scope of expertise included the ability to interpret another doctor's notes to gauge a patient's level of emotional distress and humiliation from a disfiguring diagnosis.

Again, we find the court's evidentiary ruling neither erroneous nor harmful. Under the circumstances, and with other witnesses expressing direct impressions of A.Y.'s emotional distress, the court committed no error in deeming Dr. Schwartz's inferences on A.Y.'s emotions incompetent for admission at trial.

Appellants next assert several challenges to the trial court's jury instructions. Our review of these claims is governed by the following standard:

> Error in a charge is sufficient ground for a new trial if the charge as a whole is inadequate or not clear or has a tendency to mislead or confuse rather than clarify a material issue. Error will be found where the jury was probably misled by what the trial judge charged or where there was an omission in the charge. A charge will be found

> adequate unless the issues are not made clear to the jury or the jury was palpably misled by what the trial judge said or unless there is an omission in the charge which amounts to a fundamental error. In reviewing a trial court's charge to the jury, we must look to the charge in its entirety.

Tincher v. Omega Flex, Inc., 180 A.3d 386, 397-98 (Pa.Super. 2018) (cleaned up).[4]

Appellants contend that this Court should remand for a new trial because the trial court declined to instruct the jury on a key aspect to Tennessee's Learned Intermediary Doctrine. Specifically, Janssen proposed the following instruction, which it argued would clarify for the jury that for prescription medications, unlike other consumer products, the

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[4] We note the parallel standard of Tennessee:

> [T]his Court has held that "[w]hether a jury instruction is erroneous is a question of law and is[,] therefore[,] subject to *de novo* review with no presumption of correctness." *Nye*, 347 S.W.3d at 699 (citing *Solomon v. First Am. Nat'l Bank of Nashville*, 774 S.W.2d 935, 940 (Tenn.Ct.App.1989)). As indicated, in determining whether a trial court has imparted "substantially accurate" jury instructions, we review the charge in its entirety and consider it as a whole; we will not invalidate instructions that "'fairly define[ ] the legal issues involved in the case and do[ ] not mislead the jury.'" *Id.* (quoting *Otis*, 850 S.W.2d at 446). Moreover, we may consider the jury instructions in conjunction with the verdict form in determining whether the issues were presented to the jury "in a clear and fair manner." *Hickson Corp. v. Norfolk S. Ry.*, 260 F.3d 559, 568 (6th Cir.2001).

Payne v. CSX Transportation, Inc., 467 S.W.3d 413, 448 (Tenn. 2015).

"user" to whom the warnings are directed is the physician, not the patient:

> In this action, because the product involved is a prescription medication that can only be taken with the doctor's prescription, the expected users of Risperdal, for purposes of any warnings, are the physicians who prescribed Risperdal for [A.Y.], *not* [A.Y.] or his family. This is because a prescribing physician is in the best position to understand the patient's needs and assess the risks and benefits of a particular course of treatment. In order to prevail, Plaintiff's must prove that Janssen failed to warn [A.Y.]'s healthcare providers of the risk of gynecomastia *and* that his healthcare providers were not already aware of the risks. If the risk of gynecomastia was apparent to [A.Y.]'s physicians, Janssen was not negligent even if Janssen gave no warning about it.

Appellants' First Amended Proposed Points of Charge, Proposed Instruction No.21, 6/29/16 (emphasis in original).

The trial court opted instead to rely on the Tennessee Pattern Instruction Civil 10.12 for its instruction. The instruction went as follows:

> Supplier's duty to warn. A supplier who knows or reasonably should know that a product is likely to be dangerous for its intended use or foreseeable misuse has a duty to use reasonable care to warn of the

> product's danger or to reveal its unsafe condition.
>
> Warnings should be given to those persons whom the supplier should reasonably expect to use or to handle the product or be endangered by its use or handling if the supplier reasonably should believe those persons would not realize the danger without the warnings. The failure to fulfill this duty is negligence.

N.T. 6/30/16, at 171.

Furthermore, the court directs us to the questions it presented to the jury on the verdict sheet, which the court also read to the jury before deliberation. According to the court, this reading instructed the jury specifically that the manufacturer's warning was required to be directed to A.Y.'s healthcare providers:

> Now, as you deliberate, you will receive the verdict sheet. I'll read it to you. There are four questions you must answer. The first question: Was Janssen negligent by failing to provide an adequate warning to [A.Y.'s] healthcare providers about the risk of gynecomastia from taking Risperdal? There's a line to check yes, a line to check no. If you answer yes to Question 1, please proceed to Question 2. If you answer no to Question 1, plaintiff cannot recover. Do not answer any further questions and return to this Courtroom.

N.T. 6/30/16, at 182.

The trial court opines that the explanation provided on the verdict sheet, coupled with the jury instruction regarding Defendants/Appellants' duty to warn, accurately reflected the law applicable to the present case. Appellants disagree, as they claim the court's instruction and reading of the jury sheet simply gave the jurors "contradictory" charges that could only have misled or confused them.

We disagree with Appellants' position. Viewing the court's charge as a whole, we view no key omission, fundamental error, or inherent conflict, as the jury was sufficiently apprised of a manufacturer's duty to direct its warning to healthcare providers, consistent with the learned intermediary doctrine. Therefore, Appellant is due no relief on this claim.

Next, Appellants posit that the trial court committed reversible error when it failed to apply appropriately the Tennessee Civil Justice Act Damages Cap of 2011, which imposes a limit on non-economic damages in the amount of $750,000 per plaintiff. Tenn. Code Ann. § 29-39-102(a)(2), "Civil Actions; awards" (2018).

It is undisputed that the cap applies to the present case, but Plaintiffs/Appellees argued that the facts brought this case under a statutory exception to the cap. The exception provides:

> (h) The limitation on the amount of noneconomic damages imposed by subdivision (a)(2) and subsections (b)-(e) shall not apply to personal injury and wrongful death actions:
>
> …

> (2) If the defendant intentionally falsified, destroyed or concealed records containing material evidence with the purpose of wrongfully evading liability in the case at issue; provided, however, that this subsection (h) does not apply to the good faith withholding of records pursuant to privileges and other laws applicable to discovery, nor does it apply to the management of records in the normal course of business or in compliance with the defendant's document retention policy or state or federal regulations.

Tenn. Code. Ann. § 29-39-102(h)(2).

Appellants maintain, without reference to either rules of statutory interpretation or pertinent authority, that the statute targets only spoliation of evidence during discovery, and there was no spoliation "in the case at issue."

They note Plaintiffs/Appellees did not allege that Janssen engaged in falsifying, destroying, or concealing records during the course of discovery in this case. Because, they reiterate, the statute in question is aimed at discovery conduct within a given case and not at alleged pre-litigation manipulation or concealment of documents from non-party actors, even if the documents may one day become evidence in a potential future litigation, the exception does not apply to the present matter.

The trial court found no merit to Defendants/Appellants' argument at trial, where Appellants invoked the statute when

Plaintiffs/Appellees requested the following instruction:

> You must determine whether the Defendants intentionally falsified, destroyed, or concealed records pertaining to this case[.]
>
> For you to find that Defendants intentionally falsified, destroyed, or concealed records pertaining to this case, the Plaintiff must prove by a preponderance of the evidence the following elements:
>
> 1. That Defendants intentionally falsified, destroyed or concealed Defendants' records to wrongfully evade liability in the case at issue; and
>
> 2. That Defendants' records contained material evidence pertaining to this case.

See Plaintiffs' Amended Proposed Points for Charge, 6/29/16.

Specifically, Plaintiffs/Appellees provided the following argument in support of its proposed points of charge:

> [Plaintiffs' Counsel]: Your Honor, let me give you globally what's going on. This case is going to be decided under Tennessee law, and I don't profess to be a total expert on Tennessee law. But the defendants are going to raise an issue, if there's a jury verdict and if it exceeds, I believe, $750,000, they will try to claim that there's some sort of damage cap in Tennessee. [Counsel then explains there is an exception in cases of concealment of evidence.] So what you see here is the

> instruction about what that means, and then later on in the verdict form we propose a question on it.
>
> So the two issues of concealment, there's two things they did. One is they locked up Table 21 from 2002 until 2015. That's a big part of our case. And then you also have the Bilker issue [referring to person Janssen allegedly hired to provide an alternate interpretation of the clinical studies discussed, supra]. So there's two issues of concealment because, even though they gave Table 21 to the FDA in October 2015, our claim goes to 2003. So we think this comes in, and we think you need this instruction so that we can get a jury finding on this issue in case, you know, we're fortunate enough.

N.T., 6/30/16, at 9-10.

Appellants countered:

> [Defendants' Counsel]: No, but it has to do—falsified, destroyed, or concealed to wrongfully evade liability in the case at issue. Your Honor, obviously we haven't had briefing on this, but I think it's clear from the statute and from the instruction itself that this is about concealing evidence in this litigation. It's not about whether you should or shouldn't have given facts to other people outside litigation. This is just extremely prejudicial, and it's not appropriate to this case. And to be suggesting to this jury that we destroyed evidence and kept it out of

> litigation just is irretrievably prejudicial to the defendants.

N.T., 6/30/16, at 12-13.

The trial court explains it rejected Defendants/Appellants' argument and, therefore, read Plaintiffs/Appellees' proposed charge to the jury, because ample evidence demonstrated that Appellants intentionally falsified and concealed records in this case:

> "To reiterate, Plaintiffs presented evidence that Defendants concealed Table 21, an internal Janssen document, that demonstrated a statistically significant link between Risperdal and gynecomastia. Instead of submitting this information to the FDA during the approval process, Defendants withheld and concealed the results for more than a decade. In addition, Plaintiffs presented evidence that Defendants hired Dr. Warren Bilker, a biostatistician, to perform a reanalysis of Table 21. The only specifics given to Dr. Bilker, who was under the control and direction of Dr. Findling and Dr. Daneman, were to refute the results in Table 21. N.T., 6/27/16, at 179. According to Plaintiffs, Dr. Bilker intentionally manipulated and retested the data multiple ways to get the results Defendants wanted. Once Dr. Bilker was able to refute the results in Table 21, the reanalysis was submitted as a letter by Dr. Daneman and Dr. Findling to The Journal of Clinical Psychiatry and published. These results, according to

> Plaintiffs, were inaccurate, inadequate, and misleading.

Trial Court Opinion, at 85.

We agree that such intentional conduct, if proven, was fairly contemplated within the exception set forth in subsection (h) of the statute in question. A reasonable inference arises from the record that Appellants persisted in its alleged concealment of the clinical study results recorded in Table 21 not only with an eye toward future litigation in general but also to frustrate existing lawsuits such as Plaintiffs/Appellees'. This alleged conduct was compounded by Appellants' manipulation of the data collected in Table 21 and publication of the altered results during the relevant time.

The court, therefore, properly informed the jury that it was to decide a question of fact whether Plaintiffs proved its allegations of such conduct occurring after the present lawsuit had commenced, and that if it decided in the affirmative then the damages cap no longer applied. As Appellants develop no persuasive argument to upset the court's considered interpretation of the statute, we decline to find error with the instruction at issue.

Relatedly, Appellants claim the court committed reversible error when it gave an allegedly incomplete special interrogatory on what Appellants call the spoliation issue. Specifically, the verdict form read:

> Did Janssen intentionally falsify, destroy, or conceal records containing material evidence in this case?

Trial Work Sheet/Verdict Sheet, 7/5/16.

According to Appellants, the omission of the clause, "with the purpose of wrongfully evading liability in the case at issue," deprived the jury of clear guidance on how to make the proper finding required under the law, and, therefore, prejudiced Appellants in the process. Our review of the record, however, reveals that the court provided the following jury instruction just minutes earlier:

> Trial Court: Intentional falsification, destruction, or concealment. You must determine whether the defendants intentionally falsified, destroyed, or concealed records pertaining to this case. For you to find the defendants intentionally falsified, destroyed, or concealed records pertaining to this case, the plaintiffs must prove, by a preponderance of the evidence, the following elements: Number one, that the defendants intentionally falsified, destroyed, or concealed defendant's records *to wrongfully evade liability in this case at issue* . . . .

N.T., 6/30/16, at 173. (emphasis in original).

Contrary to Appellants' contention, the court instructed the jury that it was required to consider whether Defendants/Appellants had acted in such a way to wrongfully evade liability in this case. As the record belies Appellants' assertion, we find it without merit.[5]

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[5] Also germane to this issue is the well-settled legal precept that failure to object to a flawed jury verdict prior to a jury's dismissal precludes a challenge to the verdict in post-trial

In Appellants' final issue, they contend the trial court should have granted a new trial or remitted what they perceive as an excessive damages award. We disagree.

Under Tennessee law, a trial court "may set aside a jury's verdict and order a new trial when justice so requires." *Palanki v. Vanderbilt Univ.*, 215 S.W.3d 380, 386 (Tenn.Ct.App. 2006). The role of the trial judge in this regard is well-settled:

> Although the amount of an award is primarily a consideration for the jury to determine, the trial court may suggest a remittitur when the amount of the verdict is excessive, beyond the range of reasonableness, or is excessive as the result of passion, prejudice, or caprice. *Poole v. Kroger Co.*, 604 S.W.2d 52, 54 (Tenn. 1980). However, there is no precise mathematical formula which the court can use to assure that judgments in negligence cases are uniform. *S. Ry. Co. v. Sloan*, 56 Tenn.App. 380, 407 S.W.2d 205, 211 (1965). Said the Court:
>
> > There is no exact yardstick, or measurement, which this court may

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motions. *See Stapas v. Giant Eagle, Inc.*, 198 A.3d 1033, 1041 (Pa. 2018) (holding that where both parties to litigation approved verdict sheet and did not object to verdict before jury dismissed, post-trial objections to verdict were waived); Pa.R.C.P. 227.1(b)(1) ("post-trial relief may not be granted unless the grounds therefore, (1) if then available, were raised in pre-trial proceedings or by motion, objection … or other appropriate method at trial.").

> use as a guide to determine the size of verdicts which should be permitted to stand in cases of this kind. Each case must depend upon its own facts and the test to be applied by us is not what the amount the members of the court would have awarded had they been on the jury, or what they, as an appellate court, think should have been awarded, but whether the verdict is patently excessive. The amount of damages awarded in similar cases is persuasive but not conclusive, and, in evaluating the award in other cases, we should note the date of the award, and take into consideration inflation and the reduced value of the individual dollar.

S. Ry. Co., 407 S.W.2d at 211.

Palanki, 215 S.W.3d at 386.

Pennsylvania is largely in accord:

> The assessment of damages is peculiarly within the province of the factfinder and an award will not be upset on appeal unless it is so excessive as to shock the conscience of the court or it is clearly based on partiality, prejudice or passion. *De Simone v. City of Philadelphia*, 380 Pa. 137, 110 A.2d 431 (1955). Generally, under Pennsylvania law, damages need not be proved with mathematical certainty, but only with reasonable certainty, and evidence of

> damages may consist of probabilities and inferences. *See, e.g.*, *Morin v. Brassington*, 871 A.2d 844, 852 (Pa. Super. 2005), *quoting J.W.S. Delavau Inc. v. Eastern America Transp. & Warehousing, Inc.*, 810 A.2d 672, 685 (Pa. Super. 2002); *James Corp. v. N. Allegheny Sch. Dist.* 938 A.2d 474, 494 (Pa. Cmwlth. 2007); *E.C. Ernst, Inc. v. Koppers Co., Inc.*, 626 F.2d 324, 327 (3d Cir. 1980). Where the amount of damages can be fairly estimated from the evidence, the recovery will be sustained even though such amount cannot be determined with entire accuracy. *Mass. Bonding & Ins. Co. v. Johnston & Harder*, 343 Pa. 270, 22 A.2d 709, 713-14 (1941). We review a trial court's decision whether to grant a new trial based on alleged excessiveness or inadequacy of the verdict for an abuse of discretion. *Botek v. Mine Safety Appliance Corp.*, 531 Pa. 160, 611 A.2d 1174, 1176 (1992). Judicial reduction of a jury award is appropriate only when the award is plainly excessive and exorbitant. *Haines v. Raven Arms*, 536 Pa. 452, 640 A.2d 367, 369 (1994).
>
> The refusal of a remittitur is peculiarly within the discretion of the trial court and will not be reversed absent an abuse of discretion or error of law. *Id.*, *citing Scaife Co. v. Rockwell-Standard Corp.*, 446 Pa. 280, 285 A.2d 451, 456-57 (1971).

Bailets v. Pennsylvania Tpk. Comm'n, 181 A.3d 324, 336 (Pa. 2018).

Appellants contend that such precepts should guide this Court to find that the verdict in the present case is so excessive relative to the harm suffered that a remittitur would effectively "destroy the jury's verdict," thus necessitating a retrial. *See Guess v. Maury*, 726 S.W.2d 906, 912 (Tenn.Ct.App. 1986).

Appellants note that, under Tennessee law, "[w]hen asked to determine whether a verdict should be set aside based on the amount of the damages award alone, the courts must consider the nature and extent of the plaintiff's injuries, the pain and suffering the plaintiff experienced, the expenses the plaintiff incurred as a result of the injuries, the impact the injuries have had on the plaintiff's enjoyment of life, and the plaintiff's age and life expectancy." *Duran v. Hyundai Motor America, Inc.*, 271 S.W.3d 178, 212 (Tenn.Ct.App. 2018).

"Gynecomastia[,]" Appellants submit, "is not a life-threatening condition, and Plaintiffs presented no evidence of physical pain and suffering." Appellants' brief, at 54. While surgical correction of gynecomastia is possible, Plaintiffs/Appellees did not choose to pursue this option. Appellants further stress that Plaintiffs/Appellees similarly presented no evidence of economic damages, hospital bills, and did not argue that gynecomastia would affect A.Y.'s future earnings. *Id.*

Thus essentially limited to psychological and emotional, non-economic damages, Appellants continue, Plaintiffs/Appellees' award of $70,000,000 was grossly disproportionate to the evidence. Appellants maintain the extent of such evidence was that A.Y. was bullied at school and work, teased, and

never went outside without a shirt. They conclude such a proffer simply did not support a compensatory damages award nearly 30 times larger than the next largest compensatory verdict in Philadelphia, $2,500,000 in *Pledger v. Janssen Pharmaceuticals, Inc.*, 198 A.3d 1126 (Pa.Super. 2018).

The trial court opines that the verdict was not excessive, as the jury was free to infer from the evidence that A.Y.'s pain and suffering, embarrassment, loss of enjoyment of life, and the inability to engage in normal activities in the future was considerable. In that vein, the court notes that the jury was charged to consider both economic and non-economic damages, and Tennessee law holds that a "jury has wide latitude in assessing non-economic damages." *Meals ex rel. Meals*, 417 S.W.3d at 425.

Indeed, the court notes, the jury charge instructed the jury that "no definite standard or method of calculation is prescribed by law by which to fix reasonable compensation for pain and suffering, permanent injury, disfigurement, and the loss of enjoyment of life, nor is the opinion of any witness required as to the amount of such reasonable compensation." Trial Court Opinion, at 92 (quoting N.T. 6/30/16, at 175-76). Because the courts have recognized that such damages are not easily quantified and do not lend themselves to easy valuation, the amount of these damages is appropriately left to the sound discretion of the jury. *Id.* (quoting *Duran*, 271 S.W.3d at 210-211).

We discern no reversible error with the jury's award of damages, as we do not view it as inconsistent with the evidence. A.Y. was just 4 ½ years old when

first prescribed Risperdal, and he has never since known life without gynecomastia. At sixteen years of age when the jury considered its award, A.Y. was living with severe and permanent disfigurement. The undisputed record confirms he has been routinely bullied and teased by peers and is too humiliated to ever remove his shirt in recreational or social situations where it would be customary for boys to do so when enjoying ordinary pleasures of youth.

The jurors were free to call upon their personal experiences and sensibilities to assess such intangible harms, and their valuation could reflect the length of time A.Y. would reasonably be expected to live with this disfiguring, embarrassing condition. Under such facts, the jury exercised sound discretion. Accordingly, we will not disturb the damages award.

APPELLEES' CROSS-APPEAL

In Appellees' cross-appeal, they contend the trial court erred by granting Janssen's motion for partial summary judgment on Appellees' claim for punitive damages. In entering its global order granting summary judgment as to all plaintiffs in the Risperdal litigation, the trial court determined that New Jersey had a greater interest than Pennsylvania in the application of its law on the issue of punitive damages, and the New Jersey Products Liability Act does not permit Plaintiffs to recover punitive damages.

This Court has subsequently considered the trial court's two determinations in *Murray v. Janssen Pharmaceuticals, Inc.*, 180 A.3d 1235 (Pa.Super. 2018), *Stange*, 179 A.3d at 49-50, and *Pledger*, 198 A.3d 1126 and held in each that we were required to remand for the trial court to consider conflict-of-law

principles with respect to New Jersey and the respective plaintiff's home state, which it had not done. *See Stange*, 179 A.3d at 66-67 (remanding for consideration of conflict between Wisconsin and New Jersey); *Murray* (180 A.3d at 1248-49 (remanding for consideration of conflict between Maryland and New Jersey); *Pledger*, 198 A.3d at 1148 (remanding for consideration of conflict between Alabama and New Jersey).

Here, Appellees present the same arguments made by the plaintiffs in the aforementioned cases, and both parties agree the decisions by our Court remain binding precedent. *See Marks v. Nationwide Ins. Co*, 762 A.2d 1098, 1101 (Pa.Super. 2000) (acknowledging as long as a decision by this Court has not been overturned by our Supreme Court, it remains binding precedent). Thus, as we have done previously, we reverse the order of the trial court granting partial summary judgment in favor of Janssen and remand for proceedings consistent with those in *Stange*, *Murray*, and *Pledger*.

Judgment affirmed in part, reversed in part, and remanded for proceedings wherein the trial court shall consider conflict of law principles with respect to Tennessee and New Jersey and how they bear on Plaintiffs/Appellees' punitive damages claim. Jurisdiction relinquished.

Judgment Entered.

[handwritten: signature]
Joseph D. Seletyn, Esq.
Prothonotary

Appendix C

PENNSYLVANIA COURT OF COMMON PLEAS

No. 2094

A.Y., et al.,

Plaintiffs,

v.

JANSSEN PHARMACEUTICALS INC., et al.,

Defendants.

Filed: June 20, 2018

OPINION

Patrick, J.

Defendants, Janssen Pharmaceuticals Inc., Johnson & Johnson, and Janssen Research & Development, LLC, filed an appeal from judgment entered in this matter on September 7, 2016 and from orders entered on July 1, 2016, July 5, 2016, July 25, 2016, and August 10, 2016. Plaintiffs, A.Y. and Billie Ann Yount, filed a cross-appeal from judgment entered in this matter on September 7, 2016 and from orders entered on May 2, 2014, July 18, 2014, and July 25, 2016. This Court now submits the following Opinion in support of its ruling and in accordance with the requirements of Pa.R.A.P. 1925(a). For the reasons set forth below, this Court's decision should be affirmed.

PROCEDURAL HISTORY

On April 15, 2013, Plaintiffs A.Y. and Billie Ann Yount filed a Complaint against Defendants Janssen Pharmaceuticals Inc., Johnson & Johnson, Janssen Research & Development, LLC, Elsevier, Inc., and Excerpta Medica Inc. Plaintiffs Complaint alleged the following thirteen causes of action: (1) negligence, (2) negligent-design defect, (3) fraud, (4) strict product liability—failure to warn, (5) strict product liability—design defect, (6) breach of express warranty, (7) breach of implied warranty, (8) violation of Pennsylvania Unfair Trade Practices and Consumer Protection Law, 73 P.S. § 201-1 et seq., (9) unfair and deceptive trade practices, (10) conspiracy, (11) punitive damages, (12) medical expenses incurred by parent, and (13) loss of consortium.

By Order dated May 2, 2014, the Honorable Arnold L. New ruled that New Jersey Law applied to the issue of punitive damages and that New Jersey law barred the award of punitive damages. On June 2, 2014, Plaintiffs filed a Motion for Reconsideration of the Honorable Arnold New's May 2, 2014 Order barring the award of punitive damages. On June 9, 2014, Defendants filed an Answer to Plaintiffs' Motion for Reconsideration. On July 18, 2014, Plaintiffs' Motion for Reconsideration was denied.

On November 4, 2015, the Honorable Arnold New approved a stipulation dismissing the action as to Defendants Excerpta Medica, Inc., and Elsevier Inc. On April 14, 2016, remaining Defendants, Janssen Pharmaceuticals, Inc., Johnson & Johnson, and Janssen Research & Development, LLC, filed a motion for summary judgment. On May 5, 2016, Plaintiffs

filed an Answer to Defendants' Motion for Summary Judgment. On May 11, 2016, Defendants filed a Reply. On June 10, 2016, the Honorable Arnold New ruled that Tennessee Law applies to Plaintiffs' substantive claims. Plaintiffs' claims for: negligence, negligent design defect, strict liability—failure to warn, strict liability—design defect, breach of express warranty, breach of implied warranty are subsumed into two claims: (a) Product Liability action because Risperdal was defective and (b) Product Liability action because Risperdal was unreasonably dangerous.[1] The Honorable Arnold New further ruled that Defendants' Summary Judgment was granted as to the following causes of action: (A) product liability action because Risperdal was defective, (B) fraud, (C) Pennsylvania's Unfair Trade Practices and Consumer Protection Law, (D) unfair and deceptive trade practices (under the

[1] See T.C.A. § 29-28-105(a): "A manufacturer or seller of a product shall not be liable for any injury to a person or property caused by the product unless the product is determined to be in a defective condition or unreasonably dangerous at the time it left the control of the manufacturer or seller."

See also: Definition of product liability action in T.C.A. §29-28-102(6): "Product liability action for purposes of this chapter includes all actions brought for or on account of personal injury, death or property damage caused by or resulting from the manufacture, construction, design, formula, preparation, assembly, testing, service, warning, instruction, marketing, packaging or labeling of any product. Product liability action includes, but is not limited to, all actions based upon the following theories: strict liability in tort; negligence; breach of warranty, express or implied; breach of or failure to discharge a duty to warn or instruct, whether negligent, or innocent; misrepresentation, concealment, or nondisclosure, whether negligent, or innocent; or under any other substantive legal theory in tort or contract whatsoever."

Tennessee Consumer Protection Act), (E) conspiracy, and (F) loss of consortium. Defendants' Motion for Summary Judgment was denied as to all other causes of action.

On June 16, 2016, a jury trial commenced in this matter; the Honorable Paula A. Patrick presided. On July 1, 2016, the jury returned a verdict in favor of the Plaintiffs. The jury found that Defendants negligently failed to adequately warn Plaintiffs of the risk of gynecomastia associated with Risperdal use and Defendants' negligence was a cause in bringing about A.Y.'s gynecomastia. The jury awarded Plaintiffs compensatory damages in the amount of $70,000,000.00 (seventy million dollars). On July 5, 2016, the jury's verdict was entered.

On July 8, 2016, Plaintiffs filed a Post-Trial Motion. Defendants filed a Post-Trial Motion on July 11, 2016. This Court denied both Post-Trial Motions on July 25, 2016.

On July 8, 2016, Plaintiffs filed a Motion for Delay Damages. On August 10, 2016, Plaintiffs' Motion for Delay Damages was granted. Plaintiffs were awarded $6,661,027.40 in Delay Damages. The jury verdict of $70,000,000.00 was molded to add Delay Damages of $6,661,027.40 for a total verdict of $76,661,027.40. On September 7, 2016, judgment was entered in this matter.

On September 9, 2016, Defendants filed an Appeal to the Superior Court from decisions dated July 1, 2016, July 5, 2016, July 25, 2016 and August 10, 2016. On September 13, 2016, Plaintiffs filed a cross-appeal to the Superior Court from decisions dated May 2, 2014, July 18, 2014, and July 25, 2016.

On September 22, 2016, Plaintiffs filed a Statement of Errors Complained of on Appeal pursuant to Pa.R.A.P. 1925(b). On October 12, 2016, Defendants filed a Statement of Errors Complained of on Appeal pursuant to Pa.R.A.P. 1925(b).

FACTUAL BACKGROUND

Risperdal (risperdone) is an antipsychotic medication belonging to a class of drugs which have become known as "atypical" or "second generation" ("SGA") antipsychotics. Risperdal was originally developed and approved for use in the treatment of symptoms associated with schizophrenia. The adverse effects associated with Risperdal are: rapid weight gain, hyperprolactinemia, gynecomastia (abnormal development of breasts in males), galactorrhea (lactation), pituitary tumors, microadenomas of the pituitary gland, breast cancer, osteoporosis, decreased bone mineral density, metabolic syndrome, dyslipidemia, hypertension, diabetes mellitus, diabetic ketoacidosis (DKA), hyperosmolar coma, hyperglycemia, glucose dysregulation, insulin insufficiency, insulin resistance, pancreatitis, tardive dyskinesia, extrapyramidal symptoms, involuntary movement disorders, dyskinesia, dystonia, akathisia, parkinsonism, neuroleptic malignant syndrome (NMS) and/or other related conditions. Risperdal is designed, developed, tested, labeled, packaged, distributed, marketed, and sold throughout the United States by the Janssen Defendants.

On December 29, 1993, Janssen obtained approval from the Food and Drug Administration ("FDA") to market Risperdal oral tablets for the treatment of "manifestations of psychotic disorders"

(schizophrenia) in adults. In September 2000, the FDA requested that the label be changed to more clearly indicate that Risperdal was only approved for use in treating schizophrenia in adults. In October 2006, Risperdal was approved for the treatment of irritability associated with autistic disorder in children and adolescents (between the ages of 5 and 16), including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums and quickly changing moods. Risperdal has not been approved for children younger than 5 or those older than 16 years old for irritability associated with autistic disorder.

The prescribing of drugs "off-label" occurs when a drug is prescribed by a medical professional for use beyond those contained in the drug's FDA-approved uses. This includes prescribing a drug for a condition not indicated on the label, treating the indicated condition at a different dose or frequency than specified in the label, or treating a different patient population. An example of off-label use is the treatment of a child with the drug when the drug is approved to treat adults.[2]

Plaintiff A.Y. was born in 1999. Plaintiff was diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD). In August of 2003, when A.Y. was four and a half years old, he was prescribed Risperdal by Dr. Deniz Eker, a pediatric psychiatrist. Eker Dep. 2/8/16

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[2] *See* U.S. Food & Drug Administration, *Understanding Unapproved Use of Approved Drugs "Off Label,"* available at https://www.fda.gov/forpatients/other/offlabel/default.htm (last visited February 4, 2018).

at 31-32. At the time Dr. Eker prescribed Risperdal to A.Y., she did not warn A.Y.'s mother about the risk of gynecomastia. Dr. Eker stated that she would have warned A.Y.'s mother, but Dr. Eker did not know at the time that there was such a significant risk of gynecomastia from elevated prolactin. *Id.* at 56, 61. In January 2004, four months after Plaintiff began taking Risperdal, A.Y.'s mother went to Doctor Eker and expressed concern that A.Y.'s breasts were enlarging. *Id.* at 65. Dr. Eker then began tapering the Risperdal because she was concerned about gynecomastia. *Id.* at 66. In February 2005, after the initial tapering, Dr. Eker noted that A.Y.'s breasts were getting big and that she was discontinuing Risperdal because A.Y. had gynecomastia. *Id.* Dr. Eker testified that when she first noticed gynecomastia, she began tapering off from the Risperdal but would have stopped it immediately if she had been properly informed about the risk of gynecomastia from Risperdal. *Id.* Dr. Eker believed gynecomastia was much less frequent and that A.Y.'s development of female breasts (at five years old) was a rare occurrence. When Dr. Eker believed the gynecomastia had gone down, she put A.Y. back on Risperdal. *Id.* at 76-77.

Dr. Eker transferred A.Y.'s psychiatric care to Dr. Michael Hughes in the first half of 2005. *Id.* at 78. Dr. Hughes testified that the idea to put A.Y. on Risperdal originated with Dr. Eker, and he was simply continuing the treatment. *Id.* at 279-80. Dr. Hughes could not say that he would have put A.Y. on Risperdal at all if Dr. Eker had not prescribed it first. *Id.* Dr. Hughes testified that if he had known that there was a statistically significant association between

prolactin elevation from Risperdal use and gynecomastia this information would have had a significant impact in his thinking with regard to prescribing Risperdal. *Id.* at 266-267. Dr. Hughes stated that he would have pushed against Risperdal use if he had known of the additional significant concerns. *Id.* at 83-84. Dr. Hughes treated A.Y. from May 2005 through May 2011. *Id.* at 228-29. Dr. Hughes discontinued Risperdal at the request of A.Y.'s mother because A.Y. was gaining so much weight. *Id.* at 161-62.

Dr. Brian Bonfardin, a psychiatrist, began treating A.Y. in June 2011. *Id.* at 16. In June of 2012, A.Y. was struggling, and A.Y.'s mother suggested trying Risperdal again to Dr. Bonfardin. At that time, Dr. Bonfardin's prescription of Risperdal had already plummeted because he had learned prior to 2012 that Risperdal increased prolactin levels more than other antipsychotics. *Id.* at 48-49. Dr. Bonfardin testified that he did not know of the studies showing a 5.5% and 12.5% frequency of gynecomastia among children who used Risperdal. If he had such information, he would have warned A.Y.'s mother about this significant risk. Bonfardin Dep. 2/11/16 at 16.

A.Y.'s care was transferred to Dr. Gordon Greeson in October of 2012. Dr. Greeson took A.Y. off Risperdal once he took over care because A.Y. gained quite a bit of weight and had hypertension in the short period he had been put back on Risperdal. A.Y.'s mother requested he be put back on Risperdal next month.

In 2013, A.Y.'s mother saw an advertisement discussing gynecomastia from Risperdal use. A.Y. Mother Dep. 12/14/15 at 6-8. She got in contact with

an attorney and then went to talk to A.Y.'s treating physicians about the problem. *Id.* Dr. Greeson learned of the gynecomastia from A.Y.'s mother in March 2013. Dr. Greeson immediately decided he needed to stop Risperdal because he feared making the problem worse.

ISSUES

Defendants raised the following issues in their 1925(b) Statement of Matters Complained of on Appeal:

> ***The Court Should Have Granted Judgment As A Matter Of Law Because Plaintiffs Failed To Establish That The Risperdal Warning Was Inadequate Or That Defendants Could Have Lawfully Changed The Label***

1. The Court erred in submitting the case to the jury because the Risperdal warning was adequate as a matter of Tennessee law. The pre-October 2006 Risperdal label stated in both the "Precautions" section and the "DOSAGE AND ADMINISTRATION" SECTION: "**Pediatric Use:** Safety and effectiveness in children have not been established." This unequivocal statement notified physicians that the medication was not approved for any use in children at that time—rendering the label adequate under Tennessee law. *See, e.g.*, *Strayhorn v. Wyeth Pharms., Inc.*, 887 F. Supp. 2d 799 (W.D. Tenn. 2012) *aff'd* 737 F.3d 378 (6th Cir. 2013). Moreover, the label accurately reflected the state of science at the time it was marketed.

Tenn. Code. Ann. § 29-28-105(a). Plaintiffs' expert Dr. David Kessler acknowledged that the Risperdal label included a warning as to the risk of hyperprolactinemia and the possibility of gynecomastia generally and his opinions as to the adequacy of the label were based on an incorrect interpretation of FDA regulations. As a result, judgment notwithstanding the verdict was appropriate. Mot. for Post-Trial Relief Pursuant to Pa. R.C.P. No. 227.1 of Defendants Janssen Pharm., Inc.; Johnson & Johnson; and Janssen Research & Dev., LLC (July 11, 2016) (Control No. 16071208) ("Post-Trial Mot.") at 8-11, 35-37 ¶¶ 20-27, 75-78.

2. The Court erred in submitting this case to the jury because all of Plaintiffs' failure-to-warn claims are preempted by federal law, and this issue should have been resolved by the Court. Plaintiffs' entire failure-to-warn theory rests on the notion that Janssen should have provided additional warnings as to Risperdal relative to the alleged risk of gynecomastia associated with Risperdal use by children and adolescents. This claim is preempted because federal law prohibits Janssen from taking this action. Specifically, Janssen could not comply with both Plaintiff's demands and federal regulations as evidenced by the fact that the U.S. Food and Drug Administration ("FDA") has explicitly stated that gynecomastia is not a serious adverse event, which is clear evidence that the FDA would not have approved the label change as

required by *Wyeth v. Levine*, 555 U.S. 555 (2009), and its progeny. *See* Post-Trial Mot. at 33-35, ¶¶ 71-74.

3. The Court erred in submitting Plaintiffs' failure-to-warn claim, which was based on the pre-October 2006 Risperdal label, to the jury because this claim is preempted by federal law and should have been resolved by the Court. Plaintiffs' entire theory as to the pre-October 2006 Risperdal label rests on the notion that Janssen should have provided warnings as to Risperdal relative to an unapproved population, i.e., children and adolescents. This claim is preempted because federal law prohibits Janssen from taking this action. Specifically, the FDA regulations in effect during the relevant time, including 21 C.F.R. § 201.57(e) (Mar. 2006), reflect that a warning concerning a risk as to an off-label use, i.e., an unapproved indication, must be initiated by the FDA. Post-Trial Mot. at 31-33, ¶¶ 66-70.

The Court Should Have Granted Judgment As A Matter of Law Or, In The Alternative, A New Trial Because There Was Inadequate Evidence That Any Alleged Failure to Warn Proximately Caused A.Y.'s Alleged Injuries

4. Tennessee, like Pennsylvania, has adopted the learned intermediary doctrine. *Pittman v. Upjohn Co.*, 890 S.W.2d 425, 428 (Tenn. 1994). A pharmaceutical manufacturer "may discharge their duty [to exercise reasonable

care] by distributing the drugs with proper directions and adequate warnings to those who foreseeably could be injured by the use of their products." *Id.* An allegedly inadequate warning cannot be the proximate cause of an injury where a physician is fully aware of the risks of a medication. *Harden v. Danek Med., Inc.*, 985 S.W.2d 449, 451 (Tenn. Ct. App. 1999). Post-Trial Mot. at 24, ¶¶ 50-51. Additionally, even where a warning is found inadequate, a manufacturer cannot be held liable unless plaintiff can demonstrate that an allegedly adequate warning would have been conveyed to the Plaintiff and prevented plaintiff from taking the medication. *See King v. Danek Med., Inc.*, 37 S.W.3d 429, 452-53 (Tenn. Ct. App. 2001) (citing *Harden*, 985 S.W.2d at 451). Post-Trial Mot. at 24-25, ¶ 52. Finally, Tennessee law also provides that where there is no evidence that a physician actually read the allegedly inadequate warning, the warning could not have been the proximate cause of the plaintiff's injury. *Carter v. Danek Med., Inc.*, No. CIV. 96-3243-G, 1999 WL 33537317, at *10 (W.D. Tenn. June 3, 1999). Post-Trial Mot. at 26-27, ¶ 55.

5. Here, uncontroverted testimony showed that A.Y.'s initial prescriber of Risperdal Dr. Deniz Eker, the only physician who prescribed Risperdal to A.Y. prior to the time Plaintiffs alleged he developed gynecomastia, was fully aware of the potential association between Risperdal and gynecomastia when she prescribed to A.Y. Post-Trial Mot. at 25-26,

¶ 53. Dr. Eker also testified that: she was aware that Risperdal elevates prolactin levels and that gynecomastia was a potential side effect of Risperdal since she first learned of the medication around the year 2000; that she was aware of the potential side effect the entire time she prescribed Risperdal; that she believed that the risks of causing hyperprolactinemia and gynecomastia were higher for Risperdal than they were for other medications; and that beginning at least as early as 2003, she regularly asked her patients who were taking Risperdal whether they experienced any breast discharge. Post-Trial Mot. at 25-26, ¶ 53. In fact, Dr. Eker testified that she suspected gynecomastia in A.Y. in 2004. Dep. of Dr. Deniz Eker at 126:22-128:11 (Feb. 8, 2015). Despite these suspicions, Dr. Eker restarted A.Y. on Risperdal in 2005 after discussing A.Y.'s potential gynecomastia with A.Y.'s mother. *Id.* at 177:11-21. Billie Ann Yount, A.Y.'s mother, acknowledged that Dr. Eker told her that breast enlargement was a possible side effect of Risperdal and, after being told of the risks and even after filing her lawsuit, she still requested that A.Y. stay on Risperdal. Post-Trial Mot. at 25-28, ¶¶ 53, 56. Dr. Hughes, A.Y.'s next prescriber, also testified that he was aware of the risks of gynecomastia when she [sic] prescribed Risperdal to A.Y. Post-Trial Mot. at 25-26, ¶ 53. Moreover, neither Dr. Eker nor Dr. Hughes could recall ever having read or relied

on the Risperdal label in connection with their prescriptions to A.Y. Post-Trial Mot. at 26-27, ¶ 55. Where, as here, the prescribing physicians testified that they understood the risks of a medication at the time they prescribed it to their patient, they conveyed that risk to the patient (here the patient's mother), and there is no evidence that either prescribing physician even read the product label, any alleged deficiency in the label could not be the proximate cause of A.Y.'s injury. Judgment as a matter of law therefore should have been granted.

6. In the alternative, the Court should have granted a new trial because the Court's charge to the jury and verdict form did not accurately reflect Tennessee law with respect to both medical and proximate causation. Post-Trial Mot. at 29-31, ¶¶ 58-65. The Court's verdict form failed to distinguish between medical causation and proximate causation—asking only "[w]as Janssen's negligence a substantial factor in bringing about [A.Y.]'s gynecomastia?" Post-Trial Mot. at 30, ¶ 63. The verdict form made it impossible to verify that the jury found both (a) that Risperdal caused A.Y. to develop gynecomastia, and (b) that had a different (and according to Plaintiffs adequate) warning been provided to A.Y.'s prescribing physicians they would not have prescribed Risperdal to him. Both were essential elements of A.Y.'s claim. *See, e.g.*, *Nye v. Bayer Cropscience, Inc.*, 347 S.W.3d 686, 704

(Tenn. 2011) ("Causation, an essential element of any products liability action, refers to both 'proximate cause' and 'cause in fact.'"). It is not clear from the verdict form that the jury made both necessary determinations and, as a result, the Court should have ordered a new trial.

The Court Should Have Granted Judgment As A Matter of Law Because There Was Inadequate Evidence That Risperdal Was The Medical Cause of A.Y.'s Alleged Injuries

7. The Court erred in submitting Plaintiffs' negligent failure to warn claim to the jury because Plaintiff did not establish the requisite causal connection between the alleged injury and Risperdal. Post-Trial Mot. at 12-23, ¶¶ 32-49. Plaintiffs' expert, Mark P. Solomon, M.D., did not cite to any scientific literature in support of his general causation opinion, i.e., that Risperdal causes gynecomastia because it elevates prolactin and elevated prolactin causes gynecomastia. Post-Trial Mot. at 14-18, ¶¶ 32, 34-40. He also purported to diagnose A.Y.'s alleged gynecomastia on the basis of a photograph even though he acknowledged that this was not a generally accepted means of diagnosis and that "[i]n order to make any diagnosis, you have to do a physical exam." Post-Trial Mot. at 14-15, ¶ 33. This testimony should have been excluded pursuant to Pa. R. Evid. 702, 703, Pennsylvania's *Frye* standard, and

Tennessee substantive law. *See, e.g.*, *Betz v. Pneumo Abex, LLC*, 44 A.3d 27 (Pa. 2012); *Grady v. Frito-Lay, Inc.*, 839 A.2d 1038 (Pa. 2003); *Richardson v. GlaxoSmithKline*, 412 F. Supp. 2d 863, 868 (W.D. Tenn. 2006) ("[The cause] must be such that had it not happened the injury would not have been inflicted."); *Downs v. Perstorp Components, Inc.*, 126 F. Supp. 2d 1090, 1095 (E.D. Tenn. 1999).

8. Dr. Solomon's testimony that Risperdal was the cause in fact of A.Y.'s alleged gynecomastia also should have been excluded by the Court. Dr. Solomon failed to identify the basis on which he concluded that A.Y. had gynecomastia in 2003 that did not resolve through the time he examined A.Y. in 2015. He also failed to adequately exclude other potential causes of A.Y.'s alleged gynecomastia or consider the specific dose of Risperdal taken by A.Y. These failings rendered Dr. Solomon's specific causation testimony inadmissible under Pennsylvania law and it should have been excluded by the Court. Post-Trial Mot. at 19-21, ¶¶ 41-46.

9. Additionally, Dr. Solomon's expert report failed to disclose his opinion that A.Y. had gynecomastia at "Christmastime 2003." As this opinion was not disclosed in Dr. Solomon's report, it was error for the Court to permit the testimony, alleging an opinion disclosed for the first time at trial. Post-Trial Mot. at 22-23, ¶¶ 47-49; Pa. R.C.P. No.

4003.5; *Woodard v. Chatterjee*, 827 A.2d 433, 441 (Pa. Super. Ct. 2003).

The Court Should Have Ordered A New Trial Because The Court Improperly Excluded Evidence With Regard To A.Y.'s Complete Mental Health Picture And The Benefits of Risperdal

10. The Court erred in improperly excluding considerable evidence relevant to A.Y.'s complete mental health picture, the benefits of Risperdal, and the risk-benefit analysis that A.Y.'s physicians had to undertake when determining whether to prescribe Risperdal. It is undisputed that almost every prescription medication, including Risperdal, carries some risk of side effects. In determining whether a medication is appropriate for a particular patient, the physician must weigh the potential side effects against the needs of the patient and the potential benefit to him from the medication. The Court committed fundamental error tainting the entire trial by allowing Plaintiffs to present a one-sided description of this process, focused only on risks, while preventing Defendants from fully explaining why A.Y. needed Risperdal and the factors that his physicians needed to consider when making that decision. If A.Y.'s physicians understood the risks associated with Risperdal but decided that A.Y.'s need for the medication outweighed those risks, Janssen's product label could not have been

the proximate cause of A.Y.'s injuries, regardless of content. *See, e.g.*, *Harden*, 985 S.W.2d at 451. The Court's ruling deprived the jury of critical evidence necessary to resolve one of the core issues in the case—whether A.Y.'s prescribing physicians and his parents in fact would have refused Risperdal had they been given different risk information. A reasonable jury presented with the specific facts relating to the extreme behavior by A.Y. and the substantial difficulties his parents faced with A.Y.'s behavior might well have found that different warnings would not have changed their decision to give A.Y. Risperdal. But prohibited from presenting these facts and limited to generalities, Defendants were unable to explain the depth of A.Y.'s need for Risperdal to the jury and mount a fair defense. Post-Trial Mot. at 86-87, ¶¶ 189-94.

11. The Court compounded this error with two other errors that both individually also warrant a new trial. First, the Court improperly limited the testimony of Defendants' expert Nadine Schwartz, M.D. Dr. Schwartz is a child psychologist who regularly treats the conditions for which Risperdal is prescribed and who regularly prescribes it and other medications within its class. She therefore was highly qualified to opine on Risperdal generally, the patients for whom Risperdal is appropriate, the analysis a prescriber engages in when determining whether to prescribe Risperdal, including

consideration of the risks and benefits, the psychological impact on A.Y. of his gynecomastia diagnosis, and other medications that were available for a patient such as A.Y. Testimony as to each topic, supported by Dr. Schwartz's extensive experience in the field, was appropriate expert testimony pursuant to Pa. R. Evid. 702. The Court, without basis, limited Dr. Schwartz's testimony to discussing the general benefits of Risperdal while allowing Plaintiffs' expert Dr. Kessler (who is not a psychiatrist and does not treat conditions or prescribe these medications) free rein to testify on these issues. This limitation on Dr. Schwartz's testimony was erroneous and highly prejudicial to Defendants, especially given the inconsistent treatment of her testimony compared with Dr. Keller [sic]. This warrants a new trial. *McClain v. Walker*, 761 A.2d 155, 156 (Pa. Super. Ct. 2000). Post-Trial Mot. at 44-47, ¶¶ 93-100.

12. The Court also committed error requiring a new trial by improperly precluding Defendants from presenting the testimony of A.Y.'s treating physician Gordon Greeson, M.D. who also prescribed Risperdal to A.Y. Dr. Greeson's testimony was relevant to causation because it rebutted Plaintiffs' argument that A.Y.'s parents would not have allowed him to take Risperdal had they known of its "true" risk profile. Dr. Greeson's records also discuss A.Y. having enlarged breasts in February 2016—a record that was

referenced by Plaintiffs during their opening argument, closing argument, and during the testimony of Dr. Solomon. Despite this, the Court without justification prevented Defendants from introducing the testimony of Dr. Greeson reflecting his personal observations of A.Y. and his medical diagnoses derived therefrom. The jury had a right to know A.Y.'s current physician's impressions of his physical and mental state but were deprived of this testimony by the Court's improper ruling. Post-Trial Mot. at 48-51, ¶¶ 102-114.

The Court Should Have Ordered A New Trial Because The Court Improperly Admitted Certain Testimony By Plaintiffs' Expert Dr. David Kessler

13. The Court erred in admitting large portions of Dr. David Kessler's prior deposition testimony taken in another case for four reasons. First, there was no showing or even contention that Dr. Kessler was unavailable to testify live at trial as required by the Pennsylvania Rules of Evidence. Pa. R. Evid. 804(a)(5). Plaintiffs simply decided they did not want to pay the cost of having him testify live. Post-Trial Mot. at 38-42, ¶¶ 79-89.

14. Second, allowing Dr. Kessler to testify via presentation of a stale *de bene esse* deposition intended for use in two separate and earlier cases prejudiced Defendants' ability to meaningfully cross-examine him on issues germane to *this* case. Post-Trial Mot. at 42,

¶ 90. It also precluded Defendants from cross-examining Dr. Kessler on important and relevant developments since that deposition was taken, including, but not limited to, the publication of a peer-reviewed and published reanalysis of the data from the studies addressed in the 2003 Findling article, on which Dr. Kessler offered opinions, including matters relating to "Table 21," as well as the FDA's most recent analysis of the Risperdal label. Post-Trial Mot. at 42-43, ¶ 91. The prejudice was compounded by the Court's refusal to admit evidence of the FDA's rejection of a Citizen Petition submitted by Plaintiffs' counsel as well as the Court's refusal to allow Defendants to introduce other relevant testimony Dr. Kessler gave in other cases, on the basis of a non-existent rule that if Defendants failed to ask about a matter in the *de bene esse* deposition no testimony by Dr. Kessler on that matter could be admissible. Post-Trial Mot. at 43, 83-84 ¶¶ 92, 184.

15. Third, the Court erred in permitting Dr. Kessler to offer extensive testimony regarding "off-label" promotion. This testimony was improper for two separate reasons. First, expert witnesses are not permitted to testify as to what the law is or whether certain conduct was legal—that is the exclusive province of the Court. *Waters v. State Emples. Ret. Bd.*, 955 A.2d 466 (Pa. Commw. Ct. 2008). Post-Trial Mot. at 72-73 ¶165. Second, Dr. Kessler's opinions

regarding alleged off-label promotion were irrelevant and inadmissible in this case because whether Janssen engaged in off-label promotion was irrelevant to the existence or absence of liability on Plaintiffs' claims under Tennessee law. *See, e.g.*, *Giggers v. Memphis Hous. Auth.*, 277 S.W.3d 359, 364 (Tenn. 2009). Nor is there any evidence of off-label promotion to any of A.Y.'s prescribers. Post-Trial Mot. at 73-74 ¶¶ 166-169. This lack of any nexus to the facts or law of this case renders this testimony wholly irrelevant.

16. Fourth and finally, the Court admitted extensive testimony from Dr. Kessler regarding his personal interpretation of internal Janssen documents, impermissible testimony regarding Janssen's corporate knowledge and "intent," the FDA's alleged intent, alleged violations of law by Janssen including but limited to alleged "fraud-on-the-FDA," Dr. Kessler's own personal beliefs as to what is important to doctors, patients, and parents, and an outdated and improper analysis of "Table 21." Dr. Kessler's testimony should have been excluded as to each of these topics pursuant to Pa. R. Evid. 403, 702, 703 and related decisional law. Post-Trial Mot. at 65-72, 76-84 ¶¶ 150-163, 173-184.

The Court Should Have Ordered A New Trial Because The Court Erroneously Excluded The FDA's Decision On The

Citizen Petition Submitted by Plaintiffs' Counsel

17. A new trial is warranted based upon the Court's improper exclusion of the FDA's November 25, 2014 decision on the Citizen Petition submitted by Plaintiff's counsel. The denial letter sent by the FDA provided valuable information concerning the FDA's opinion on the adequacy of the Risperdal label's warnings and the benefits of Risperdal in pediatric populations. The denial letter is powerful evidence that the FDA itself disagrees with the conclusions of Plaintiffs' expert witnesses, including Dr. Kessler, whose credibility Plaintiff attempted to bolster by citing his prior experience at the FDA. Defendants were prejudiced by the Court's refusal to admit this relevant evidence. That the denial of the petition was at the time of trial the subject of an appeal to the United States Court of Appeal for the Third Circuit from dismissal of the challenge by Plaintiffs' counsel to the denial by the United States District Court for the Eastern District of Pennsylvania, is immaterial to its relevance or its admissibility. The letter was fully effective pending judicial review unless a Court stayed its effect which did not occur here. See 5 U.S.C. § 705. Post-Trial Mot. at 84-85, ¶¶ 185-89.

The Court Should Have Ordered A New Trial Because The Court Improperly Charged The Jury In Several Respects

18. The Court also made several errors in its jury charge that necessitate a new trial. First, the Court failed to instruct the jury as to the learned intermediary doctrine. A pharmaceutical manufacturer "may discharge their duty [to exercise reasonable care] by distributing the drugs with proper directions and adequate warnings to those who foreseeably could be injured by the use of their products." *Pittman*, 890 S.W.2d at 428. Under the learned intermediary doctrine, the duty to warn runs to the prescribing physician, not the end user of the medication. Not only did the Court fail to instruct the jury that it was required to determine whether Janssen provided A.Y.'s ***physicians*** with an adequate warning, the court charged that "[w]arnings should be given to those persons whom the supplier should reasonably expect to use or handle the product or be endangered by its use or handling if the supplier reasonably should believe those persons would not realize the danger without the warnings." This instruction suggested to the jury that Janssen needed to supply A.Y. (or his parents) with a warning adequate to put them on notice of a potential risk, which is contrary to controlling Tennessee law. Post-Trial Mot. at 51-54, ¶¶ 115-21.

19. The Court also fundamentally misapplied Tenn. Code Ann. §§ 29-39-102(a)(2), (h)(2), and improperly instructed the jury that it should determine whether Janssen intentionally falsified, destroyed, or

concealed evidence. Neither party disputed at trial that Tenn. Code Ann. §§ 29-39-102(a)(2), (h)(2) applied to this case. That statute limits the amount of non-economic damages that can be awarded to any plaintiff to $750,000 unless "the defendant intentionally falsified, destroyed or concealed records containing material evidence with the purpose of wrongfully evading liability in the case at issue." *Id.* The Court should not have instructed the jury on this issue at all because there is no evidence whatsoever that Janssen falsified, destroyed, or concealed any evidence to avoid liability in ***this*** case, let alone that it did so intentionally. The statute's exception, in effect, is a safeguard against spoliation of evidence. *See, e.g.*, Tenn. Code Ann. §§ 29-39-102(a)(2), (h)(2) ("this subsection (h) does not apply to the good faith withholding of records pursuant to privileges and other laws applicable to discovery . . ."); Tenn. Prac. Series, Tenn. Pattern J.I. —Civ § 14.57A (2015). These provisions make clear that the exception to the statute is concerned with discovery abuses, not the merits of the underlying conduct. In order to invoke the exception, Plaintiffs argued that Defendants withheld two pieces of evidence—Table 21 and the "Bilker issue"—but there is no evidence that either document was falsified, withheld or destroyed to evade liability. To the contrary, the documents were produced to Plaintiffs during discovery and in fact were admitted into evidence in this case. Moreover,

the Court exacerbated the error by failing to include the phrase "for the purpose of wrongfully evading liability in this case" which does not accurately describe the jury findings necessary to invoke the exception to the cap. As a result, the damages cap should have applied and the jury should not have been instructed on the exception which did not apply as a matter of law. Post-Trial Mot. at 54-56, ¶¶ 122-29.

20. The Court erred in failing to instruct the jury on Tennessee's statutory presumption of adequacy in its charge and that failure necessitates a new trial. Tennessee law provides that "[c]ompliance by a manufacturer or seller with any federal or state statute or administrative regulation existing at the time a product was manufactured and prescribing standards for … labeling, warning or instructions for use of the product, shall raise a rebuttable presumption that the product is not in an unreasonably dangerous condition in regard to matters covered by these standards." Tenn. Code Ann. § 29-28-104(a). Where there is evidence, as here, that a defendant complied with federal regulations, a jury must be instructed on the statutory presumption. *See, e.g.*, *Clarksville-Montgomery Cnty. School Sys. v. United States Gypsum Co.*, 925 F.2d 993, 1004-05 (6th Cir. 1991). The Court's failure to do so in this case requires a new trial. Post-Trial Mot. at 56-58, ¶¶ 130-34.

21. The Court also erred in failing to instruct the jury that Defendants could not be liable for failing to provide information to the FDA, that Defendants could not be found liable for truthful off-label promotion, or that punitive damages were not at issue, despite Plaintiffs' counsel's repeated and improper invitations to "punish" defendants. In light of the minimal evidence regarding damages in this case, *see infra* ¶ 22, and the $70,000,000 verdict, the jury's award cannot rationally be understood as anything other than a punitive award given the gross disproportion between the evidence of harm and the amount of the verdict. These errors too require a new trial. Post-Trial Mot. at 58-65, ¶¶ 135-49.

The Court Should Have Ordered A New Trial Or In The Alternative Remittitur Because The Amount Of Damages Awarded By The Jury Was Unsupported By The Evidence At Trial

22. The Court erred in not ordering a new trial given the excessive nature of the jury's verdict. Tennessee Courts have held that "[t]he amount of a verdict alone can be so large that it reflects passion, prejudice, or caprice." *Duran v. Hyundai Motor Am., Inc.*, 271 S.W.3d 178, 212 (Tenn. Ct. App. 2008). "When asked to determine whether a verdict should be set aside based on the amount of the damage award alone, the courts must consider the nature and extent of the plaintiff's injuries, the pain and suffering the

plaintiff experienced, the expenses the plaintiff incurred as a result of the injuries, the plaintiff's loss of earning capacity as a result of the injuries, the impact the injuries have had on the plaintiffs enjoyment of life, and the plaintiff's age and life expectancy." *Id.* Additionally, where a remittitur would effectively "destroy[] the jury's verdict" a new trial is required. *See, e.g.*, *Guess v. Maury*, 726 S.W.2d 906, 907, 913 (Tenn. Ct. App. 1986) (overruled in part on other grounds). Here, the jury's verdict of $70,000,000 was so blatantly excessive that a new trial was required. The only evidence at trial in support of A.Y.'s claim for damages was the testimony of A.Y.'s father, Terry Yount, who testified that A.Y. was teased at school and at Mr. Yount's workplace. He also testified that A.Y. is "doing okay, considering what he's been through. He's doing all right." Plaintiffs also presented the deposition testimony of A.Y. and Ms. Yount which was consistent with Mr. Yount's testimony. Plaintiffs introduced no testimony of any out-of-pocket expenses, medical expenses, lost wages, or lost-earning potential. This evidence alone was inadequate to support a $70,000,000 compensatory damages verdict. To the contrary, numerous Tennessee cases have remitted much smaller awards or ordered a new trial where the plaintiff introduced far more extensive evidence of pain and suffering. *See, e.g.*, *Guess*, 726 S.W.2d 906. Plaintiffs conceded they have not incurred

any expenses as a result of A.Y.'s injuries, and did not introduce any evidence to show any loss of earning capacity or ongoing injury. Given the discrepancy between the evidence as to damages and the jury's monetary award, a remittitur cannot cure the error and a new trial is required. Post-Trial Mot. at 89-95, ¶¶ 198-214.

23. In the alternative, the jury's award must be significantly remitted in order to be in line with Tennessee case law with respect to damages. Post-Trial Mot. at 89-95, ¶¶ 198-214.

The Court Should Have Granted Judgment Notwithstanding The Verdict As To Johnson & Johnson And Janssen Research & Dev., LLC Because Plaintiffs Introduced No Evidence Of Wrongdoing As To Those Defendants

24. The Court should have granted judgment notwithstanding the verdict as to both Johnson & Johnson and Janssen Research & Dev., LLC because Plaintiffs introduced no evidence of any wrongdoing as to either Defendant—neither of whom manufactured Risperdal. Tenn. Code Ann. § 29-28-105(a). The verdict form only asked the jury to render a verdict as to Janssen and no evidence was introduced at trial that Janssen is simply an alter-ego of either company. As a result, both Johnson & Johnson and Janssen Research & Dev., LLC should have been granted

judgment notwithstanding the verdict. Post-Trial Mot. at 96-98, ¶¶ 218-29.

Plaintiffs raised the following issue in their 1925(b) Statement of Matters Complained of on Appeal:

1. On May 2, 2014, the trial court granted Defendants' global motion for partial summary judgment as to the Plaintiffs' claims for punitive damages asserted in *In re: Risperdal® Litigation*, March Term 2010, No. 296, reasoning that New Jersey law applied globally to the issues of punitive damages in this litigation and that Defendants could not incur punitive liability in any of the Risperdal cases filed in Philadelphia County as a matter of New Jersey law. The May 2, 2014 Order had global application to all Risperdal cases pending in the First Judicial District. Did the trial court err by granting that motion, where ample evidence supported a claim of punitive damages against Defendants and warranted the submission of that issue to the jury under either Tennessee or New Jersey law?

DISCUSSION

DEFENDANTS' STATEMENT OF MATTERS COMPLAINED OF ON APPEAL:

This Court has consolidated the twenty-four points enumerated in Defendants' Statement of Matters Complained of on Appeal into the following thirteen issues: (1) whether this Court should have granted judgment as a matter of law because Plaintiffs failed to establish that the Risperdal warning was inadequate or that Defendants could have lawfully

changed the label; (2) whether this Court erred in submitting the case to the jury because all of Plaintiffs' failure to warn claims were preempted by federal law; (3) whether Plaintiffs' claims were barred by the learned intermediary doctrine; (4) whether this Court's verdict form was proper; (5) whether the evidence was sufficient to establish medical causation; (6) whether this Court erred in excluding evidence of specific instances of aggressive conduct; (7) whether this Court erred in limiting the testimony of Nadine Schwartz, M.D.; (8) whether this Court improperly precluded the testimony of Gordon Greeson, M.D.; (9) whether this Court erred in admitting Dr. Kessler's *de bene esse* deposition; (10) whether this Court erred in excluding the FDA's decision on the Citizen Petition; (11) whether this Court's jury instructions were proper; (12) whether the verdict was excessive; and (13) whether this Court should have entered judgment notwithstanding the verdict as to Johnson & Johnson and Janssen Research & Development, LLC. This Court finds no merit in any of the assignments of error.

I. THIS COURT PROPERLY REFUSED TO GRANT JUDGMENT AS A MATTER OF LAW BECAUSE DEFENDANTS FAILED TO PROVIDE AN ADEQUATE LABEL AND DEFENDANTS, NOT THE FDA, WERE RESPONSIBLE FOR PROVIDING SUCH A LABEL

On appeal, Defendants claim, in part, that this Court erred in submitting the case to the jury because the Risperdal label was adequate as a matter of Tennessee law. Defendants' claim should be

dismissed. As discussed in detail below, Defendants were aware of the extent of the statistical link between Risperdal and gynecomastia and they failed to provide this information either on their label or to the FDA. As such, Defendants' claim for judgment as a matter of law as it pertains to the adequacy of their label fails.

Defendants additionally claim that they were entitled to judgment notwithstanding the verdict based on what they perceived as a concession from Plaintiffs' expert, Dr. David Kessler, to an allegedly "incorrect interpretation of FDA regulations." Contrary to Defendants' claim, there was no such concession on the record. Moreover, even if such a concession was made, the standard for judgment notwithstanding the verdict would not have been met.

Judgment notwithstanding the verdict will only be granted "in a clear case where the facts are such that no two reasonable minds could fail to agree." *DiFrancesco v. Excam, Inc.*, 642 A.2d 529, 531 (Pa. Super. Ct. 1994).

> In reviewing a denial of judgment notwithstanding the verdict, an appellate court must decide whether there was sufficient evidence to sustain the verdict; our [the Superior Court of Pennsylvania's] scope of review is very narrow: all evidence and all reasonable inferences drawn therefrom must be considered in the light most favorable to the verdict winner.

Mitchell v. Moore, 729 A.2d 1200, 1203 (Pa. Super. Ct. 1999). Here, in viewing the evidence in the light most favorable to the Plaintiffs, it is clear that there was sufficient evidence to sustain the verdict.

A. Defendants failed to provide an adequate Risperdal label

It is essential to the safety of prescription drug users across the country that manufacturers be held to the standard of providing adequate labels for their drugs. The Court in *Strayhorn v. Wyeth Pharms. Inc.*, explained the following:

> Tennessee law effectively requires a manufacturer to alter its label if it wishes to avoid tort liability. Indeed, prescription drug manufacturers must market and distribute their products while minimizing the risk of danger; **adequate warnings and proper instructions reduce this risk.** Thus, if a manufacturer distributes a drug without adequate warnings, it exposes itself to liability … To avoid that liability, the manufacturer would have to alter its label to strengthen its warning …

Strayhorn v. Wyeth Pharms. Inc., 887 F. Supp. 2d 799, 818 (W.D. Tenn. 2012) *aff'd* 737 F.3d 378 (6th Cir. 2013) (emphasis added). The *Strayhorn* Court went on to say that:

> … [T]he Tennessee Supreme Court has noted that manufacturers of prescription drugs "have a duty to market and distribute their products in a way that minimizes the risk of danger. They may discharge their duty by distributing the drugs with proper directions and **adequate warnings to those who foreseeably could be injured** by the use of their products. Warnings are reasonable when they both convey a fair indication of the

> dangers involved in taking a prescription drug and warn with the **degree of intensity** required by the nature of the risk.

Id. at 814 (emphasis added) (citation omitted). Here, the Risperdal label was inadequate because Defendants were well aware of off-label pediatric use of Risperdal at the time it was prescribed to A.Y., and as discussed at length in the Learned Intermediary section of this Opinion, Defendants failed to provide a label that demonstrated the degree of intensity, or likelihood and seriousness, of the risks associated with Risperdal use, despite their knowledge to the contrary.[3]

1. Pediatric use of Risperdal was foreseeable

The evidence presented at trial established that the Defendants foresaw pediatric use of Risperdal. The following deposition testimony was elicited from Plaintiffs' expert, Dr. David Kessler, who served as the commissioner of the FDA for seven years:

> **Q.** And in documents that you have reviewed, was Janssen interested in not only

[3] Although both pediatric and adult patients with psychosis, later changed to schizophrenia, could be considered "foreseeable" Risperdal users, this opinion focuses on pediatric users specifically. Kessler Dep. 5/19/15 at 37. In 2006, Risperdal was specifically approved for irritability associated with autism in adolescents and children; subsequently it was approved for use in bipolar pediatric patients. *Id.* at 35. Patients with these conditions who Defendants were aware would likely be prescribed Risperdal from their physicians, were foreseeable Risperdal users.

> maintaining but developing the market of what was an off-label usage of the drug?
>
> **A.** So certainly by documents that I've seen around 2000, 2001, those statements about growing and maintaining the market was in Janssen's agenda.

Kessler Dep. 5/19/15 at 86. The discussion later continued:

> **Q.** Was there an obligation to get this information [meaning known higher rates between Risperdal and gynecomastia] which was known to Janssen in 2000/2001, and certainly in 2001 by July, to the physicians who are prescribing this drug widely off-label [meaning to children]?
>
> **A.** In my opinion, yes, there was such an obligation, because Janssen, if you look carefully at this time period, was marketing this drug for its use in children. And if you're going to market a drug for use in children, then you have an obligation to tell the good as well as the bad. So you want to make sure—I mean, if you're marketing a drug, you've got to tell the good and the bad.
>
> **Q.** Okay. Is there evidence which you have seen that Janssen was marketing the drug for children and adolescents back in 2000/2001?
>
> **A.** Yes.

Id. at 125-126. As the transcript demonstrates, Defendants clearly foresaw pediatric use of Risperdal because Defendants specifically targeted the pediatric population through their marketing efforts.

2. Defendants failed to disclose the true statistical relationship between Risperdal and gynecomastia

Defendants failed to report the statistically significant association between Risperdal and gynecomastia, both within itself as a drug, and in comparison to other drugs, despite having evidence of a causal link in their internal studies. The 2002 Risperdal label in effect at the time that A.Y. was first prescribed the drug stated that "gynecomastia is rare" indicating under industry standards the chance of occurrence was "fewer [than] one out of a 1000." Eker Dep. 2/8/16 at 43. The 2002 label also stated that "as with other drugs that antagonize Dopamine D2 receptors," Risperidone "elevates prolactin levels." *Id.* at 4-6. This label was not changed until 2006 whereupon it stated that gynecomastia occurred in 2.3% of users and that Risperdal caused a higher occurrence of hyperprolactinemia than other antipsychotics. *Id.* at 56-58. Still, the label was inaccurate and misleading according to Defendants' own internal studies.

In mid-May 2002, Janssen conducted a pooled analysis of five studies which looked at prolactin levels in children and adolescents. The data was summarized in a chart referred to as Table 21. At the time of this analysis, Defendants already knew that the pure incident rate of gynecomastia was 4 to 5%. Kessler Dep. 5/19/15 at 176. This is because Janssen had previously conducted a special attention study in November 2000 (RIS-INT-41), which showed such a

correlation.[4] During Dr. Kessler's deposition, he testified about Janssen's internal studies, the information contained therein, and the knowledge that Defendants had regarding the true rate of gynecomastia. The following exchange occurred:

> **Q.** Now my question is, was it known to Janssen Pharmaceuticals well before 2006 that the rate of gynecomastia in children and adolescents in their studies exceeded 2.3 percent?
>
> **A.** Yes. You certainly have earlier studies that were completed years before that show a higher incidence. That is the average of—across studies by 2006.
>
> **Q.** Yes. But my focus is on timing, not on—not on average. We'll talk about average.
>
> **A.** Okay.
>
> **Q.** As to timing, did Janssen Pharmaceuticals know by 2000, by November of 2000, that the rate of gynecomastia actually exceeded 2.3 percent [despite their label at the time still saying "rare" and indicating less than .001% incidence]?
>
> **A.** Yes. In certain studies, that was exactly correct.

Id. at 64.

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[4] The final results of this study established that 5.5% of boys taking Risperdal developed gynecomastia. It should also be noted that Defendants subsequently conducted an extension study (RIS-INT-70) which showed that the incidence rate of gynecomastia was 12.5%.

Not only did Defendants know that Risperdal elevated prolactin in children and adolescents and caused gynecomastia at a rate higher than 2.3%, Defendants also knew that Risperdal was associated with an increased risk of hyperprolactinemia compared to other antipsychotics long before the label was changed. This was evidenced by a September 2006 email from Dr. Gahan Pandina, a scientist who was involved in Janssen drug development and Risperdal development; it stated the following: "[w]e have known for years that RIS [Risperdal] elevates prolactin more so than other second-generation antipsychotics. First-generation antipsychotics also elevate prolactin either comparably or less than RIS, a fact that has been known for years." Kessler Dep. 5/19/15 at 72-73. As this email makes clear, Defendants knowingly concealed that Risperdal was connected to higher rates of hyperprolactinemia than other antipsychotics for "years."[5]

Based on the foregoing, Defendants' claim that the Risperdal label was adequate must fail. Defendants foresaw pediatric use of Risperdal given that they specifically targeted the pediatric population, and Defendants deliberately misrepresented and understated both the incidence

[5] A second email was shown to the Court demonstrating that the same knowledge of the increased relationship between hyperprolactinemia and Risperdal as compared to other anti-psychotics was known in 2003 and likely before. *See* Kessler Dep. 5/19/15 at 71-72 ("[In an email from Janssen employee, Olga Mitelman on January 28, 2003,] [w]hen compared to competitors … only RIS [Risperdal] causes prolactin elevation at the recommended low doses. Other atypicals would show the same elevations, but only at doses seldom seen.").

rate of gynecomastia and the increased risks associated with Risperdal as compared to other antipsychotics.

B. Defendants had the responsibility to warn users of potential Risperdal risks and due to their failure to disclose important statistical information to the FDA, the FDA's refusal to accept initial label change requests is irrelevant

It is the responsibility of the drug manufacturer to ensure that it provides an adequate label to foreseeable consumers. *See Wyeth v. Levine*, 555 U.S. 555, 567-68 (2009) ("Congress adopted a rule of construction to make it clear that manufacturers remain responsible for updating their labels"). The United States Supreme Court clearly states that "the very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to the CBE [Changes Being Effected] regulation is difficult to accept—neither [the manufacturer Defendant] nor the United States has identified a case in which the FDA has done so." *Id.* at 570. This Court is equally unconvinced by Defendants' claim that they were prohibited by the FDA from providing an adequate drug label.

FDA regulation provides that "if a manufacturer is changing a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction' or to 'add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product,' it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA

approval." *Id.* at 568. Per the regulations, a drug manufacturer need merely to submit the "revised warning for review and approval" at a later time. *Id.* at 562. The FDA mandates that "analysis of any other data or information relevant to the safety and effectiveness of the drug" must be provided to the agency along with requests for changes in a drug label. Kessler Dep. 5/19/15 at 263.

Here, Defendants are correct that the FDA rejected their attempts to add pediatric information to the Risperdal label for years. When Defendants first applied for a change in the Risperdal label in 1997, the FDA rejected their changes because they had "not identified any pediatric indication for—for which [they] believe[d] Risperdal could be approved." *Id.* at 82-84. In 2000, the FDA rejected Defendants' proposed label changes again; this time the rejection was due to the fact that the FDA did not find Defendants' proposed pediatric usage for "conduct disorder" to be valid as either a diagnosis or disorder. *Id.* at 88-90. In 2005, Defendants filed for label changes specific to irritability associated with autism, instead of conduct disorder, but were denied yet again for failing to present adequate information. Kessler Dep. 5/20/15 at 337-341.

Defendants neglected to submit testing information pertaining to the statistically significant association between Risperdal and gynecomastia with any of their applications to the FDA. The following testimony was elicited from Dr. Kessler:

> **Q.** From what you know and what you've reviewed in this litigation, did Janssen have, among the information in their files, Table 21

> and the statistically significant association [between Risperdal and gynecomastia]?
>
> **A.** Yes.
>
> **Q.** Okay. And from what you see and what you know, was that submitted to the FDA as part of the process?
>
> **A.** I do not see it being submitted.
>
> **Q.** And, in fact, do you see eventually the opposite being represented?
>
> **A.** Yes, I do.

Id. at 339. In attempting to garner FDA approval for a drug label, Dr. Kessler made clear that as a drug manufacturer, "…you'd want to make sure that physicians and the FDA had the full set of data." Kessler Dep. 5/19/15 at 316. Defendants failed provide a full set of data. While the statistical association between Risperdal and prolactin-related adverse events was presented in the drafts of labels for FDA approval, the same information did not appear in the final version presented to the FDA. *See* Kessler Dep. 5/19/15 at 263-264 ("The incidence appears, but the statistical association is taken out between Version 4 and the final publication.").

As Dr. Kessler explained, due to the complete lack of knowledge of the statistically significant relationship between Risperdal and gynecomastia, the FDA "advisory committee . . . . recommended against monitoring [prolactin] [and therefore changing the Risperdal label to adjust for pediatric use], because there was no association [so far as they were aware]. But, in fact, we know that [there was such an association and it was known to Defendants]. And,

therefore, we don't know what the—those advisors would have recommended had they been told about the association." *Id.* at 268-269. As the *Wyeth* Court stated, in the absence of "clear evidence that the FDA would have approved a change to [the drug's] label, [the Supreme Court] will not conclude that it was impossible for [the manufacturer] to comply with both federal and state requirements." *Wyeth*, 555 U.S. at 571. There is no clear evidence here as to whether the FDA would, or would not have, approved a change to Risperdal's label had they known of the true statistical relationship between Risperdal and gynecomastia. This Court therefore cannot conclude that it would have been impossible for Defendants to comply with both federal and state requirements.

In sum, the FDA repeatedly rejected Defendants' attempts to change the label, not because they were refusing to provide safety information to Risperdal users, but because Defendants repeatedly submitted vague drug information with little research or support. Defendants can hardly blame the FDA's approval process for their failure, and choice, to withhold crucial safety information from the FDA, and consequentially, foreseeable users.

Defendants' claim that they could not have lawfully changed the Risperdal label due to FDA regulations fails based on legal precedent stating they could have provided warning prior to approval if they had so chosen. It also fails due to factual evidence that they failed to provide, and in fact actively attempted to conceal, adequate drug safety information to, and from, the FDA.

For the foregoing reasons, Defendant's claim should be dismissed. Defendants did not meet the burden of proof required for either judgment as a matter of law or judgment notwithstanding the verdict.

II. PLAINTIFFS' CLAIMS WERE NOT PREEMPTED BY FEDERAL LAW

On appeal, Defendants contend that this Court erred in submitting the case to the jury because all of Plaintiffs' failure to warn claims were preempted by federal law. According to Defendants, a conflict between Tennessee law and federal regulation made it impossible for Defendants to adequately warn of Risperdal's gynecomastia risk. As discussed above, Defendants' arguments are without merit.

According to the U.S. Supreme Court, "[a] proper pre-emption analysis is dependent upon a comparison of the federal statute or regulation and the particular state law applicable." *Hassett v. Dafoe*, 74 A.3d 202, 214 (Pa. Super. Ct. 2013) (citing *Foster v. Love*, 522 U.S. 67, 71 (1997) ("holding preemption must turn on whether state law conflicts with the text of the relevant federal statute or regulation")). A state statute is preempted only "where compliance with both federal and state regulations is a physical impossibility or where the state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *CTS Corp. v. Dynamics Corp. of America*, 481 U.S. 69, 79 (1987) (internal citations and quotations omitted). Since "[s]tates are independent sovereigns in our federal system," there is a strong presumption against preemption. *See Medtronic, Inc. v. Lohr*, 518 U.S. 470,

485 (1996) ("Congress does not cavalierly pre-empt state-law causes of action"). Here, Plaintiffs' failure to warn claims were not preempted because it was possible for Defendants to comply with both their state law duty to adequately warn foreseeable users of Risperdal, and their federal labeling duties.

Defendants rely on *Wyeth v. Levine*, 555 U.S. 555 (2009) in support of their claim that Plaintiffs' failure-to-warn claims were preempted by federal law. Such reliance is misplaced. In *Wyeth*, the Supreme Court expressly rejected the argument that FDA drug labeling regulations preempt state-law failure to warn claims. The Court asserted the following:

> [I]t has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.

Id. at 570-71. The Court explained that "[a]lthough a manufacturer generally may change a drug label only after the FDA approves a supplemental application, the agency's 'changes being effected' (CBE) regulation permits certain preapproval labeling changes that add or strengthen a warning to improve drug safety." *Id.* at 573. The Court noted that the FDA retains the authority to reject labeling changes made pursuant to CBE regulation; however, in order to conclude that it was impossible for a drug manufacturer to comply with both state and federal requirements, there must be clear evidence that the FDA would not have approved a change to the drug's label. The Court

ultimately found that the drug manufacturer in *Wyeth* could have unilaterally strengthened its drug label without the FDA's prior approval pursuant to the CBE process and that there was no evidence that the FDA would have rejected such a label change.

Here, like the drug manufacturer in *Wyeth*, Defendants were responsible for the content of their Risperdal label at all times; they were responsible for providing all relevant safety research to the FDA, and to ensure that any safety concerns about Risperdal were made known to foreseeable users. Despite this responsibility, Defendants failed to adequately warn of the risks associated with Risperdal even though they knew there was a higher than reported statistical link between Risperdal and gynecomastia. As discussed above, Defendant *did* propose label changes to the FDA; however, they provided the FDA with inaccurate and incomplete information. Had Defendants presented accurate information to the FDA about the statistically significant relationship between Risperdal and gynecomastia, the label change may have been approved. Since there was no clear evidence as to whether the FDA would, or would not have, approved a change to Risperdal's label had they known of the true statistical relationship between Risperdal and gynecomastia, this Court could not conclude that it was impossible for Defendants to comply with both federal and state labeling requirements.

Based on the foregoing, Defendants' claim should be dismissed. Defendants failed to sustain their burden of demonstrating that it was impossible to comply with both federal and state law.

III. THE LEARNED INTERMEDIARY DOCTRINE FAILS AS A DEFENSE

On appeal, Defendants attempt, unsuccessfully, to raise the learned intermediary doctrine as a defense. The purpose of the learned intermediary doctrine is to ensure that makers of "unavoidably unsafe products" with a duty to give warnings may "reasonably rely on intermediaries [often, physicians] to transmit their warnings and instructions." *Pittman v. Upjohn Co.*, 890 S.W. 2d 425, 429 (Term. 1994). The Court in *Harden v. Danek Med., Inc.* held the following:

> In order to recover for failure to warn under the learned intermediary doctrine, a plaintiff must show: (1) that the defendant failed to warn the physician of a risk associated with the use of the product not otherwise known to the physician; and (2) that the failure to warn the physician was both a cause in fact and proximate cause of the plaintiff's injury.[6]

Harden v. Danek Med., Inc., 985 S.W. 2d 449, 451 (Tenn. Ct. App. 1998). "[I]t is generally held that the learned intermediary doctrine may shield a manufacturer from liability when the physician was independently aware of the risks involved" because "the failure to warn cannot be the proximate cause of the user's injury if the user had actual knowledge of

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[6] Cause in fact will be addressed in a separate part of this opinion. For the purposes of this discussion, the Court is proceeding with the understanding that it has already been proven that Defendants' failure to warn was a cause in fact of A.Y.'s gynecomastia.

the hazards in question" and the "consumer [in this case, physician] was already aware of the danger." *Id.*

Here, Defendants' attempted application of the learned intermediary doctrine through both Deniz Eker, M.D. and Michael Hughes, M.D. fails as (A) Defendants failed to produce adequate notice of the full risk associated with Risperdal and its connection to gynecomastia and (B) neither physician was independently aware of the full risk of Risperdal and its relationship to gynecomastia.

A. The learned intermediary doctrine fails because Defendants did not provide adequate notice of the risk of gynecomastia on the Risperdal label

"[P]hysicians can be learned intermediaries only when they have received adequate warnings." *Pittman*, 890 S.W. 2d at 429. "The adequacy of a drug manufacturer's warnings is normally a question of fact." *Id.* In *Pittman*, a case holding that a drug label was adequate and the manufacturer not at fault, adequate warnings were defined as follows:

> Warnings concerning prescription drugs generally are adequate when they contain a full and complete disclosure of the potential adverse reactions to the drug. A reasonable warning not only conveys a fair indication of the dangers involved, but also warns with the **degree of intensity** required by the nature of the risk.

Id. (emphasis added).

Here, unlike *Pittman*, the Risperdal label was inadequate as it failed to state the correct degree of

intensity of the risk of gynecomastia by (1) understating the relationship between Risperdal and gynecomastia and (2) falsely advertising that Risperdal's connection to hyperprolactinemia was comparable to other drugs.[7]

1. Defendants understated the relationship between Risperdal and gynecomastia

As discussed above, Dr. Eker first prescribed Risperdal to A.Y. in August of 2003. At that time, the Risperdal label stated that "gynecomastia is rare." Eker Dep. 2/8/16 at 42. Rare, as defined on the Risperdal label, meant "events … occurring … fewer [than] one out of 1000." *Id.* at 43.

At trial, Plaintiffs introduced evidence that Defendants were aware that the relationship between Risperdal and gynecomastia was higher than rare since 2001. It was revealed that instead of the likelihood of gynecomastia being 1/1000 (or .001%), a clinical trial of 1,885 children showed an incidence rate of 2.3%. *Id.* at 48. The Risperdal label was not altered to reflect this higher percentage until 2006. *Id.* at 56. *But see* Hughes Dep. 3/10/16 at 80-81 ("[T]here are internal [Defendants'] studies that say 12.5 percent [occurrence rate of gynecomastia] and there are internal studies that say 5—or 12 percent, other internal studies that say 5.5 percent … that label says 2.3 percent, and before that it doesn't mention the 2.3 percent").

[7] Hyperprolactinemia refers to elevated levels of prolactin. Prolactin is the hormone that causes gynecomastia.

During Dr. Eker's deposition, Plaintiffs' counsel questioned Dr. Eker about how she would address a "rare" side effect with her patients:

> **Q.** When you have a side effect like gynecomastia and you're being told that it occurs in fewer than one out of 1000 users or it's rare, is that the type of thing that you typically have to counsel patients about, or is that one of the lesser?
>
> **A.** It's a less likelihood.
>
> …
>
> … [I]f the risk is rare, I do not discuss usually with the patient because there might be a lot of rare side effects.

Eker Dep. 2/8/16 at 43-44. Dr. Eker's response dramatically changed when Plaintiffs' counsel asked her how a higher than rare risk of a side effect would affect her decision to prescribe a drug:

> **Q.** There are lots of different side effects—
>
> **A.** Huh-huh.
>
> **Q.** —different quality and different likelihood of developing them; correct?
>
> **A.** Yes.
>
> **Q.** And when you're doing a risk benefit analysis, is that [severity] one of the things you're trying to balance, how severe the side effect is with how likely the patient is to get it?
>
> **A.** That's right.
>
> …

> **Q.** Is that [gynecomastia] the type of thing as a Doctor that, if you thought was a frequent side effect you would want to be on the lookout for?
>
> …
>
> **A.** Yes, I would.

Id. at 40-42.

Dr. Hughes, who began treating A.Y. in 2005, had a similar response. During Dr. Hughes's deposition, Plaintiffs' counsel questioned him about how the higher than "rare" relationship between gynecomastia and Risperdal would have affected his risk-benefit analysis and advice to A.Y.'s mother. The following exchange occurred:

> **Q.** … I mean, wouldn't you have found 5.5—a 5.5 percent incidence rate significant enough to impact the type of risk benefit discussions you were having with the mother?
>
> …
>
> **A** [Hughes]: Sure. So I'm going back in time—
>
> **Q.** Right.
>
> **A.** —giving you my best gues[s]. My best guess is that I probably would have but it's speculation on my part, but I think I would have but—
>
> **Q.** Sure.
>
> **A.** —I can't—I can't go back in time and say for certain, but it's—it would be important to know, I mean, yeah.

Hughes Dep. 3/10/16 at 82-83.

As the above-referenced testimony demonstrates, the Risperdal label understated the "degree of intensity" of the relationship between Risperdal and gynecomastia. It failed to disclose to either Dr. Eker or to Dr. Hughes the true incidence rate of gynecomastia and was therefore inadequate. The inadequacy of the Risperdal label is one factor that causes Defendants' learned intermediary doctrine defense to fail.

2. Defendants falsely presented Risperdal's connection to hyperprolactinemia as being comparable to other drugs

In 2003, when Dr. Eker first prescribed Risperdal to A.Y., the label indicated that the risk of hyperprolactinemia in patients taking Risperdal was comparable to other drugs. *See* Eker Dep. 2/8/16 at 45 ("[A]s with other drugs that antagonize Dopamine D2 receptors with Risperidone elevates prolactin levels"). In 2006, the label was changed to state that "Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents." *Id.* at 58.

During her deposition, Dr. Eker made clear that had she known of the greater risk of hyperprolactinemia associated with Risperdal as compared to other drugs, she would never have prescribed it in 2003:

> **Q.** [A]nd you were just telling us a second ago if you had—if they had included this information about Risperidone is associated with higher levels of prolactin elevation than other psychotics—antipsychotic agents—excuse me—you wouldn't have prescribed it in '03?

A. That's right.

Id. at 59-60.

Dr. Hughes also addressed the increased relative risk of hyperprolactinemia with Risperdal use:

> **Q.** … And if one thing you're concerned about is prolactin levels when you're prescribing a medication, would it be important for you as a doctor to know whether Risperidone or Risperdal elevates those prolactin levels higher than its competitors?
>
> **A.** Certainly.
>
> …
>
> Just to be clear … if there was an elevation of prolactin and there was a correlation directly made clinically in relation to increased gynecomastia would that be important to know?
>
> **Q.** Yes, sir.
>
> **A.** Sure, any medication certainly.
>
> **Q.** And if you to page—I mean, you want to know the clinical significance—let me ask you this: Is the more information you have as a doctor, better? Does it help you treat your patients?
>
> **A.** Of course.
>
> **Q.** And if a drug company was aware of information that would be clinically significant, would you want them to tell you that so you can help treat your patients better?
>
> **A.** Of course.

Hughes Dep. 3/10/16 at 66-69.

By hiding the true nature of the risk of hyperprolactinemia with Risperdal behind an inaccurate depiction of Risperdal as similar to other drugs, the warnings were inadequate. Consequentially, the learned intermediary doctrine does not apply.

B. The learned intermediary doctrine fails because neither physician had knowledge of the risk of gynecomastia

As Tennessee courts have explained, a physician must be "fully aware of the risks" of a product to have independent knowledge sufficient to overcome an inadequate product label. *Harden*, 985 S.W. 2d at 452.

Here, in addition to the foregoing, the learned intermediary doctrine defense fails because 1) neither Dr. Eker nor Dr. Hughes had sufficient experience with gynecomastia and 2) the jury found that there was insufficient evidence that either physician relied upon independent knowledge instead of Defendants' provided material.

1. Neither physician had experience with gynecomastia

The first factor often addressed by the Court is the experience of physicians with a specific product. *See Carter v. Danek Med., Inc.*, 1999 WL 33537317 (W.D. Tenn. June 3, 1999) (finding that the physician could be held to have independent knowledge of risks associated with the surgical equipment because he had extensive experience with the equipment, having performed over 100 spine fusions with the device); *see also King v. Danek Med., Inc.*, 37 S.W.3d 429, 431-32,

453 (Tenn. Ct. App. 2000) (noting that both of the plaintiffs' implanting physicians in the case were "well experienced" with a device used in spinal fusion surgeries: one physician, who performed spinal surgery on the first plaintiff, was the chief of orthopedic surgery and chief of orthotics at the United States Air Force Academy Hospital; the other physician, who performed a disc removal surgery on the second plaintiff, was a board certified orthopedic surgeon and past president of the Western New York Orthopedic Society").

Here, neither Dr. Eker nor Dr. Hughes had experience or training pertaining to gynecomastia. During Dr. Eker's deposition, defense counsel asked Dr. Eker about her experience with diagnosing gynecomastia. The following exchange occurred:

> **Q.** Did you ever make a diagnosis of true gynecomastia—
>
> **A.** Then or in the past?
>
> **Q.** —of [A.Y.]?
>
> **A.** I had concerns. I never saw gynecomastia before and I thought he had it.
>
> …
>
> **Q.** Based on your review of the records, did you ever send [A.Y.] for a prolactin test?
>
> **A.** I did not.
>
> **Q.** Have you ever diagnosed anyone with gynecomastia?
>
> **A.** Not since then.
>
> **Q.** So, [A.Y.] would be the only person who you've had a suspicion of gynecomastia?

A. Yes.

Eker Dep. 2/8/16 at 126-128. Plaintiffs' counsel also questioned Dr. Eker about her experience:

> **Q.** And do you get any training as a psychiatrist on the difference between, for instance, gynecomastia caused by hormonal changes—you know, breast growth as opposed to fatty tissue?
>
> …
>
> In your career have you received training on that?
>
> **A.** Not specifically.
>
> **Q.** Okay.
>
> **A.** I can't differentiate that.

Id. at 68-69.

Similar questions were posed to Dr. Hughes. Dr. Hughes testified that he had "concerns with gynecomastia before" but decided not to diagnose gynecomastia. Hughes Dep. 3/10/16 at 122-124. As Dr. Hughes explained, he took a "baseline [prolactin test] so [he] could monitor it going forward." *Id.* When asked about his specific experience with diagnosing or treating gynecomastia, Dr. Hughes stated the following:

> **Q.** … And is gynecomastia—have you ever treated patients with gynecomastia?
>
> **A.** It would have been so long ago.
>
> **Q.** Sure. It's not your focus?
>
> **A.** No.

Id. at 91.

Given their testimony, it would be implausible to suggest that Dr. Eker, having diagnosed exactly one case of gynecomastia, and Dr. Hughes, with no training or specialization in treating gynecomastia, had similar experience to the *Carter* physician who had performed 100 times with the device at issue. It would be equally implausible to suggest that the two *King* orthopedic surgeons, performing spinal and disc removal surgeries well within their specialty, were acting with the same experience as two psychiatrists observing the physical symptoms of gynecomastia in A.Y. It is evident that neither Dr. Eker nor Dr. Hughes had sufficient experience with gynecomastia to have independent knowledge sufficient for the learned intermediary doctrine to apply.

2. Neither physician ignored manufacturer warnings to rely upon their own independent knowledge

To supplement the determination of independent knowledge, Courts consider whether the physician relied upon information provided by the manufacturer in determining the product's risk. *See Harden*, 985 S.W. 2d at 452 (stating that the physician acknowledged that he was familiar with the FDA regulatory status of the product but that he did "not rely upon certain literature distributed or sponsored by the defendant in making his determinations"). If a physician did rely upon the literature of the defendant, he was not utilizing "independent knowledge." *See King*, 37 S.W.3d at 453 ("Both of the plaintiffs' implanting physicians … testified that they relied upon their own knowledge and judgment in deciding to implant the devices into the plaintiffs. The

plaintiffs [therefore had] not shown that these decisions [pertaining to utilizing the product] were influenced by any representation which the defendants made or failed to make. Thus, the plaintiffs' claims in this [attempted suit of the manufacturer] fail because they have failed to establish that, had additional warnings been given, the plaintiffs would not have sustained their injuries [as the physicians' risk analysis was in no way based upon information provided by the manufacturer]").

Here, when Dr. Eker was asked whether she recalled "consulting and relying upon any portion of the Risperdal label when deciding to prescribe" Risperdal thirteen years before, she admitted that she did not remember. Eker Dep. 2/8/16 at 111. Still, she was "not aware of the significance of gynecomastia at" the time she prescribed Risperdal to A.Y. *Id.* at 66. Dr. Eker was also asked where she found information pertaining to Risperdal in her patients in 2001 and 2002. The following exchange occurred:

> **Q.** What information, if any, did you review that led you to first prescribe Risperdal to your patients in 2001 or 2002?
>
> **A.** It was a discussion, of course, with my supervisors and the journals I have read, case reports, review articles.
>
> **Q.** And what did you consult in 2001 and 2002, to learn about the side effects associated with Risperdal?
>
> **A.** I would check the PDR [physician's desk reference].

Id. at 100. The fact that Dr. Eker checked the physician's desk reference, a guide commonly used by doctors in determining which medication to prescribe for a patient, intrinsically means that Dr. Eker most likely did look to the Risperdal label before prescribing it to patients.

Dr. Hughes testified that he was not "relying exclusively" on the package insert of Risperdal but on "multiple sources." Hughes Dep. 3/10/16 at 99. Nonetheless, when asked what his understanding of a package insert (or label) was, Dr. Hughes made clear that "it talks about things that are important about the medication" and it is "certainly" something that he understands that a pharmaceutical company uses to convey "important" information to prescribing physicians. *Id.* at 55-56.

Unlike the physician in *Harden*, neither Dr. Eker nor Dr. Hughes explicitly stated that they did not rely upon the literature provided by manufacturers. Moreover, unlike the physicians in *King*, neither physician here claimed to have had independent knowledge of gynecomastia and neither claimed to have relied upon their own knowledge.

Ultimately, the jury was not convinced that the inability to remember actions taken over a decade ago, or choosing not to exclusively rely upon labels for Risperdal's side effects, was the equivalent to either physician having independent knowledge of Risperdal's side effects or consciously ignoring Defendants' Risperdal label. As neither physician was found to ignore the Defendants' label or to possess independent knowledge of the risks associated with

Risperdal, the learned intermediary doctrine does not apply.

IV. THIS COURT'S VERDICT FORM WAS PROPER

On appeal, Defendants claim that this Court's verdict form made it impossible to verify that the jury found that Defendants were both the cause in fact and the legal cause of A.Y.'s injuries because it only asked whether Janssen's negligence was a substantial factor in bringing about A.Y.'s gynecomastia. Accordingly, Defendants contend that a new trial was warranted. For the reasons discussed below, Defendants' claim must fail.

It is axiomatic that the trial court's jury instructions guide the jury in its deliberations. The instructions must inform the jury of each applicable legal principle and must "be presented in a way that will be readily understandable to the jury." *Alexander v. Inman*, 903 S.W.2d 686, 704 (Tenn. Ct. App. 2014) (citing *Sasser v. Averitt Express, Inc.*, 839 S.W.2d 422, 430 (Tenn. Ct. App. 1992)). "[W]here the trial court's instructions clearly and definitely set forth the elements upon which liability must be based, the failure to recite each element in the verdict form will not render the verdict invalid." *Goodale v. Langenberg*, 243 S.W.3d 575, 584 (Tenn. Ct. App. 2007) (citing *State v. Faulkner*, 154 S.W.3d 48, 62 (Tenn. 2005)).

Here, this Court's instructions clearly and definitely set forth the elements upon which liability was to be based. Relying on the Tennessee Pattern Jury Instructions, this Court instructed the jury, in relevant part, as follows:

Plaintiffs allege that Janssen was negligent because there was a defect in Risperdal's warning label. A manufacturer who knows or reasonably should know that a product is likely to be dangerous for its intended use has a duty to use reasonable care to warn of the product's danger or to reveal its unsafe condition.

…

A negligence claim requires proof of two types of causation, cause in fact and legal cause. Cause in fact and legal cause are distinct elements of a negligence claim, and both must be proven by the plaintiff by a preponderance of the evidence.

The defendant's negligent conduct is a cause in fact of the plaintiff's injury if, as a factual matter, it directly contributes to the plaintiff's injury and, without it, plaintiff's injury would not have occurred. It is not necessary that a defendant's act be the sole cause of the plaintiff's injury, only that it can be—only that it be a cause.

Once you have determined that a defendant's negligence is the cause in fact of a plaintiff's injury, you must decide whether the defendant's negligence was also a legal cause of the plaintiff's injury . . . . To be a legal cause of an injury, there is no requirement that the cause be the only cause, the last act, or the nearest to the injury, so long as it is a substantial factor in producing the injury or the damage. The foreseeability requirement

> does not require the person guilty of negligence to foresee the exact manner in which the injury takes place or the exact person who would be injured. It is enough that the person guilty of negligence could foresee or, through the use of reasonable care, should have foreseen the general manner in which the injury or the damage occurred.

N.T. 6/30/16 a.m. at 167-170. *See also* T.P.I.-Civil 3.20, 3.21 and 3.22. As these instructions clearly indicate, after finding that the Defendants breached their duty to warn, the jury was required to determine whether Defendants' negligent conduct was a cause in fact of A.Y.'s injuries. If the jury made such a finding, it was then required to determine whether Defendants' negligence was also a legal cause of A.Y.'s injuries. As this Court explained, both cause in fact and legal cause are elements of negligence that Plaintiffs must prove. *See Kilpatrick v. Bryant*, 868 S.W.2d 594, 612 (Tenn. 1993) (Proximate cause or legal cause "concerns a determination of whether legal liability should be imposed where cause in fact has been established").

After all instructions were read to the jury, this Court presented the jury with the verdict form; the form included, inter alia, the following question, which the jury answered in the affirmative:[8]

---

[8] The first interrogatory on the verdict form asked the following: "Was Janssen negligent by failing to provide an adequate warning to [A.Y.]'s healthcare providers about the risk of gynecomastia from taking Risperdal?" The jury responded "Yes" and were directed to "proceed to Question 2."

> 2. Was Janssen's negligence a substantial factor in bringing about [A.Y.]'s gynecomastia?
>
> Yes____ No____
>
> *If you answered "Yes" to Question 2, please respond to Question 3. If you answered "No" to Question 2, Plaintiff cannot recover. Do not answer any further questions and return to the courtroom.*

Contrary to Defendants' claim on appeal, this interrogatory accurately reflected the law as described in the jury instructions and was sufficient to establish that the jury found Defendants to be the cause in fact and the legal cause of A.Y.'s injuries. To reiterate, the jury could not have found that Defendants' negligence was a substantial factor in bringing about A.Y.'s gynecomastia unless it first found that Defendants' negligence was the cause in fact of A.Y.'s injuries.

Upon consideration of the foregoing, Defendants' claim should be dismissed. This Court, in instructing the jury, clearly set forth the elements upon which liability was to be based. These instructions, combined with the jury's affirmative response to the above-referenced interrogatory, were sufficient to establish that the jury found that Defendants were both the cause in fact and the legal cause of A.Y.'s injuries.

V. THE EVIDENCE WAS SUFFICIENT TO ESTABLISH MEDICAL CAUSATION

On appeal, Defendants contend that this Court should have granted judgment as a matter of law because there was inadequate evidence that Risperdal was the medical cause of A.Y.'s injuries. Defendants'

claim is meritless. As discussed in detail below, the testimony of Dr. Solomon, Plaintiffs' medical causation expert, was sufficient to support the conclusion that A.Y. developed gynecomastia while on Risperdal. Since the law does not require a verdict in Defendants' favor, this claim should be dismissed.

A. Dr. Solomon's testimony was proper under Pennsylvania and Tennessee law

First, Defendants argue that Dr. Solomon's testimony should have been precluded at trial because he purported to diagnose A.Y.'s gynecomastia on the basis of a photograph and he did not cite to scientific literature in support of his general causation opinion. According to Defendants, Dr. Solomon's testimony should have been excluded pursuant to Pennsylvania Rules of Evidence 702 and 703, Pennsylvania's *Frye* standard, and Tennessee substantive law. Defendants' claim must fail.

According to Rule 702, "[a] witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if: (a) the expert's scientific, technical, or other specialized knowledge is beyond that possessed by the average layperson; (b) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; and (c) the expert's methodology is generally accepted in the relevant field." Pa.R.E. 702. Relatedly, Rule 703 provides that "[a]n expert may base an opinion on facts or data in the case that the expert has been made aware of or personally observed. If experts in the particular field would reasonably rely on those kinds

of facts or data in forming an opinion on the subject, they need not be admissible for the opinion to be admitted." Pa.R.E. 703.

Here, Dr. Solomon's testimony was admissible under Rules 702 and 703. Dr. Solomon is a board certified general and plastic surgeon with over thirty years of experience. N.T. 6/22/16 p.m. at 13, 17. Dr. Solomon is amply familiar with gynecomastia; he routinely makes diagnostic, treatment, and causation decisions in his private practice. *Id.* at. 17. By his own estimation, Dr. Solomon has treated hundreds of patients with gynecomastia. *Id.* Dr. Solomon clearly possesses knowledge beyond that of the average layperson and was qualified to give expert testimony about whether Risperdal caused A.Y.'s gynecomastia in this case.

In forming his opinion, Dr. Solomon relied on a variety of factors, including A.Y.'s medical records, his own examination of A.Y, and his personal experience. Dr. Solomon's opinion that A.Y.'s gynecomastia was caused by his use of Risperdal was well-reasoned, scientifically supported, and helpful to the trier of fact.

1. Contrary to Defendants' claim, Dr. Solomon did not diagnose A.Y.'s gynecomastia solely on the basis of a photograph

Defendants' claim that Dr. Solomon purported to diagnose A.Y.'s gynecomastia on the basis of a photograph is a mischaracterization of Dr. Solomon's testimony. At trial, Dr. Solomon was asked whether he *could* diagnose gynecomastia from a picture. Dr. Solomon answered in the affirmative. N.T. 6/22/16 p.m. at 49. Dr. Solomon did not, however, diagnose

A.Y.'s gynecomastia solely on the basis of a photograph as Defendants intimate. Rather, in forming his opinion regarding the cause of A.Y.'s gynecomastia, Dr. Solomon relied on a number of factors, which he discussed in his expert reports and at trial.

Dr. Solomon authored two reports in the instant action. In his first report, dated December 8, 2015, Dr. Solomon stated that it was his impression that A.Y. had bilateral gynecomastia due to his exposure to Risperdal. Dr. Solomon's finding was based on A.Y.'s medical history and a physical examination of A.Y on November 30, 2015. Dr. Solomon testified regarding this examination at trial:

> **DR. SOLOMON:** I met with Andrew and his mother [on November 30, 2015], and I took the history of his exposure to the Risperdal, of the development of his breasts, of his other medical issues, which we talked about and I put in my report. And I asked about his exposure to other drugs, both legal and illegal, other habits, drinking, for example, which can contribute to gynecomastia, which he does not do, nor does he have any illicit drug history that I could elicit from him. So I did basically a standard medical intake exam, allergies, medications, any kind of surgery that he underwent, and then I did an exam that I would describe as problem-focused but focused toward the issues related to exposure to Risperdal.
>
> …

> I examined his breasts. I made measurements of his breasts. I photographed his breasts.

N.T. 6/22/16 p.m. at 92-94, 99. After evaluating A.Y., Dr. Solomon wrote the December 8th report, wherein he detailed his findings.

Dr. Solomon wrote a second report on February 17, 2016. This report was based on Dr. Solomon's review of supplemental data. Dr. Solomon reviewed medical records, pharmacy records, and deposition testimony from A.Y., A. Y.' s mother, Dr. Eker, Dr. Bonfardin, Dr. Philips and Jessica Livingston, APRN. The information contained in these documents buttressed Dr. Solomon's initial findings and he was able to establish a causal link between Risperdal and A.Y.'s gynecomastia.

> **DR. SOLOMON:** So what I decided prior to my completing this review was that he had gynecomastia. I hadn't made a causal link until I reviewed all the supplementary data.

N.T. 6/22/16 p.m. at 156. After reviewing the above-referenced information, Dr. Solomon opined, to a reasonable degree of medical certainty, that exposure to Risperdal caused A.Y. to suffer from gynecomastia. *See Report of Dr. Solomon dated February 17, 2016.*

Dr. Solomon thoroughly explained all of the facts and data upon which his opinion was based at trial:

> **Q.** You have testified you reviewed the medical literature about Risperdal; right?
>
> **A.** Yes.
>
> **Q.** You reviewed Andrew's medical history; right?

A. Yes.

Q. You've examined Andrew?

A. Yes.

Q. You've talked with his mother as well?

A. Yes.

Q. Looked at the photograph evidence?

A. Yes.

Q. You have brought to bear your training, your knowledge, and experience in evaluating Andrew; correct?

A. Yes.

Q. Do you have opinions about whether or not he has gynecomastia?

A. I do.

Q. What is your opinion about whether he has gynecomastia?

A. He absolutely has gynecomastia.

Q. Okay. Do you have an opinion as to what caused his gynecomastia?

A. I do.

Q. And in reaching that opinion, did you rely upon all those things you've described, the medical records, your knowledge of the scientific research, your training, your experience, the whole gamut of expertise that you bring to bear on this?

A. That's correct.

> **Q.** I assume you didn't just consider the good parts and the bad parts. You considered everything; is that right?
>
> **A.** Correct, the totality.
>
> …
>
> **Q.** So based on the records you've reviewed, your training, your experience, your examination, your knowledge of the scientific literature, can you tell us to a reasonable degree of scientific and medical certainty what caused Andrew's gynecomastia?
>
> **A.** Andrew's exposure to Risperdal at a very young age is the direct and proximate cause of his gynecomastia.
>
> **Q.** Doctor, all your opinions have been to a reasonable degree of medical and scientific certainty?
>
> **A.** Absolutely.

N.T. 6/22/16 p.m. at 112-113, 117-118. As the transcript demonstrates, Dr. Solomon reviewed and relied on a variety of factors and information in forming his opinion that Risperdal caused A.Y.'s gynecomastia, not just a photograph.

2. The *Frye* test is not applicable

Defendants' claim that Dr. Solomon's testimony should have been excluded pursuant to Pennsylvania's *Frye* standard must fail. The *Frye* test does not apply to the instant action.

As the Superior Court has stated, the test set forth in *Frye* only applies when a party seeks to introduce novel scientific evidence; it does not apply

every time science enters the courtroom. *Trach v. Fellin*, 817 A.2d 1102, 1109 (Pa. Super. Ct. 2003). When novel scientific evidence is presented, the proponent of that evidence must demonstrate that the expert's methodology is generally accepted by scientists in the relevant field as a method for reaching the conclusion to which the expert will testify at trial. *Grady v. Frito-Lay, Inc.*, 839 A.2d 1038, 1045 (Pa. 2003). Under *Frye*, trial judges are required to "pay deference to the conclusions of those who are in the best position to evaluate the merits of scientific theory and technique when ruling on the admissibility of scientific proof[.]" *Id.* As the Supreme Court explained, the purpose of the *Frye* test is to insure that "only reliable expert scientific evidence is admitted at trial." *Id.*

Here, Plaintiffs did not introduce novel scientific evidence; rather, the methodology used by Dr. Solomon in rendering his opinion was generally accepted in the medical community. As the record demonstrates, Dr. Solomon reviewed and analyzed A.Y.'s medical records and relied on his personal expertise in reaching his conclusion that Risperdal caused A.Y.'s gynecomastia. This type of methodology is generally accepted among the medical community for diagnosis and treatment. *See Cummins v. Rosa*, 846 A.2d 148, 151 (Pa. Super. Ct. 2004) (finding the *Frye* test inapplicable where the methodology employed by plaintiffs' medical experts in reaching their conclusions regarding the source of plaintiff's injuries consisted of an analysis of the plaintiff-wife's medical records and reliance upon their respective personal expertise).

Since there was nothing scientifically novel about the methodology used by Dr. Solomon in this case, the *Frye* test does not apply.

3. The weight to be given to Dr. Solomon's testimony was a question for the jury

Defendants' claim that Dr. Solomon's testimony should have been excluded because he did not cite to scientific literature in support of his general causation opinion should be dismissed. This claim goes to the weight of Dr. Solomon's testimony, not the admissibility.

As Pennsylvania appellate courts have explained, "[i]f a witness has any reasonable pretension to specialized knowledge on the subject under investigation he may testify, and the weight to be given to his [testimony] is for the jury." *Lira v. Albert Einstein Medical Center*, 559 A.2d. 550, 552 *quoting Kuisis v. Baldwin-Lima-Hamilton Corp.*, 319 A.2d 914, 924 (Pa. 1974). *See e.g.*, *Joyce v. Boulevard Physical Therapy Rehab. Ctr. P.C.*, 694 A.2d 648, 656 (Pa. Super. Ct. 1997) (finding that an orthopedic surgeon, who testified to the applicable standard of care, did not need to cite to treatises and medical periodicals to support his opinion; his thirty years in the field of orthopedic medicine was sufficient to support his opinion regarding the relevant standard of care); *Smith v. Grab*, 705 A.2d 894, 900-01 (Pa. Super. Ct. 1997) (finding that an oncologist's opinion regarding the effect of a three-week delay in diagnosing breast cancer was based upon his knowledge, education, reading, and experience of twenty-five years as a practicing oncologist, and the

"failure to cite an article or text on point goes to the weight of his testimony, not its admissibility").

The weight to be afforded to Dr. Solomon's testimony was for the jury to decide. Thus, this claim should be dismissed.

B. Dr. Solomon's testimony that Risperdal was the cause in fact of A.Y.'s gynecomastia was properly admitted

Second, Defendants contend that Dr. Solomon's testimony that Risperdal was the cause in fact of A.Y.'s alleged gynecomastia should have been excluded. According to Defendants, Dr. Solomon failed to identify the basis on which he concluded that A.Y. had gynecomastia in 2003 that did not resolve through the time he examined A.Y. in 2015. He also failed to adequately exclude other potential causes of A.Y.'s alleged gynecomastia or consider the specific dose of Risperdal taken by A.Y. These failings, according to Defendants, rendered Dr. Solomon's specific causation testimony inadmissible under Pennsylvania law and it should have been excluded by the Court. Defendants' claims are baseless.

1. Dr. Solomon identified the basis for his conclusion

Contrary to Defendants' claim, Dr. Solomon identified the basis upon which he concluded that A.Y. had gynecomastia in 2003 that did not resolve through the time he examined A.Y. in 2015. This is evident from the record.

The evidence presented at trial established that A.Y. was first prescribed Risperdal on August 22, 2003 by Dr. Eker. N.T. 6/22/16 p.m. at 136. Dr. Eker

prescribed 0.25 milligrams of Risperdal to be taken twice a day, once in the morning and once at night. N.T. 6/22/16 p.m. at 43. A.Y. began showing signs of gynecomastia just a few months later. In a photograph taken of A.Y. during Christmastime 2003, A.Y.'s breasts appeared to be disproportionate to the rest of his body. At that time, A.Y. was not taking any other medications. *Id.* at 115. The Christmastime photograph was the first documented evidence of gynecomastia. This evidence was substantiated by a claim made by A.Y.'s mother a few weeks later. On January 12, 2004, during an appointment with Dr. Eker, A.Y.'s mother expressed concern that A.Y.'s "breasts have been enlarging." *Id.* at 55. Dr. Eker decided to "gradually taper the Risperdal to be discontinued," noting that the "patient is gaining weight and has possible ? gynecomastia." *See Report of Dr. Eker dated January 12, 2004.* Less than a month later, on February 9, 2004, A.Y. had a medication check with Dr. Eker. At that time, Dr. Eker noted in her records that A.Y. "has gynecomastia." N.T. 6/22/16 p.m. at 62. *See also Report of Dr. Eker dated February 9, 2004.*

At trial, Dr. Solomon was asked whether gynecomastia could be stopped at this point if A.Y. stopped taking Risperdal. The following exchange occurred:

> **Q.** If they stop the Risperdal, do they stop the gynecomastia from continuing to form?
>
> **A.** It does not stop it.
>
> **Q.** Is there some pill, some treatment, some shock, anything that we have medically available to us in 2004, or even today, that Dr.

> Eker could have done on February 9, 2004 to stop the gynecomastia?
>
> **A.** No. Once you've started that process, once the cells have been stimulated to do what they're going to do, they're now beyond the scope of normal control, and there are no medications, as I stated previously, that would change that course.
>
> **Q.** The match has been lit is what I think you said.
>
> **A.** Yes. The match is lit. The fire is going.

N.T. 6/22/16 p.m. at 62-63. As Dr. Solomon made clear, once the breast tissue has been stimulated and an abnormal pattern of growth has been established, the breast tissue will continue to grow beyond normal boundaries. *Id.* at 50, 53. In other words, there was no way to stop the gynecomastia from continuing to form at this point.

On May 26, 2005, a prolactin test was performed. At the time, A.Y. was taking 0.25 milligrams of Risperdal once a day, and had been since March 9, 2005.[9] *Id.* at 69, 78-79. The lab results came back the following day, May 27, 2005. The results revealed that A.Y.'s prolactin level was "highly elevated" at 23.7 milligrams per milliliter. N.T. 6/22/16 p.m. at 78. Dr. Solomon explained the significance of the results at trial:

> **A.** Prolactin is a hormone secreted by the pituitary gland that, in the presence of

[9] Prior to March 9, 2005, Risperdal had been discontinued for a period of time.

Risperdal, goes up above normal levels and is associated with the presence or production of gynecomastia.

Q. Prolactin is in all of our bodies?

A. Yes.

Q. What happens in boys if their prolactin levels get too high?

A. They get breasts, among other things.

Q. That is called hyperprolactinemia I think we've heard?

A. Yes, that's correct.

Q.... So they do this prolactin test; is that right?

A. That's correct.

…

Q. What do the prolactin results come back at?

…

A. So it's 23.7 milligrams per milliliter. That's the quantity of the hormone per milliliter, or cubic cc, that's what a milliliter is, of blood circulating in his body. We have a six-and-a-half-year-old boy at this point. When you look at those reference ranges, you know, when they call that normal there, it's normal for a non-pregnant woman or a pregnant woman. So the lab doesn't distinguish the age or the sex of the person they're getting the specimen from. Adult males have a normal range of 2 to 18 milligrams per milliliter. That's an adult male.

…

It's highly elevated for an adult male. For a young boy, for whom the reference range is probably 10 to 12 at most, it's more than double. And, in fact, I've seen data from the Janssen folks where the reference range is 7, so that would be triple what the company describes as normal.

…

Q. Does that high prolactin level mean the gynecomastia started in 2005?

A. It does not, no. We already know it started in—around Christmastime of 2003, and we have evidence of it then. So it started then.

Q. So if I tried to argue that it started in '05, that would be wrong or misleading; fair?

A. It would certainly be incorrect based on the evidence that we've reviewed already in the court.

Q. What significance then can we draw from the elevated prolactin test in 2005?

A. The evidence that we can draw is that, when this young man is exposed to the Risperdal, his prolactin level goes up at any age.

Q. He's sensitive to the medicine?

A. Correct.

Q. Because not—fair point not everybody that takes Risperdal will end up with gynecomastia; right?

A. Correct.

…

Q. We can put that 5/27/05 record back on. And I think where we left off, and I don't want to put words into your mouth, but by this point, even though we've got this elevated prolactin, it's your testimony that the damage is already done?

A. Yes.

N.T. 6/22/16 p.m. at 72-73, 75-76, 78, 83. As Dr. Solomon explained, the stimulus for the growth of A.Y.'s breast tissue occurred in 2003, when A.Y. began taking Risperdal. A.Y.'s gynecomastia was observable shortly thereafter. A photograph taken around Christmastime that year showed that Defendants' breasts were disproportionate to the rest of his body. The elevated prolactin test in May 2005 was additional evidence of A.Y.'s gynecomastia. Dr. Solomon's explanation was consistent with Dr. Solomon's prior testimony that once gynecomastia has formed, it will not go away on its own.

Moreover, Dr. Solomon's explanation was consistent with his own findings from his physical examination of A.Y. in December 2015. To reiterate, when Dr. Solomon physically examined A.Y. in December 2015, he found that A.Y.'s gynecomastia did not resolve. Dr. Solomon stated the following regarding his physical examination of A.Y.:

Q. You actually put your hands on him; is that right?

A. Absolutely.

> **Q.** Were you able to feel the glandular tissue you described at the beginning of your examination?
>
> **A.** Yes.
>
> **Q.** You're sure this isn't just fat?
>
> **A.** It's breast tissue. It's gynecomastia beyond any doubt.

N.T. 6/22/16 p.m. at 98. Dr. Solomon explained his finding to the jury:

> **A.** The thing that I think the jury needs to remember is, even if he was a little toward the higher side in that Christmas photograph, his breasts were beyond that. They were out of proportion to that. And it is my determination, based on the records, the photographs, and my own physical examination, that that pattern has continued into his present-day status.

Id. at 58.

As the transcript demonstrates, Dr. Solomon explained the basis upon which he concluded that A.Y. had gynecomastia in 2003 that did not resolve through the time he examined A.Y. in 2015. Based on the foregoing, Defendants' claim should be dismissed.

2. Dr. Solomon excluded other potential causes of gynecomastia

Contrary to Defendants' claim, Dr. Solomon adequately excluded other potential causes of A.Y.'s gynecomastia. Dr. Solomon ruled out gynecomastia associated with puberty, gynecomastia from Klinefelter syndrome, gynecomastia caused by other

medications, gynecomastia from kidney and/or liver disease, gynecomastia caused by a thyroid condition, and family history of gynecomastia. Dr. Solomon specifically testified as follows:

> **Q.** … did you consider whether the gynecomastia was caused by puberty?
>
> **A.** I did.
>
> **Q.** How do we know the gynecomastia was not caused by puberty?
>
> **A.** Because at the age of four, he wasn't in puberty when he got breasts.
>
> **Q.** Four-year-olds aren't in puberty; right?
>
> **A.** By definition.
>
> **Q.** So we can eliminate that as a cause; fair?
>
> **A.** Correct.
>
> **Q.** You mentioned something called Klinefelter syndrome; is that right?
>
> **A.** Yes.
>
> **Q.** Can you rule out Klinefelter syndrome as a cause of his gynecomastia?
>
> **A.** I did.
>
> **Q.** How?
>
> **A.** Based on the fact that he is sexually mature. Patients with Klinefelters have a different hair pattern in their gonads. They have breast tissue but they tend to be thin. And, again, he has sexual maturity. He's achieved sexual function. And I examined his gonads, as I said, and, well, he had an undescended testicle. That's a different

discussion. But he certainly has a normal penis and testicle, and except for the undescended one, he's normal. Klinefelters often have small gonads, small testes, for example, and pubic hair does not look like adult male pubic hair.

Q. He also has facial hair?

A. He has facial hair. He has acne, consistent with his issue of puberty on his chest.

Q. Can we rule out Klinefelters as a potential cause of his gynecomastia?

A. Correct.

Q. What about family history? Does he have anybody in the family that's got—you know, his dad, his mom, did you look into that?

A. Again, that's part of the questions I routinely ask, and the answer is there's no family history.

Q. Not showing in the records a history of gynecomastia in the family?

A. Correct.

Q. Can we rule that out?

A. Yes.

Q. We talked about this a little bit already, but he's been on some other medications; right?

A. That's correct.

Q. How do we know—well, first of all, how do we know it wasn't the other medications?

A. Because the only medication he was on when he first got the condition was Risperdal.

Q. And, I mean, I can—I'm circling here the December 25, '03 picture. At that time he was only on the Risperdal; is that right?

A. That's correct.

Q. That was the triggering event?

A. That's correct.

Q. So all these other medicines—Risperdal, Depakote, lithium, Abilify—can you rule those out as the cause?

A. After the trigger event, that's correct.

Q. What about issues with his thyroid?

A. Again, he's got a number of measurements of thyroid function throughout the chart, the medical records that I read, I believe even up to the exam of February 2016. They're all normal.

Q. So we can eliminate that as well?

A. Yes.

Q. I hear people with chronic liver disease can get gynecomastia.

A. Correct.

Q. Does Andrew have chronic liver disease?

A. He has no history of hepatitis. He does not drink. His liver function studies that I saw in the chart that were drawn periodically throughout his life have all been normal.

Q. Can we rule chronic liver disease out?

A. Correct.

Q. I hear people with chronic kidney disease can also end up with gynecomastia.

A. Rarely, but yes.

Q. Does Andrew have chronic kidney disease?

A. He has no evidence of kidney disease either in history or biochemical assays that are, again, present in the chart.

Q. We rule that out; is that right?

A. Correct.

Q. That leaves us with Risperdal?

A. That's correct.

Q. Can we rule out Risperdal as the cause of his gynecomastia?

A. No. It's the culprit.

Q. So based on the records you've reviewed, your training, your experience, your examination, your knowledge of the scientific literature, can you tell us to a reasonable degree of scientific and medical certainty what caused Andrew's gynecomastia?

A. Andrew's exposure to Risperdal at a very young age is the direct and proximate cause of his gynecomastia.

Q. Doctor, all your opinions have been to a reasonable degree of medical and scientific certainty?

A. Absolutely.

N.T. 6/22/16 p.m. at 113-117. As the transcript demonstrates, Dr. Solomon adequately ruled out other potential causes of AY's gynecomastia.

3. There is no support for Defendants' claim that Dr. Solomon failed to consider the dose of Risperdal

Defendants' claim that Dr. Solomon failed to consider the dose of Risperdal taken by A.Y. is baseless. As discussed above, Dr. Solomon testified that, in forming his opinion, he relied, in part, on medical records from several physicians. These medical records contained information regarding the dates in which Risperdal was prescribed to A.Y., as well as the dose of Risperdal that was prescribed. Not only did Dr. Solomon review this information, he discussed it at trial. *See* e.g., N.T. 6/22/16 p.m. at 43-44, 56, 61, 69, 173-175. Dr. Solomon's testimony refutes Defendants' claim that Dr. Solomon failed to consider the specific dose of Risperdal taken by A.Y. Since there is no support for Defendants' claim, it should be dismissed.

C. Dr. Solomon's testimony was proper under Pennsylvania Rule 4003.5

Finally, Defendants contend that Dr. Solomon's expert report failed to disclose his opinion that A.Y. had gynecomastia at "Christmastime 2003." As this opinion was not disclosed in Dr. Solomon's report, it was error for the Court to permit the testimony, alleging an opinion disclosed for the first time at trial. Defendants' claim should be dismissed. This Court did not err in admitting Dr. Solomon's testimony.

Pennsylvania Rule of Evidence 4003.5, which governs discovery of expert testimony, states, in relevant part, as follows:

> (c) To the extent that the facts known or opinions held by an expert have been developed in discovery proceedings under subdivision (a)(1) or (2) of this rule, the direct testimony of the expert at the trial may not be inconsistent with or go beyond the fair scope of his or her testimony in the discovery proceedings as set forth in the deposition, answer to an interrogatory, separate report, or supplement thereto. However, the expert shall not be prevented from testifying as to facts or opinions on matters on which the expert has not been interrogated in the discovery proceedings.

Pa.R.E. 4003.5(c). Rule 4003.5 "favors the liberal discovery of expert witnesses and disfavors unfair and prejudicial surprise." *Woodard v. Chatterjee*, 827 A.2d 433, 441 (Pa. Super. Ct. 2003) (quoting *Jones v. Constantino*, 631 A.2d 1289, 1294 (Pa. Super. Ct. 1993)). In determining whether an expert's trial testimony is within the "fair scope" of his report, "[t]he question to be answered is whether, under the circumstances of the case, the discrepancy between the expert's pre-trial report and his trial testimony is of a nature which would prevent the adversary from preparing a meaningful response, or which would mislead the adversary as to the nature of the appropriate response." *Bainhauer v. Lehigh Valley Hospital*, 834 A.2d 1146, 1150-51 (Pa. Super. Ct.

2003). Here, Dr. Solomon's testimony did not exceed the fair scope of his expert reports.

1. Dr. Solomon's testimony was within the fair scope of his reports

Defendants received a copy of Dr. Solomon's December 8, 2015 report, as well as his February 17, 2016 report prior to trial. In his February report, Dr. Solomon stated, in relevant part, that the cause of A.Y.'s gynecomastia was "exposure to Risperdal starting in 2003 and ongoing at intervals until 2013." *See Report of Dr. Solomon dated February 17, 2016.* Dr. Solomon explained this portion of his report on cross-examination at trial:

> **A.** My second report stated that he has gynecomastia due to the exposure to Risperdal. His exposure to Risperdal began in 2003. Therefore, that's when his gynecomastia began.

N.T. 6/22/16 p.m. at 124-125. Dr. Solomon also provided support for the conclusions set forth in his report at trial:

> A. … the stimulus for the growth of his breast tissue occurred in 2003 and was documented first, we can see it in that photograph, the Christmas photograph I'll call it, and in the subsequent visit with Dr. Eker, when discussions about gynecomastia were first entertained, when his mom said he was growing breasts.

N.T. 6/22/16 p.m. at 88. Dr. Solomon's testimony was proper.

Although not specifically stated in his expert reports, Dr. Solomon's testimony that A.Y.'s gynecomastia began shortly after starting Risperdal in 2003 and was observable in a photograph taken around Christmastime that year did not improperly exceed the fair scope of the reports. As our appellate courts have explained, the fair scope rule is not "a trap for the unwary, requiring that every word a witness utters on the stand be traceable to his or her pre-trial report." *Andaloro v. Armstrong World Industries, Inc.*, 799 A.2d 71, 84 (Pa. Super. Ct. 2002). Rather, "'fair scope' contemplates a reasonable explanation and even an enlargement of the expert's written words." *Hickman v. Fruehauf Corp.*, 563 A.2d 155 (Pa. Super. Ct. 1989). Dr. Solomon's explanation for his conclusion was reasonable and consistent with his theory of causation. Since Dr. Solomon's testimony was within the fair scope of his reports, Defendants' claim should be dismissed.

2. No harm resulted from the admission of Dr. Solomon's testimony

Even if Dr. Solomon's testimony was outside of the fair scope of his reports, Defendants were neither surprised nor prejudiced by the admission of his testimony. Defendants had an opportunity to rebut Dr. Solomon's testimony through their own causation expert, Dr. Moltich, who specifically addressed, and called into question, the opinions of Dr. Solomon at trial. Since any discrepancy between Dr. Solomon's reports and his trial testimony was not of a nature which prevented Defendants from making a meaningful response, this Court did not err in admitting it.

VI. THIS COURT DID NOT ERR IN EXCLUDING EVIDENCE OF SPECIFIC INSTANCES OF AGGRESSIVE CONDUCT

On appeal, Defendants claim that this Court should have ordered a new trial because it improperly excluded evidence with regard to A.Y.'s complete mental health picture and the benefits of Risperdal. Defendants' claim is without merit and a new trial is not warranted. It is well-established that "[t]he grant or refusal of a new trial will not be reversed on appeal, absent an abuse of discretion or error of law which controlled the outcome of the case." *Weed v. Kerr*, 205 A.2d 858, 859 (Pa. 1965). Here, this Court did not commit an abuse of discretion or error of law in limiting the scope of evidence related to A.Y.'s mental health. Thus, Defendants' claim should be dismissed.

The Pennsylvania Rules of Evidence "vest the trial court with the authority to determine the admissibility of evidence as well as to control the scope of examination." *Rettger v. UPMC Shadyside*, 991 A.2d 915, 925 (Pa. Super. Ct. 2010). To be admissible, evidence must be relevant; "evidence that is not relevant is not admissible." Pa.R.E. 402 cmt. "Evidence is relevant if it logically tends to establish a material fact in the case, tends to make a fact at issue more or less probable, or supports a reasonable inference or presumption regarding the existence of a material fact." *Commonwealth v. Spiewak*, 617 A.2d 696, 699 (Pa. 1992). According to Rule 403, the trial court may exclude relevant evidence if its probative value is outweighed by a danger of unfair prejudice.[10]

[10] "Pa.R.E. 403 differs from F.R.E. 403. The Federal Rule provides that relevant evidence may be excluded if its probative

Pa.R.E. 403. As our appellate courts have explained, "'[u]nfair prejudice' supporting exclusion of relevant evidence means a tendency to suggest decision on an improper basis or divert the jury's attention away from its duty of weighing the evidence impartially." *Commonwealth v. Wright*, 961 A.2d 119, 151 (Pa. 2008). It is the function of the trial court to "balance the alleged prejudicial effect of the evidence against its probative value and it is not for an appellate court to usurp that function." *Commonwealth v. Parker*, 882 A.2d 488, 492 (Pa. Super. Ct. 2005).

Here, at trial, Defendants sought to introduce evidence of specific instances where A.Y. exhibited aggressive behavior as well as certain encounters A.Y. had with the justice system. This evidence, according to Defendants, was relevant because it related to the risk/benefit analysis used by his physicians in deciding to prescribe Risperdal to A.Y. Defendants specifically argued the following:

> … [T]o the extent that he's had encounters with the justice system that have been discussed and dealt with by his physicians in choosing to prescribe him Risperdal and other drugs, that's all important evidence to understanding what was in the mind of the prescribers at the time that they choose to put him on Risperdal or other medications.

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value is 'substantially outweighed.' Pa.R.E. 403 eliminates the word 'substantially' to conform the text of the rule more closely to Pennsylvania law. *See Commonwealth v. Boyle*, 498 Pa. 486, 447 A.2d 250 (1982)." Pa.R.E. 403 cmt.

N.T. 6/20/16 a.m. at 10. This Court disagreed. This was not a failure to diagnose case. Plaintiff was diagnosed correctly and was placed on the correct medication; therefore, specific incidents of rage or violence was not necessary for this failure to warn claim. Not only was the proffered evidence not relevant to Plaintiffs' failure-to-warn claim, it was prejudicial to Plaintiffs. As such, this Court precluded Defendants from introducing said evidence. This Court specifically stated the following in support of its decision:

> … [I]n terms of getting into all these specific incidents, had to call the police 2 o'clock in the morning, he was doing this, doing all that, no, I'm not going to allow that, because I think that that is very prejudicial. It's not probative. The only thing the jury has to know is that this person had mental health issues. They were severe and had some violent outbursts and he was prescribed this medication. Anything specific, you know, about what he did when he was being violent, what he did as a result of being on this medication or not being on, that's not relevant, it really isn't, to the failure-to-warn issue . . . . I will allow you to bring out the fact that, of course, he had, you know, he was violent and he had some issues, you know. That's why he had to take the medication because of his mental health, extensive mental health issues.

Id. at 14. As the transcript demonstrates, this Court permitted Defendants to discuss the fact that A.Y. had

extensive mental health issues, was violent at times, and had outbursts. *Id.* at 15. Although this Court precluded Defendants from introducing evidence of specific instances where A.Y. exhibited aggressive conduct, Defendants were not deprived of the ability to mount a fair defense as they contend. Defendants were able to adequately explain why A.Y. needed Risperdal and the factors that his physicians considered in making the decision to prescribe the medication.

This Court's decision was not an abuse of discretion or contrary to law. This Court properly weighed the relevant and probative value of the proffered evidence against the prejudicial impact. In doing so, this Court found that evidence of specific instances of A.Y.'s aggressive conduct was not relevant to the underlying issue of whether Defendants failed to adequately warn of the risks associated with Risperdal. Moreover, the prejudicial effect of the proffered evidence outweighed its probative value. Based on the foregoing, Defendants' claim should be dismissed.

VII. THIS COURT DID NOT ERR IN LIMITING THE TESTIMONY OF NADINE SCHWARTZ, M.D.

On appeal, Defendants claim that this Court erred in limiting the scope of testimony of Defendants' expert, Nadine Schwartz, M.D. According to Defendants, Dr. Schwartz "was highly qualified to opine on Risperdal generally, the patients for whom Risperdal is appropriate, the analysis a prescriber engages in when determining whether to prescribe Risperdal, including consideration of the risks and

benefits, the psychological impact on A.Y. of his gynecomastia diagnosis, and other medications that were available for a patient such as A.Y." *See Defendants' 1925(b) Statement.* Despite being qualified to testify as to each topic, Defendants' contend that "[t]he Court, without basis, limited Dr. Schwartz's testimony to discussing the general benefits of Risperdal[.]" *Id.* For the reasons discussed below, Defendants' claim must fail.

It is well-settled that "[t]he admissibility of evidence is a matter addressed solely to the discretion of the trial court." *Klein v. Aronchick*, 85 A.3d 487, 491 (Pa. Super. Ct. 2014) (quoting *Commonwealth v. Marshall*, 743 A.2d 489, 492 (Pa. Super. Ct. 1999)). Thus, the standard of review is very narrow. The reviewing court "may only reverse upon a showing that the trial court clearly abused its discretion or committed an error of law." *Turney Media Fuel, Inc. v. Toll Bros., Inc.*, 725 A.2d 836, 839 (Pa. Super. Ct. 1999) (citations omitted). "To constitute reversible error, an evidentiary ruling must not only be erroneous, but also harmful or prejudicial to the complaining party." *Id.* Here, this Court did not abuse its discretion in limiting the testimony of Dr. Schwartz at trial.

Dr. Schwartz is a pediatrician and a general and child psychiatrist in Philadelphia. N.T. 6/24/16 p.m. at 6-7. Dr. Schwartz is board certified in pediatrics, general pediatrics, general psychiatry, and child and adolescent psychiatry. *Id.* at 7. In this case, Dr. Schwartz was offered by Defendants as an expert in pediatrics, general psychiatry, child and adolescent psychiatry, the prescription of psychiatric medications

and the risk/benefit analyses performed in connection with those prescriptions, and the pharmacology of pediatric psychiatric medications. *Id.* at 22. This Court permitted Dr. Schwartz to testify as an expert witness; however, it limited the scope of examination. *See Rettger v. UPMC Shadyside*, 991 A.2d 915, 925 (Pa. Super. Ct. 2010) (the Pennsylvania Rules of Evidence "vest the trial court with the authority to determine the admissibility of evidence as well as to control the scope of examination"). This Court did not, however, limit the scope of Dr. Schwartz's testimony as described by Defendants.

A. Dr. Schwartz was not limited to only discussing the general benefits of Risperdal

Contrary to Defendants' claim, Dr. Schwartz was not precluded from testifying about Risperdal generally, the patients for whom Risperdal is appropriate, and the analysis a prescriber engages in when determining whether to prescribe Risperdal, including consideration of the risks and benefits. As the transcript demonstrates, Dr. Schwartz testified regarding these matters and more at trial. The following testimony was elicited:

> **Q.** In your practice as a child and adolescent psychiatrist, do you perform risk/benefit analyses in deciding whether or not to prescribe a particular medication?
>
> **A.** With every patient that I see and with every patient that I supervise on, yes.
>
> **Q.** … [W]ould you just generally describe what a risk/benefit analysis is in connection with making a decision to prescribe a

medication for a patient in child and adolescent psychiatry.

A. Sure. So a risk/benefit analysis is a fancy way of saying that you consider the pros and cons of what the best treatment or what the right treatment or what the various treatment options should or shouldn't be for any given patient or patient situation. You look at what you're trying to do for someone and you look at what the various options are that might exist and you figure out if the treatment is hopefully going to give you the benefit that you want without making things worse than what you started off with.

…

Q. Dr. Schwartz, you've told us earlier that you've reviewed medical and educational records and testimony relating to [A.Y.]. Based on your review of all the information relating to [A.Y.], did you determine whether he was diagnosed with any psychiatric conditions?

A. I did.

Q. And what conditions was he diagnosed with during the course of his treatment?

A. He was diagnosed with several different conditions. He was diagnosed with attention deficit hyperactivity disorder, oppositional defiant disorder, and he was diagnosed with mood disorder that at various points was called different things, which is okay, because mood disorder is sort of an umbrella or

overarching term that can include a number of different things. And so at different points he was labeled as either just mood disorder or depressed or bipolar. So all those things collectively kind of indicated the same thing.

Q. Did you reach any opinion with respect to how serious these conditions were?

A. I did.

Q. And without describing specific acts or events that you reviewed in the course of his treatment, what was your opinion with respect to the severity of his condition?

A. [A.Y.] had, over the course of the records that I reviewed, very serious symptoms.

Q. Is the severity of the condition relevant to the risk/benefit analysis that a psychiatrist does in deciding whether to prescribe a medication?

A. It's pretty much the most essential piece, yes.

Q. And how is that so?

A. Well, first of all, somebody doesn't usually show up to the doctor unless something's bothersome in the first place. And then in a case of psychiatric or psychological problems, if something is not that severe, especially with a child, we're probably not going to consider medication in the first place. We'll probably consider some other kind of route like therapy, behavior therapy, individual talk therapy, family therapy. There are a variety of different kinds of therapies out

there. So the only time we're going to think about medication for a child is if something reaches a certain level of severity. And so that's why severity is critical, is an essential piece of a risk/benefit analysis.

Q. Could you briefly explain to the jury what a mood disorder is?

A. Sure. So the primary piece of a mood disorder is that your—the person's mood is—I guess the best way to explain this is the analogy that I always use when I'm talking to patients and families, and that is the globe of the Earth. If you think about the globe of the Earth, the widest part is at the equator. And most of us live not on the equator all the time because people's moods aren't flat. They're not supposed to be flat. But we live within range of the equator. So maybe we go up as high as North Carolina or south as Brazil, but we don't go all the way to the two different Poles. That would be a big, far stretch from the equator. And a mood disorder is when your mood varies very widely, from around the equator. So to be depressed would be to be way down south, towards the South Pole. And to stay there not just for a little bit, but to stay there for a significant enough period of time that it was interfering with your functioning. And the opposite, bipolar disorder, meaning something where you have mania and also some amount of depression, would be way up north, up at the North Pole. And, again, not just for a split second or a minute or a tiny

little bit of time, but for enough time that it created dysfunction in your life. So that's the basic premise of a mood disorder. And then there are symptoms that go along with mood disorders that people can manifest in all sorts of ways. But that's really the crux of a mood disorder, is that your mood is very different from what it's supposed to be and it stays there for a while and it interferes with your functioning in a way that is significant that can be interfering with your relationships with people. It can interfere with your relationship with your family, with your relationship with peers. It can interfere with your achievement in terms of academic accomplishments, your ability to be or remain employed. It can be so severe that it can cause you to feel suicidal or, in fact, attempt to take your life. And if they go on for a while and are untreated, they can even lead to psychosis, which is the same kind of symptoms that people have when they're schizophrenic.

…

Q. Would you explain to the jury what the benefits of Risperdal are in the treatment of the types of disorders with which [A.Y.] was diagnosed?

A. Okay. I'm going to start with mood disorder. Risperdal and drugs similar to Risperdal in that class are used for mood disorder as a way of helping with aggressive or explosive outbursts of mood and also as mood stabilizers. So what that means is that

what I was talking about before, those deviations from the more stable mood that typically people have, their moods are varying, from highs to lows, and helping to rein those unstable moods back in towards stability. So that when persons are having a mood disorder and their mood is not reined in towards the more typical stable, Risperdal can—has been shown to help with mood stabilization. It also has been shown to help with aggressive and impulsive outbursts of mood and with people being able to stay more in control and have less aggressive outbursts type behaviors. Another thing that happens for some people with mood disorders is that they have difficulty sleeping, either getting to sleep or staying asleep or both. And so one of the things that sometimes—not necessarily an intended effect, but one of the side effects of Risperdal that can be beneficial for people with that problem is that it will help them with their sleep. And, again, another not necessarily intended effect but beneficial effect for some people with mood disorder is that Risperdal can help with appetite. For some people that turns into a bigger problem than it is intended to be, so that can be both a benefit and a not benefit, but for some people it is a benefit. But really the primary benefit for mood disorder is helping to rein those very explosive and aggressive outbursts of mood that some people have, what we call irritability, in so that people can stay in better control of their moods when they have

> mood disorder. The same thing is often seen with people who have behavior disorders such as ADHD or oppositional defiant disorder. So with those kinds of disorders, oftentimes there's a component of impulsivity that leads to outbursts of behavior. And those can sometimes be very quick and very severe. And, again, the same kinds of benefit are seen with Risperdal and the agents like it in helping the people with those disorders not necessarily have such a short fuse, so that there's a little bit more time between when they are aggravated by something and their ability to not necessarily fly off the handle so quickly so that they get a little bit more time to think maybe and to come up with a different response so that aggression and violence are not necessarily the immediate response, but maybe there's a more thought-out or measured response.

N.T. 6/24/16 p.m. at 21-26, 54-56. The above-referenced testimony belies Defendants' claim that this Court limited Dr. Schwartz to only discussing the general benefits of Risperdal. As the transcript demonstrates, Dr. Schwartz testified about Risperdal as a treatment for certain mood disorders, the patients for whom Risperdal is appropriate, and the factors to be considered when prescribing such a medication. Dr. Schwartz also discussed A.Y.'s medical conditions, the seriousness of his symptoms, and why the severity of the conditions is relevant to a psychiatrist's risk/benefit analysis.

Given that the substance of Dr. Schwartz's testimony covered more than just a discussion of the general benefits of Risperdal, this claim must fail.

B. This Court did not err in precluding Dr. Schwartz from testifying about certain topics

In addition to the foregoing, Defendants' claim that this Court improperly precluded Dr. Schwartz from testifying about the psychological impact on A.Y. of his gynecomastia diagnosis and from discussing other medications that were available must also fail.

First, Dr. Schwartz was not qualified to testify about the psychological impact the gynecomastia diagnosis had on A.Y. Dr. Schwartz never interviewed, examined or treated A.Y.; she never even met with him or any member of his family in connection with her work on this case. Dr. Schwartz did not have any first-hand knowledge of A.Y.'s psychological state, which varied at certain points in time, nor could she adequately ascertain this information from the medical records. Thus, any opinion regarding how A.Y.'s gynecomastia diagnosis affected him would have been based on speculation and conjecture. As our appellate courts have explained, "an opinion based on mere possibilities is not competent evidence. This means that expert testimony cannot be based solely upon conjecture or surmise." *Viener v. Jacobs*, 834 A.2d 546, 558 (Pa. Super. Ct. 2003). *See also Duquesne Light Company v. Woodland Hills School District*, 700 A.2d 1038, 1047 (Pa. Cmwlth. 1997) ("Speculative testimony or testimony made without reasonable certainty does not aid the trier of fact and should be stricken"). Since Dr. Schwartz's opinion regarding how

A.Y.'s diagnosis affected him would not have assisted the trier of fact, it was properly precluded at trial.

Second, Defendants suffered no prejudice as a result of this Court's decision to preclude Dr. Schwartz from testifying about other medications that were available to A.Y. Throughout trial, the jury heard testimony that A.Y. was placed on numerous medications to help with treatment of his conditions. Specifically, the jury heard testimony that A.Y. was prescribed Clonidine, Strattera, Dexedrine, Abilify, Tenex, Ritalin, Seroquel, Zoloft, Zyprexa, Lithium, Prozac, Depakote, Fluoxetine, Paxil, Geodon, Trileptal, Invega, and Fanapt. The jury also heard testimony that these medications were not effective in treating A.Y.'s symptoms. As the transcript demonstrates, A.Y.'s mother told doctors that Risperdal was "the only med[ication] which has really helped." N.T. 6/28/16 p.m. at 16. She also acknowledged that she restarted A.Y. on Risperdal because she thought it was more effective than any other medication. N.T. 6/29/16 p.m. at 141.

Since the jury heard testimony regarding the other medications that were available, Defendants were not harmed or prejudiced by this Court's decision to preclude Dr. Schwartz from testifying in this regard. As such, Defendants' claims should be dismissed.

VIII. THIS COURT DID NOT ABUSE ITS DISCRETION IN PRECLUDING THE TESTIMONY OF GORDON GREESON, M.D.

On appeal, Defendants claim that this Court erred in precluding the testimony of Gordon Greeson, M.D., at trial. Defendants' claim must fail. Dr.

Greeson's testimony was not relevant to Plaintiffs' failure to warn claims as it did not have a tendency to make the existence of any fact more or less probable. *See* Pa.R.E. 401.

As discussed above, "the admissibility of evidence is a matter addressed solely to the discretion of the trial court and may be reversed only upon a showing that the court abused its discretion." *Klein v. Aronchick*, 85 A.3d at 491. Here, this Court did not abuse its discretion in precluding Dr. Greeson's testimony at trial.

Dr. Greeson is a child and adolescent psychiatrist at the Helen Ross McNabb Mental Health Center ("Health Center") in Knoxville, Tennessee. Greeson Dep. 3/1/16 at 13-14. Dr. Greeson began treating A.Y. in October 2012 after A.Y.'s psychiatrist, Dr. Brian Bonfardin, left the Health Center. *Id.* at 15. At the time Dr. Greeson inherited A.Y. as a patient, A.Y. was having behavioral issues. According to Dr. Greeson, A.Y. "presented with mood issues, primarily irritability and aggression." *Id.* at 17. Dr. Greeson treated A.Y. for these issues, and others, until February 2016. *Id* at 22.

During one particular doctor's visit in March 2013, A.Y.'s mother informed Dr. Greeson that she filed a lawsuit against the manufacturer of Risperdal. *Id.* at 105-106. According to A.Y.'s mother, she saw a commercial run by lawyers who were advertising for potential clients who had taken Risperdal and developed gynecomastia. A.Y.'s mother brought this to Dr. Greeson's attention and stated that she believed Risperdal caused A.Y. to develop gynecomastia. *Id.* at 106-109. At trial, Defendants sought to introduce the

testimony of Dr. Greeson, contending that his discussion with A.Y.'s mother was relevant to the issue of causation. Plaintiffs disagreed. The following arguments were advanced by both parties with respect to the admissibility of Dr. Greeson's testimony:

> **THE COURT:** What is this doctor? What is the offer of proof for that one?
>
> **DEFENSE COUNSEL:** It's a little different in that Dr. Greeson has testimony with regard to gynecomastia and discussion of gynecomastia with [A.Y.'s mother], and so it definitely goes to causation.
>
> **THE COURT:** I'm sorry. The testimony is that he had discussion with her about gynecomastia?
>
> **DEFENSE COUNSEL:** About gynecomastia, that's right, Your Honor, and that differs from Dr. Bonfardin, for example, such that the jury's entitled to hear this testimony, part of their consideration about whether [A.Y.] really had gynecomastia, part of the causation question.

N.T. 6/24/16 a.m. at 86.

> **THE COURT:** What was the basis of this doctor discussing any gynecomastia with the plaintiff?
>
> **DEFENSE COUNSEL:** Because [A.Y.'s mother] brought it to his attention. They had a discussion about it in 2013.
>
> **THE COURT:** I'm trying to find out—

DEFENSE COUNSEL: The discussion that we just heard about from [A.Y.'s father] related to the lawsuit. So when she had heard the commercial, she came in and asked Dr. Greeson for the first time about whether he had gynecomastia, and it's relevant for the jurors' understanding of whether or not [A.Y.] had gynecomastia and it goes to the causation question.

THE COURT: I don't think it does. Go ahead.

PLAINTIFFS' COUNSEL: Your Honor, if I may, I think you're right on. What it said was there was a conversation after she filed the lawsuit. She told her doctor. He got her off generic Risperdal. [Dr. Greeson] never evaluated [A.Y.] for gynecomastia. He never made a determination on it. It really has nothing to do with anything. It's after Bonfardin. We're talking even more removed than his testimony.

Id. at 87-88.

PLAINTIFFS' COUNSEL: [Dr. Greeson] didn't do any evaluation for gynecomastia. He didn't put his hands on him, pinch test, any of that stuff.

THE COURT: So how would he know?

PLAINTIFFS' COUNSEL: He doesn't know . . . . He doesn't ever say he knows. Dr. Bonfardin prescribed generic Risperdal. This is a doctor that continued on. I think they shared a note together at one point where they write on the same medical record. All he

> did was keep prescribing what Dr. Bonfardin did. The mother goes in and says—
>
> **THE COURT:** This was a doctor after Bonfardin?
>
> **PLAINTIFFS' COUNSEL:** Correct. And the mother goes in and says the thing about the lawsuit, gynecomastia. He never confirms or denies whether he has it. He never does an evaluation. All they did was taper him off the drug, and that was it.

Id. at 97-98. This Court ultimately determined that Dr. Greeson's testimony was not relevant to Plaintiffs' failure to warn claims. Dr. Greeson never conducted a physical examination of A.Y.'s chest and did not diagnose A.Y. with gynecomastia. In fact, Dr. Greeson had never diagnosed *any* patient with gynecomastia. Greeson Dep. 3/1/16 at 108. Thus, contrary to Defendants' claim, Dr. Greeson's testimony would not have been relevant for the jurors' understanding of whether or not A.Y. had gynecomastia at the time. Moreover, the jury already heard testimony that A.Y.'s mother filed the underlying lawsuit after seeing the above-referenced commercial for Risperdal. The following testimony was elicited from A.Y.'s father at trial:

> **Q.** You mentioned that your wife saw a commercial advertising about the fact that a drug Risperdal made people grow female breasts. Do you remember talking about that with your lawyer a few minutes ago?
>
> **A.** I do.

Q. And it was shortly after that that your wife filed this lawsuit; right?

A. She did.

N.T. 6/24/16 a.m. at 52. As such, Dr. Greeson's testimony regarding his conversation with A.Y.'s mother would have been duplicative of testimony that was already presented to the jury.

Based on the foregoing, Defendants' claim should be dismissed. This Court did not abuse its discretion in precluding the testimony of Dr. Greeson at trial.

IX. THIS COURT DID NOT ERR IN ADMITTING THE TESTIMONY OF DR. KESSLER

On appeal, Defendants claim that this Court improperly admitted certain testimony by Plaintiffs' expert, David A. Kessler M.D, J.D. According to Defendants, Dr. Kessler's testimony should have been precluded because (1) there was no showing or contention that Dr. Kessler was unavailable to testify live at trial; (2) Defendants were unable to meaningfully cross-examine Dr. Kessler on issues germane to this case; (3) Dr. Kessler improperly offered testimony regarding off-label promotion; and (4) Dr. Kessler improperly testified regarding his personal interpretation of internal corporate documents. For the reasons discussed below, Defendants' claims should be dismissed.

Dr. Kessler holds a bachelor's degree from Amherst College, a law degree from the University of Chicago Law School, and a medical degree from Harvard Medical School. Dr. Kessler completed his internship and residency in pediatrics at Johns Hopkins Hospital. In 1990, President George H.W.

Bush appointed Dr. Kessler as the Commissioner of the Food and Drug Administration. Dr. Kessler served in this role for seven years and was responsible for enforcing the United States Food, Drug, and Cosmetic Act. From 1997 to 2003, Dr. Kessler was the Dean of Yale University School of Medicine, where he also taught pediatrics, epidemiology, public health. Since 2003, Dr. Kessler has worked at the University of California at San Francisco, where he is a professor of pediatrics, epidemiology, and biostatistics. Dr. Kessler has authored numerous professional articles in legal medical and scientific journals on federal regulation of food, drugs, and medical devices.

In this case, Plaintiffs introduced a *de bene esse* deposition of Dr. Kessler at trial. Given Dr. Kessler's knowledge, skill, education, experience, and training, he was qualified to give expert testimony about general topics relating to FDA regulatory process, a pharmaceutical company's obligation to warn of safety hazards, and Defendants' failure to warn about the risks associated with Risperdal. Dr. Kessler's testimony was relevant and helpful to the trier of fact in understanding the evidence and was properly admitted at trial.

A. Dr. Kessler's testimony was admissible under Pa.R.C.P. 4017(g)

Defendants' claim that this Court erred in admitting Dr. Kessler's deposition testimony because there was no showing or contention that he was unavailable to testify live at trial must fail. Dr. Kessler's testimony was admissible under Pennsylvania Rule of Civil Procedure 4017.1(g).

According to Rule 4017.1(g), "a video deposition of a medical witness or any witness called as an expert, other than a party, may be used at trial for any purpose whether or not the witness is available to testify." This Rule is intended to "allay the problem of attendance at trial that is commonly experienced with medical and other expert witnesses." Goodrich Amram 2d § 4017.1(g):1.

Here, Dr. Kessler's opinions have been thoroughly explored in the Risperdal litigation. Prior to the trial at issue, Dr. Kessler had been deposed three times and testified at two trials. In May 2015, Plaintiffs obtained a *de bene esse* videotaped deposition of Dr. Kessler for use in all Risperdal trials. The purpose of this deposition was to lower litigation costs and for the convenience of Dr. Kessler, who resides in California. In his deposition, Dr. Kessler addressed issues germane to all Risperdal cases and offered opinions regarding the Defendants' duty of care and Defendants' breach of their duty to warn. As Plaintiffs explained, Dr. Kessler's testimony was Defendant-specific but Plaintiff-generic. Since Dr. Kessler's *de bene esse* deposition was relevant to all Risperdal trials, including this one, his deposition was properly admitted. This is so even if Dr. Kessler was available to appear live at trial. To reiterate, Rule 4017.1 permits use of a videotaped deposition of a medical witness even if the witness is available to appear at trial. As such, this claim should be dismissed.

B. The Findling reanalysis was not relevant to Dr. Kessler's testimony

Second, Defendants contend that they were unable to meaningfully cross-examine Dr. Kessler on

issues germane to this case. Specifically, Defendants claim they were precluded from cross-examining Dr. Kessler about the reanalysis of data which appeared in the 2003 article, "Prolactin Levels During Long-Term Risperidone Treatment in Children and Adolescents" by Findling et al. ("Findling"). This claim must also fail.

Our Superior Court has explained that "an expert witness may be cross-examined on the contents of a publication upon which he or she has relied in forming an opinion, and also with respect to any other publication which the expert acknowledges to be a standard work in the field. In such cases, the publication or literature is not admitted for the truth of the matter asserted, but only to challenge the credibility of the witness' opinion and the weight to be accorded thereto." *Majdic v. Cincinnati Mach. Co.*, 537 A.2d 334, 339 (Pa. Super. Ct. 1988).

Here, as Plaintiffs' counsel pointed out at trial, Dr. Kessler's testimony focused on Defendants' failure to warn in 2003 when the Findling article was operative and A.Y. was being prescribed Risperdal. In his *de bene esse* deposition, Kessler referred to various drafts of the Findling article and discussed the fact that data included in the initial drafts of the article, which showed a statistically significant association between Risperdal ingestion and gynecomastia, did not appear in the published article. Dr. Kessler testified that, by omitting this data, Janssen misled physicians and the scientific community. Dr. Kessler ultimately concluded that the Defendants failed to warn of the gynecomastia risk associated with Risperdal.

In forming his opinions, Dr. Kessler did not acknowledge the Findling article to be a standard work in the field upon which he relied. In addition, Dr. Kessler did not rely on the reanalysis of the Findling article in formulating his opinions. The reanalysis was published in 2016. As discussed above, Dr. Kessler's opinions focused on Defendants' failure to warn in 2003. As such, the reanalysis had no bearing on Dr. Kessler's testimony. Moreover, because Dr. Kessler did not consider or rely on the reanalysis in forming his opinions, there was no need to cross-examine him about an opinion he did not offer. Defendants were permitted to present their own expert witnesses to discuss the reanalysis and to challenge Dr. Kessler's credibility.

Finally, the results of the reanalysis were available at the time that Dr. Kessler's *de bene esse* deposition was taken. Thus, Defendants could have cross-examined Dr. Kessler regarding the reanalysis at that time. Defendants' failure to do so did not justify requiring Dr. Kessler to testify live at trial.

For the foregoing, Defendants' claim should be dismissed. The Findling reanalysis was not relevant to Dr. Kessler's testimony.

C. Dr. Kessler's testimony regarding off-label promotion was properly admitted

Third, Defendants contend that this Court erred in permitting Dr. Kessler to offer extensive testimony regarding "off-label" promotion. According to Defendants, expert witnesses are not permitted to testify as to what the law is or whether certain conduct was legal. Moreover, Defendants contend that Dr. Kessler's opinions regarding off-label promotion were

inadmissible because whether Janssen engaged in off-label promotion was irrelevant to the existence or absence of liability on Plaintiffs' claim under Tennessee law. Defendants' claims are meritless and should be dismissed.

As discussed above, it is well-settled that evidence is relevant if it has any tendency to make a fact more or less probable than it would be without the evidence and the fact is of consequence in determining the action. Pa.R.E. 401. "Whether evidence has a tendency to make a given fact more or less probable is to be determined by the court in the light of reason, experience, scientific principles and the other testimony offered in the case." Pa.R.E. 401 cmt. Relevant evidence may be excluded "if its probative value is outweighed by a danger of one or more of the following: unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence." Pa.R.E. 403. Here, Dr. Kessler's testimony regarding off-label promotion was relevant to the issues in this case and its probative value outweighed the danger of unfair prejudice.

Off-label means the practice of prescribing prescription drugs for use that is not approved by the FDA. Off-label use of prescription drugs is lawful. That is, doctors are allowed, in the practice of medicine, to prescribe drugs that have been approved by the FDA for purposes or uses other than the ones approved by the FDA. It is not lawful, however, for drug companies to promote their drug for a use that has not been approved by the FDA. Dr. Kessler

testified in this regard during his *de bene esse* deposition.

> [I]f I can just say, the drug can be used off-label. Nothing wrong with that. What the law says is that doctors can use their individual, his or her—any doctor can use his or her judgment. It just prevents a company from promoting the use.

Kessler Dep. 5/19/15 at 88. Dr. Kessler explained the purpose behind the FDA's policy against off-label promotion by pharmaceutical companies:

> It's one of the—it's a very important policy issue. It underlies, really, the whole structure of our drug regulatory system. We have a system where companies have incentives to do studies, get information, and that information goes to doctors and patients. And that comes from doing studies and getting the information. And if you can go promote, go market, outreach—call it what you want—you can go sell, market, promote, outreach, for indications that you're not approved, where is the incentive to get the kind of information, to evaluate that information appropriately, and assure safety and efficacy? So if you allow unapproved marketing for off-label indications, unapproved indications, then you're not going to—you're going to basically unravel the whole system of drug regulation.

Kessler Dep. 5/20/15 at 367-68. As Dr. Kessler explained, off-label promotion undercuts the FDA's ability to ensure safety and efficacy of a drug.

> … [I]t deprives physicians and patients of the basic safety and effectiveness evaluation that companies and the FDA work hard to do to assure the public that its drugs are safe and effective. If a company promotes off-label, it undercuts that system. All right. And when you couple that off-label promotion with powerful medicines for whom the risk is not fully disclosed, what you're doing, when you—if you sell this medicine, if you sell Risperdal for a broad range of indications, for a whole set of behavioral indications, ADHD, Tourette's, other indications that are not—have never been approved, you are going to expose more children to that risk. And when that exposure accompanies—is accompanied by an increased risk and risks that are not fully disclosed, that puts those kids in harm's way.

Id. at 474-75. Despite the FDA's policy, Plaintiffs presented evidence that Defendants promoted off-label use of Risperdal for children and adolescents years before it was approved for that indication by FDA. According to Dr. Kessler, Defendants created business and marketing plans specifically targeting children and adolescents for the use of Risperdal. Defendants directed its sales force to go out and talk to pediatricians, pediatric psychiatrists, and other medical professionals who primarily treated children, and to market Risperdal as safe and effective for symptoms of various disorders in children. Dr. Kessler testified as follows:

> **Q.** Was there a sales force for Janssen?

A. Yes.

Q. And did the sales force for Janssen visit doctors regularly?

A. Yes. I reviewed sales notes, yes.

Q. Did Janssen doctors [sic] visit routinely and consistently with physicians who were pediatric psychiatrists, pediatric neurologists, and pediatric pediatricians in particular?

A. I think you said Janssen doctors. I think you meant—

Q. Sales force.

A. Thank you very much. Yes. There are documents that talk about those visits.

Kessler Dep. 5/20/15 at 403.

Q. From your review of the documents, can you tell us, first of all, in the period of 2000 through 2006 before the approval for autism, was Janssen promoting the drug Risperdal for children and adolescents?

A. I have no doubt in my mind.

Q. From the documents that you reviewed, have you reached that conclusion?

A. Yes.

Q. Was Janssen marketing the drug for adolescents and children?

A. Certainly.

Q. Is there any doubt in your mind?

A. No.

Id. at 365. In addition to promoting Risperdal for unapproved use in children, Defendants failed to warn of its risks despite knowing that Risperdal was associated with an increased risk of gynecomastia in young males and despite having ample opportunity to warn. The following testimony was elicited from Dr. Kessler.

> **Q.** … I want you to just, if you would, list for me and tell me those ways that the—that Janssen could have and should have warned pediatric practitioners prescribing this drug off-label to children.
>
> **A.** In all—in all ways, whenever they touched a physician.
>
> **Q.** Okay. Let me—let me see if I can catalogue them for you.
>
> **A.** Yes.
>
> **Q.** Could they and should they have done it through their sales force?
>
> **A.** Sure.
>
> **Q.** Tell me how.
>
> **A.** What—if they're going—if they're in there visiting, they can warn.
>
> **Q.** Is every opportunity—is every time that a salesperson went to a doctor who they knew was prescribing to children and adolescents an opportunity to give them the information which you've mentioned here?
>
> **A.** As long as it's safety and warning, yes.
>
> **Q.** Okay. How about through the medical education that they were doing? Could they

have and should they have warned in that way?

A. Absolutely.

Q. Is there something called a "Dear Doctor" letter?

A. Yes.

Q. What is a "Dear Doctor" letter? And could and should Janssen under these circumstances have disseminated a "Dear Doctor" letter? First, describe it and tell me could they have and should they have here.

A. Yes. Yes, they could have. Yes, they should have. FDA was very specific going back several decades. If you look at the Federal Register and you look at the language that my predecessors set out in the Federal Register, there—companies can warn. If there is a safety issue, you can warn in a "Dear Doctor" letter. It's a letter to physicians. It's a—it's a form of communication.

Q. If you're not sure, can you go to the FDA and tell the FDA, "I'm going to send this letter out. Is this okay?"

A. In fact, Janssen—there's examples where Janssen sent out "Dear Doctor" letters before talking to the FDA, and after talking to the—the FDA. Certainly you would want to talk to the FDA. I would think that would be a good idea. But the fact is, if you know of a safety issue, okay, there are many forms, including a "Dear Doctor" level—letter, that you can warn.

> **Q.** We've mentioned the "Dear Doctor" letter, the sales representatives, the medical—the educational approach when they are having these regional advisory committee meetings. Was that a place where they could have and should have warned?
>
> **A.** Absolutely. You would think, right, that the number one thing you would want if you have doctors there—I mean, call it an advisory committee—is you talk about the safety issues. You talk about the incidence. You talk about hyperprolactinemia being—Risperdal causing more hyperprolactinemia. You talk about the fact that you have this increase in 8 to 12 weeks, and you talk about all the data.
>
> **Q.** And did they do the opposite?
>
> **A.** They did not do—they did not sufficiently warn. They failed to warn.

Id. at 460-63. As Dr. Kessler explained, Defendants had every opportunity to warn pediatric practitioners prescribing Risperdal off-label to children but intentionally failed to do so.

Dr. Kessler's testimony regarding off-label promotion was proper. Dr. Kessler was qualified and well-equipped to testify regarding the policies and procedures at the FDA given his extensive knowledge and experience in the field of food and drug regulation. Dr. Kessler explained his experience, in relevant part, as follows:

> **Q.** As part of your role at the FDA, were you knowledgeable about and did you oversee marketing and promotion of drugs?
>
> **A.** I was intimately involved in the regulation of advertising, marketing, and communication of prescription drugs. That was done by an office at the time that was called—the acronym was DDMAC. And it had a director, but I worked directly with that director on implementing a number of policies.
>
> **Q.** And would you also be familiar with the regulation of drugs; that is to say, the regulations which are promulgated which are—those documents which say what can and can't be done?
>
> **A.** Yes. Both the laws, the regulations, the guidances. I've also served, sir, since I was FDA commissioner on certain corporate boards and, in fact, chaired the compliance committee of those corporate boards as they relate to both drugs and devices.

Kessler Dep. 5/19/15 at 25-26.

> **Q.** And you're familiar with the sales activities of pharmaceutical companies?
>
> **A.** I certainly was responsible for overseeing the regulation of the advertising and marketing when I was at the agency, and I've seen it from the inside being on pharmaceutical company boards.

Kessler Dep. 5/20/15 at 435. Given Dr. Kessler's background, he was qualified to testify regarding the

FDA's policy on off-label promotion by pharmaceutical companies and whether he believed Defendants acted in accordance with that policy.

Moreover, contrary to Defendants' claim, evidence of off-label promotion was relevant to Plaintiffs' failure to warn claims. Under Tennessee law, "[m]anufacturers of prescription drugs, like the manufacturers of any other unavoidably dangerous product, have a duty to market and distribute their products in a way that minimizes the risk or danger. They may discharge their duty by distributing the drugs with proper directions and adequate warnings to those who foreseeably could be injured by the use of their products." *Pittman v. Upjohn Co.*, 890 S.W.2d 425, 428 (Tenn. 1994). Warnings are considered adequate "when they contain a full and complete disclosure of the potential adverse reactions to the drug. A reasonable warning not only conveys a fair indication of the dangers involved, but also warns with the degree of intensity required by the nature of the risk." *Pittman v. Upjohn Co.*, 890 S.W.2d at 429 (citing *Seley v. G.D. Searle & Co.*, 67 Ohio St.2d 192, 423 N.E.2d 831, 837 (1981)).

As discussed above, Dr. Kessler testified that Defendants were promoting Risperdal for unapproved use in children for many years, evidenced by their marketing materials. Since Defendants specifically targeted the pediatric population, Risperdal use in pediatric patients was foreseeable. Under Tennessee law, Defendants had a duty to disclose the known risks that Risperdal posed to this pediatric population. As Dr. Kessler explained, Defendants not only failed to adequately warn of the known risks, they concealed

and misrepresented information about the side effects of Risperdal. This testimony was undeniably relevant to Plaintiffs' failure to warn claim.

Based on the foregoing, Defendants' claim should be dismissed. Dr. Kessler's testimony was relevant to the issues in the case and helpful to the trier of fact in understanding the evidence.

D. Dr. Kessler was permitted to testify regarding internal corporate documents

Finally, Defendants contend that this Court erred in admitting extensive testimony from Dr. Kessler regarding his personal interpretation of internal Janssen documents as well as the intent of Janssen and the FDA. Defendants' claim is unfounded. Dr. Kessler did not exceed the permissible scope of expert testimony.

Courts have held that an expert may testify about his review of internal corporate documents to explain the basis for his opinions. *In re Flonase Antitrust Litigation*, 884 F. Supp. 2d 184 (E.D. Pa. 2012). Here, in forming his opinions, Dr. Kessler reviewed, inter alia, internal documents from Janssen and the FDA. Dr. Kessler discussed the meaning and significance of these documents and how they fit into the FDA's scheme for regulating pharmaceutical drugs. Using the information contained in these documents, Dr. Kessler explained what knowledge was available to Defendants and what information they should have known as the manufacturer of a prescription drug. Dr. Kessler also discussed what Defendants should have done in terms of disclosing certain information and what their own internal documents showed they failed to do. Dr. Kessler was permitted to offer such

testimony given his extensive knowledge and experience with FDA regulations and procedures, as well as his knowledge of the obligations of a pharmaceutical company to disclose clinical data and analyses of data pertinent to safety. This testimony was helpful to the jury in understanding FDA regulatory requirements and the ways in which Defendants failed to comply with those requirements.

The substance of Dr. Kessler's testimony did not exceed the bounds of permissible expert testimony. While Dr. Kessler discussed what Defendants should have known, should have done, and failed to do, he did not testify regarding Defendants' intent. In fact, at one point during his deposition, Dr. Kessler expressly stated that he did not "want to … get into intention." Kessler Dep. 5/20/15 at 415. As such, Defendants' claim must fail.

X. THIS COURT DID NOT ERR IN PRECLUDING THE FDA'S RESPONSE TO THE CITIZEN PETITION

On appeal, Defendants contend that this Court erred in excluding the FDA's response to the Citizen Petition submitted by Plaintiffs' counsel. Defendants' claim is baseless and should be dismissed. This Court did not err in precluding this evidence at trial.

By way of background, on July 27, 2012, Plaintiffs' counsel submitted a Citizen Petition (the "Petition"), requesting the FDA to exercise its authority to request information relating to Risperdal, gynecomastia, and prolactin.[11] Additionally, Plaintiffs' counsel requested the FDA to revoke the pediatric indication for

[11] The Petition was amended on August 27, 2012.

Risperdal (risperidone), for all generic versions of risperidone, and for Invega (paliperidone), unless and until the long-term safety of those drug products can be demonstrated. Alternatively, Plaintiffs' counsel requested that the FDA require a black-box warning for Risperdal and all generic versions of risperidone based on the lack of sufficient data to prove the drugs' safety. The FDA responded to the Petition on November 25, 2014 and denied Plaintiffs' counsel's requests for a ban or black box warning.[12]

Prior to the start of trial in this case, Plaintiffs moved to exclude evidence, arguments, references, or inferences to the FDA's November 25, 2014 response. According to Plaintiffs, the FDA's response constituted inadmissible hearsay and had no relevance to the main issues in the case. The Defendants, however, claimed the FDA's response was relevant and admissible under the official records exception to the hearsay rule. This Court ultimately granted Plaintiffs' motion and precluded the FDA's response at trial. This Court's decision was proper for the following reasons.

First, the FDA's response was inadmissible hearsay. Hearsay is defined as "a statement, other than one made by the declarant, while testifying at trial or hearing, offered in evidence to prove the truth of the matter asserted." Pa.R.E. 801(c). Hearsay is generally inadmissible unless an exception applies. One exception to the hearsay rule is the official records

[12] Plaintiffs' counsel subsequently sued the FDA, challenging its decision. At the time of trial in this case, the matter was on appeal.

exception. Section 42 Pa.C.S.A. § 6103, provides the following:

> An official record kept within this Commonwealth by any court, magisterial district judge or other government unit, or an entry therein, when admissible for any purpose, may be evidenced by an official publication thereof or by a copy attested by the officer having the legal custody of the record, or by that officer's deputy, and accompanied by a certificate that the officer has the custody. The certificate may be made by any public officer having a seal of office and having official duties with respect to the government unit in which the record is kept, authenticated by the seal of that office[.]

According to 42 Pa.C.S.A. § 6104, when an official record has been properly certified pursuant to the requirements set forth in 42 Pa.C.S.A. § 6103, the record is admissible as evidence that the governmental action or inaction disclosed therein was in fact taken. 42 Pa.C.S.A. § 6104(a). In addition, "a copy of a record authenticated as provided in section 6103 disclosing the existence or nonexistence of facts which have been recorded pursuant to an official duty … shall be admissible as evidence of the existence or nonexistence of such facts, unless the sources of information or other circumstances indicate lack of trustworthiness." *Id.* at (b).

Here, contrary to Defendants' claim, the FDA's response contained out of court statements which Defendants purported to use as evidence to prove the truth of the matter asserted and did not fit under the

official records exception to the rule against hearsay. Defendants sought to introduce the information contained in the FDA's response through Janet Arrowsmith, M.D., an expert in regulatory matters relating to pharmaceutical regulation. Dr. Arrowsmith authored an expert report, wherein she offered several opinions regarding the intent of the FDA's response. Dr. Arrowsmith specifically opined, in relevant part, that the FDA's response confirmed that Risperdal is safe and effective for children and adolescents, that gynecomastia is not a serious or clinically significant hazard, that the Risperdal label is adequate, that Risperdal's association with increases in prolactin levels and gynecomastia were well-known as possible side effects associated with antipsychotic drugs, and that reports of hyperprolactinemia and gynecomastia in the post-1993 Risperdal trials were not new events and did not meet the "newly acquired information" standard that would have necessitated a CBE change to the existing label. *See Report of Dr. Arrowsmith dated February 12, 2016*. Dr. Arrowsmith's interpretations of the FDA's out of court statements were offered for the truth of the matter asserted therein and were inadmissible as the FDA's response did not fit under the official records exception to the rule against hearsay.

Second, even if the FDA's response did not constitute inadmissible hearsay, it was nonetheless inadmissible because it was not relevant to Plaintiffs' failure to warn claims. As previously discussed, A.Y. was initially prescribed Risperdal in 2003; he stopped using Risperdal in 2013. The FDA responded to the Petition in November 2014, after the relevant time

period at issue, and did not address Plaintiffs' counsel's contentions regarding the current labeling of Risperdal. Rather, it only addressed Plaintiffs' counsel's requests to revoke the pediatric indication for Risperdal and all generic versions of risperidone or to require a black-box warning. Dr. Arrowsmith's opinions regarding the FDA's response to these requests were not relevant to whether Defendants adequately warned of the risks associated with Risperdal use, whether A.Y.'s physicians would not have prescribed Risperdal had they known of the risks, and whether Risperdal use caused A.Y.'s gynecomastia. Since Dr. Arrowsmith's opinions in this regard would not have been helpful to the jury in determining a fact in issue or in understanding the evidence, they were precluded at trial.

Finally, *assuming arguendo* that the FDA's response had evidentiary value, the danger of unfair prejudice outweighed its minimal probative value. Pa.R.E. 403. As our courts have explained, "'[u]nfair prejudice' means a tendency to suggest decision on an improper basis or to divert the jury's attention away from its duty of weighing the evidence impartially." *Id.* at cmt. Here, admitting the FDA's response at trial would have confused and distracted the jury from a fair consideration of the evidence in this case. For this reason and the others mentioned above, Defendants' claim should be dismissed.

XI. THIS COURT'S JURY INSTRUCTIONS WERE PROPER

On appeal, Defendants claim that this Court "made several errors in its jury charge that necessitate a new trial." According to Defendants, this Court erred

in (A) improperly suggesting to the jury that Janssen needed to provide A.Y. or his parents with a warning adequate to put them on notice; (B) improperly instructing the jury that it should determine whether Janssen intentionally falsified, destroyed, or concealed evidence; (C) failing to instruct the jury on Tennessee's statutory preemption of adequacy; and (D) failing to instruct the jury that punitive damages could not be awarded. Defendants' claims must fail; there was no error with regard to the jury instructions.

"Whether a jury instruction is erroneous is a question of law and is therefore subject to de novo review with no presumption of correctness." *Solomon v. First Am. National Bank of Nashville*, 774 S.W.2d 935, 940 (Tenn. Ct. App. 1989). "The legitimacy of a jury's verdict is dependent on the accuracy of the trial court's instructions […], [t]herefore, a trial court is under a duty to impart substantially accurate instructions concerning the law applicable to the matters at issue." *Hensley v. CSX Transp., Inc.*, 310 S.W.3d 824, 833 (Tenn. Ct. App. 2009). However, "[t]he judgment of a trial court will not be set aside based on an erroneous jury instruction unless it appears that the erroneous instruction more probably than not affected the judgment of the jury." Tenn. R. App. P. 36(b); *Gorman v. Earhart*, 876 S.W.2d 832, 836 (Tenn. 1994).

Trial courts need not grant a request for a jury instruction if the general jury charge already covers the substance of the requested instruction. *Borne v. Celadon Trucking Servs., Inc.*, 532 S.W.3d 274, 300 (Tenn. 2017). "Appellate courts review the entire charge as a jury would, rather than through the

practiced eye of a judge or lawyer." *Id.* at 297. In addition, jury instructions are not measured against the standard of perfection and the jury charge will not be invalidated if it "fairly defines the legal issues involved in the case and does not mislead the jury." *City of Johnson City v. Outdoor West, Inc.*, 947 S.W.2d 855, 858 (Tenn. Ct. App. 1996). Moreover "a particular instruction must be considered in the context of the entire charge." *Id.*

Reversal of a judgment is appropriate "only when the improper denial of a request for a special jury instruction has prejudiced the rights of the requesting party." *Johnson v. Tennessee Farmers Mut. Ins. Co.*, 205 S.W.3d 365, 372 (Tenn. 2006). It is not sufficient that refusal to grant the requested instruction may have affected the result, "it must affirmatively appear that it did in fact do so." *Otis v. Cambridge Mut. Fire Ins. Co.*, 850 S.W.2d 439, 446 (Tenn. 1992). "Tennessee courts view the jury charge in its entirety and consider the charge as a whole in order to determine whether the trial judge committed prejudicial error." *Id.* "It is not error to deny a requested instruction if its substance is covered in the general charge." *Id.* at 445. Here, this Court's jury instructions, when read as a whole, were proper.

A. This Court did not improperly suggest to the jury that Janssen needed to provide A.Y. or his parents with a warning adequate to put them on notice of the risks associated with Risperdal

First, Defendants argue that this Court failed to instruct the jury as to the supplier's duty to warn. N.T. 6/30/16 p.m. at 184. Defendants argue that they had a

duty to make only A.Y.'s physician aware of the risk of gynecomastia when taking Risperdal, and did not have a duty to warn A.Y. or his parents. According to Defendants, this Court's jury charge failed to adequately convey this standard. Defendants' claim is baseless.

At trial, Defendants submitted proposed jury instructions. Defendants requested, in relevant part, that this Court instruct the jury as follows:

> In this action, because the product involved is a prescription medication that can only be taken with the doctor's prescription, the expected users of Risperdal, for purposes of any warnings, are the physicians who prescribed Risperdal for [A.Y.], not [A.Y.] or his family. This is because a prescribing physician is in the best position to understand the patient's needs and assess the risks and benefits of a particular course of treatment. In order to prevail, Plaintiffs must prove that Janssen failed to warn [A.Y.]'s healthcare providers of the risk of gynecomastia and that his healthcare providers were not already aware of the risks. If the risk of gynecomastia was apparent to [A.Y.]'s physicians, Janssen was not negligent even if Janssen gave no warning about it.

This Court did not read Defendants' proposed jury charge verbatim. Rather, in instructing the jury regarding the supplier's duty to warn, this Court relied on Tennessee Pattern Instruction Civil 10.12. This Court specifically instructed the jury as follows:

> Supplier's duty to warn. A supplier who knows or reasonably should know that a product is likely to be dangerous for its intended use or foreseeable misuse has a duty to use reasonable care to warn of the product's danger or to reveal its unsafe condition.
>
> Warnings should be given to those persons whom the supplier should reasonably expect to use or to handle the product or be endangered by its use or handling if the supplier reasonably should believe those persons would not realize the danger without the warnings. The failure to fulfill this duty is negligence."

N.T. 6/30/16 a.m. at 171.

The questions presented to the jury on the verdict sheet, and read to the jury before deliberation, specified that the warning must have been directed to A.Y.'s healthcare providers:

> Now, as you deliberate, you will receive the verdict sheet. I'll read it to you. There are four questions you must answer. The first question: Was Janssen negligent by failing to provide an adequate warning to [A.Y.]'s healthcare providers about the risk of gynecomastia from taking Risperdal? There's a line to check yes, a line to check no. If you answer yes to Question 1, please proceed to Question 2. If you answer no to Question 1, plaintiff cannot recover. Do not answer any further questions and return to this Courtroom.

N.T. 6/30/16 p.m. at 182. This explanation of the verdict sheet, coupled with the above-referenced instruction regarding Defendants' duty to warn, accurately reflected the law applicable to this case. Thus, this claim should be dismissed.

B. This Court did not err in instructing the jury that it should determine whether Janssen intentionally falsified, destroyed, or concealed evidence in this case

Defendants argue that this Court improperly instructed the jury that it should determine whether Janssen intentionally falsified, destroyed, or concealed evidence. According to Defendants, there was no evidence whatsoever that Janssen falsified, destroyed, or concealed any evidence to avoid liability in the instant action. Just as this Court found no merit in Defendants' argument at trial, it finds no merit in their argument on appeal.

At the conclusion of all the evidence presented at trial, Plaintiffs requested, in part, that this Court instruct the jury as follows:

> You must determine whether the Defendants intentionally falsified, destroyed or concealed records pertaining to this case[.]
>
> For you to find that Defendants intentionally falsified, destroyed or concealed records pertaining to the case, the Plaintiff must prove by a preponderance of the evidence the following elements:
>
> 1. That Defendants intentionally falsified, destroyed or concealed Defendants' records to

> wrongfully evade liability in the case at issue; and
>
> 2. That Defendants' records contained material evidence pertaining to this case.

See Plaintiffs' Amended Proposed Points for Charge dated June 29, 2016. Plaintiffs argued the following in support of their request:

> **MR. ITKIN:** Your Honor, let me give you globally what's going on. This case is going to be decided under Tennessee law, and I don't profess to be a total expert on Tennessee law. But the defendants are going to raise an issue, if there's a jury verdict and if it exceeds, I believe, $750,000, they will try to claim that there's some sort of damage cap in Tennessee. I don't know that that claim is accurate. What our research indicates is that, if you get a finding of concealment of medical records, there's no question the cap would not apply. So what you see here is the instruction about what that means, and then later on in the verdict form we propose a question on it. So the two issues of concealment, there's two things they did. One is they locked up Table 21 from 2002 until 2015. That's a big part of our case. And then you also have the Bilker issue. So there's two issues of concealment because, even though they gave Table 21 to the FDA in October 2015, our claim goes to 2003. So we think this comes in, and we think you need this instruction so that we can get a jury finding on this issue in case, you know, we're fortunate enough.

N.T. 6/30/16 a.m. at 9-10. Defendants objected, arguing that the instruction was not applicable to this case:

> **MR. ABERNETHY:** No, but it has to do—falsified, destroyed, or concealed to wrongfully evade liability in the case at issue. Your Honor, obviously we haven't had briefing on this, but I think it's clear from the statute and from the instruction itself that this is about concealing evidence in litigation. It's not about whether you should or shouldn't have given facts to other people outside litigation. This is just extremely prejudicial, and it's not appropriate to this case. And to be suggesting to this jury that we destroyed evidence and kept it out of litigation just is irretrievably prejudicial to the defendants.

N.T. 6/30/16 a.m. at 12-13. This Court found Defendants' argument unconvincing and ultimately read Plaintiffs proposed charge to the jury.[13] N.T. 6/30/16 a.m. at 173. This Court's decision was proper.

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[13] It should be noted Defendants were permitted to rebut Plaintiffs' claims of concealment in their closing argument. Defense counsel specifically stated the following in support of their position: "I need to talk about one other question, which is Question 4, this question about Janssen falsifying, destroying, or concealing records. This is about Table 21, according to Mr. Itkin. It's about the slide from Dr. Bilker, according to Mr. Itkin. Ladies and gentlemen, those documents, even though the plaintiffs never proved what they mean or why they're important, those documents were not falsified, destroyed, or concealed. They were produced in the litigation. You saw them in this lawsuit. They are in evidence for whatever you may think of them. We didn't destroy these documents. We provided these documents. The

As discussed at length above and contrary to Defendants' claim, there was ample evidence presented at trial that Defendants intentionally falsified and concealed records in this case. To reiterate, Plaintiffs presented evidence that Defendants concealed Table 21, an internal Janssen document, that demonstrated a statistically significant link between Risperdal and gynecomastia. Instead of submitting this information to the FDA during the approval process, Defendants withheld and concealed the results for more than a decade. In addition, Plaintiffs presented evidence that Defendants hired Dr. Warren Bilker, a biostatistician, to perform a reanalysis of Table 21. The only specifics given to Dr. Bilker, who was under the control and direction of Dr. Findling and Dr. Daneman, were to refute the results in Table 21. N.T. 6/27/16 p.m. at 179. According to Plaintiffs, Dr. Bilker intentionally manipulated and retested the data multiple ways to get the results Defendants wanted. Once Dr. Bilker was able to refute the results in Table 21, the reanalysis was submitted as a letter by Dr. Daneman and Dr. Findling to The Journal of Clinical Psychiatry and published. These results, according to Plaintiffs, were inaccurate, inadequate, and misleading.

Since there was disputed evidence as to whether Defendants intentionally falsified and concealed records, it was not error for this Court to give the above-referenced instruction to the jury.

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answer to that question is no. And I've talked about that a little earlier, so I won't repeat myself on it." N.T. 6/30/16 a.m. at 126-27.

C. Defendants were not entitled to an instruction on the rebuttable statutory presumption

Next, Defendants claim that this Court failed to instruct the jury on the statutory presumption of adequacy. Defendant's claim must fail.

Under Tennessee law, there exists "a rebuttable presumption in favor of a manufacturer who complies with 'any federal or state statute or administrative regulation' in existence at the time the product was manufactured." *Tuggle v. Raymond Corp.*, 868 S.W.2d 621, 624 (Tenn. Ct. App. 1992). "The rebuttable presumption created is that the manufacturer's product is not in an 'unreasonably dangerous condition in regard to matters covered by those standards.'" *Id.* Tennessee Code Annotated Section 29-28-104 specifically provides the following:

> Compliance by a manufacturer or seller with any federal or state statute or administrative regulation existing at the time a product was manufactured and prescribing standards for design, inspection, testing, manufacture, labeling, warning or instructions for use of a product, shall raise a rebuttable presumption that the product is not in an unreasonably dangerous condition in regard to matters covered by these standards.

Tenn. Code Ann. § 29-28-104 (West). The purpose of this statute is to "give refuge to the manufacturer who is operating in good faith and [in] compliance of what the law requires him to do." *Tuggle v. Raymond Corp.*, 868 S.W.2d at 625.

According to Defendants, there was evidence presented in this case that Defendants complied with federal regulations; thus, this Court should have instructed the jury on the statutory presumption of adequacy. Defendants cited to *Clarksville-Montgomery Cnty. School Sys. v. United States Gypsum Co.*, 925 F.2d 993, 1004-05 (6th Cir. 1991) in support of their argument. Such reliance is misplaced.

In that case, the Plaintiff, Clarksville-Montgomery County School System, filed suit against the Defendant, United States Gypsum Co., for manufacturing Audicote, a product containing asbestos which was used in the construction of Plaintiff's school buildings from 1966-1970. Years later, "[i]n 1982, the Environmental Protection Agency ("EPA") issued a regulation requiring every school district in the country to inspect for the existence of friable asbestos by June 1983." *Id.* at 995. To comply with this requirement, Plaintiff hired "consultants to conduct a survey of its schools and scheduled the removal of Audicote from its buildings to take place from 1983 to 1987." *Id.* Per the regulation, all asbestos-containing materials were to be "separately removed with stringent precautions." *Id.* Plaintiff incurred significant expense as a result of Audicote's disposal. "The total cost [Plaintiff] incurred, including survey and inspection, architectural services, and removal and replacement of asbestos ceiling plaster and other contaminated material, was $1,618,135.12." *Id.*

In the suit against Defendant, Plaintiff alleged that Audicote was defective and unreasonably dangerous and that Defendant was negligent in

manufacturing Audicote due to its health hazards. Defendant denied that Audicote created any risk of harm and argued that Audicote adhered to industry standards at the time of installation. The case proceeded to trial and, after all the evidence presented, the District Court instructed the jury regarding the rebuttable presumption that arises from a manufacturer's compliance with governmental standards; the Court specifically stated the following:

> You have heard testimony in this case concerning standards governing the manufacture of acoustical plasters. If you find that the defendant complied with these regulations or standards at the time its products were manufactured concerning design, inspection or testing, this shall raise the rebuttable presumption that the product is not in an unreasonably dangerous condition in regard to the matters covered by these standards.
>
> Such a presumption is controlling only in the complete absence of contradicting facts and circumstances. Thus, if there is evidence in the case contradicting the presumption, the presumption disappears and it's for you the jury to weigh the evidence and to reach what appears to be the most probable conclusion.

Clarksville-Montgomery Cty. Sch. Sys. v. U.S. Gypsum Co., 925 F.2d 993, 1004 (6th Cir. 1991). The jury ultimately returned a verdict in favor of the Defendant. Plaintiff filed an appeal, challenging the District Court's instruction regarding the rebuttable presumption. According to Plaintiff, there was no

evidence or testimony in the record addressing Audicote's compliance with any federal or state statute or administrative regulation. The Sixth Circuit upheld the District Court's instruction against Plaintiff's assertion of reversible error, holding that although the record did not contain an overabundance of evidence on Audicote's compliance with governing standards, there was enough evidence and testimony to support the District Court's decision to instruct the jury regarding the rebuttable presumption. The Sixth Circuit specifically pointed to testimony from the building's architects who testified that they referred to federal and state codes, regulations and ordinances in preparing the building's specifications. The testimony revealed that, at the time of construction, there was no indication that asbestos was hazardous; rather, "building code inspectors considered asbestos a valuable asset." *Id.* at 1004. Only later did the regulations concerning asbestos change. This testimony "created the inference that Audicote's compliance with governing standards was one of many factors considered in preparing the specification" and provided the basis for charging the jury on the rebuttable presumption. *Id.*

The facts of the instant action are distinguishable from *Clarksville-Montgomery Cty. Sch. Sys.* Unlike the Defendant in that case, there was ample evidence in the instant action that the Janssen Defendants did not act in good faith and in compliance with government regulations. As discussed at length above, under FDA regulations, Defendants were responsible for the content of their label at all times. Defendants had a duty to create a label that adequately warned of the risks associated with Risperdal and to ensure that

the warnings remained adequate as long as Risperdal was on the market. As demonstrated by Plaintiffs at trial, Defendants failed to comply with this requirement. Defendants' label did not accurately reflect the frequency and severity of the risk of gynecomastia despite Defendants' knowledge of the true rate of gynecomastia. In addition to withholding information, Plaintiffs presented evidence that Defendants actively concealed data about Risperdal's gynecomastia risk. Since Plaintiffs presented sufficient evidence that Risperdal was not adequately labeled in compliance with FDA standards, Defendants were not entitled to an instruction on the rebuttable statutory presumption. Compare *Goins v. Clorox Co.*, 926 F.2d 559 (6th Cir. 1991) (Plaintiff introduced no evidence to challenge defendants' compliance with federal regulations; therefore, defendants were entitled to a rebuttable presumption that their products were not unreasonably dangerous).

D. This Court did not err in denying Defendants' request for an instruction on punitive damages

Finally, Defendants argue this Court failed to instruct the jury that punitive damages were not at issue and could not be awarded in this case.[14] Defendants' claim must fail. As mentioned above, the trial court is under a duty to impart substantially

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[14] Defendants also claim that this Court failed to instruct the jury that Defendants could not be liable for failing to provide information to the FDA, and that Defendants could not be liable for truthful off-label promotion. Contrary to their claim, Defendants were not entitled to any such instructions. *See e.g.*, Sections I, II, IX of this opinion.

accurate instructions concerning the law applicable to the matters at issue. Here, punitive damages were not at issue; thus, an instruction regarding punitive damages was not warranted.

On October 22, 2015, the Honorable Arnold L. New filed an Opinion wherein he ruled that Risperdal plaintiffs were barred from seeking punitive damages in Risperdal litigation pursuant to New Jersey product liability law. *See In Re: Risperdal Litigation Applicable to All Cases* (Court of Common Pleas of Philadelphia County, March Term 2010, No. 296). As such, only compensatory damages were recoverable.

Since punitive damages were not available in this case, all parties were precluded from presenting evidence on punitive damages at trial. At the conclusion of all the evidence presented, Defendants requested that this Court instruct the jury that it may not award punitive damages. This Court denied Defendants' request and instructed the jury, in relevant part, as follows:

> Damages. The fact that I'm instructing you about damages does not imply any opinion on my part as to whether damages should be awarded. If you find that the defendant is liable to the plaintiff, you must then find an amount of money damages you believe will fairly and adequately compensate the plaintiff for all the physical injury he has sustained as a result of this occurrence. The amount you award today must compensate the plaintiff completely for damages sustained in the past as well as damages the plaintiff will sustain in the future.

> Compensatory damages. If, under the Court's instructions, you find that the plaintiff is entitled to damages, then you must award plaintiff damages that will reasonably compensate the plaintiff for claimed loss or harm which has been proven by a preponderance of the evidence, provided you also find it was or will be suffered by the plaintiff and was legally caused by the act or omission upon which you base your finding of liability.
>
> Each of these elements of damages is separate. You may not duplicate damages for any element by also including that same loss or harm in another element of damage.
>
> In determining the amount of damages, you should consider the following elements: Physical pain and mental suffering. Physical pain and suffering is reasonable compensation for any physical pain and suffering, physical and mental discomfort suffered by the plaintiff, and the present cash value for pain and suffering likely to be experienced in the future. Mental suffering includes anguish, grief, shame, or worry.

N.T. 6/30/16 a.m. at 173-74. As the instruction clearly indicates, the jury was required to determine whether Plaintiffs were entitled to compensatory damages for physical pain and mental suffering. This instruction was clear and adequately conveyed the law applicable to the matters at issue.

This Court's decision not to instruct the jury on punitive damages was proper. Such an instruction

was neither relevant nor applicable to this case because punitive damages were not at issue. Introducing punitive damages for the first time during the jury charge would have confused the jury by diverting its attention to an issue that was not germane to the trial. Since the issue of damages was adequately covered in this Court's compensatory damages charge, Defendant's claim should be dismissed.

XII. THE VERDICT WAS NOT EXCESSIVE

On appeal, Defendants claim that this Court should have ordered remittitur because the amount of damages awarded by the jury was unsupported by the evidence at trial. This Court disagrees.

Appellate courts operate under the presumption that "juries are honest and conscientious and they have followed the instructions given to them." *Duran v. Hyundai Motor Am., Inc.*, 271 S.W.3d 178, 212 (Tenn. Ct. App. 2008). Whenever possible, the reviewing court must "give effect to the jury's verdict." *Id.* at 210. A judgment based on a jury's verdict may be invalidated "only when there is no material evidence to support the verdict or when the amount of the verdict is so excessive or unconscionable that it shocks the judicial conscience and amounts to a palpable injustice." *Id.* (internal citations omitted). Material evidence is "evidence material to the question in controversy, which must necessarily enter into the consideration of the controversy and by itself, or in connection with the other evidence, be determinative of the case." *Meals ex rel. Meals v. Ford Motor Co.*, 417 S.W.3d 414, 422 (Tenn. 2013).

Here, the record contained material evidence to support the jury's verdict of seventy million dollars. At trial, the jury heard testimony from Dr. Kessler, M.D., Dr. Solomon, M.D., Dr. Eker, M.D., Dr. Hughes, M.D., and A.Y.'s father, among others. As discussed at length above, these witnesses testified about the knowledge Defendants had regarding the risks associated with Risperdal, the information that Defendants concealed and withheld from the FDA and prescribers, and the ultimate effect that Defendants' actions had on A.Y. and will continue to have on him in the future.

As discussed above, at the conclusion of all the evidence presented at trial, this Court instructed the jury regarding damages. In addition to the instructions discussed in Section XI(C) above, this Court also instructed the jury as follows:

> Permanent injury. A permanent injury is an injury that the plaintiff must live with for the rest of the plaintiff's life that may result in inconvenience or the loss of physical vigor. Damages for permanent injury may be awarded whether or not it causes any pain or inconvenience.
>
> Disfigurement. Disfigurement is a specific type of permanent injury that impairs a person's beauty, symmetry, or appearance.
>
> Loss of enjoyment of life. Loss of enjoyment of life takes into account the loss of the normal enjoyments and pleasures in life in the future as well as limitations on the person's life still resulting from the injury.

> Pain and suffering, permanent injury, disfigurement, and loss of enjoyment of life are separate types of losses. A plaintiff is entitled to recover for these losses if the plaintiff proves by a preponderance of the evidence that each was caused by the defendant's fault.
>
> No definite standard or method of calculation is prescribed by law by which to fix reasonable compensation for pain and suffering, permanent injury, disfigurement, and the loss of enjoyment of life, nor is the opinion of any witness required as to the amount of such reasonable compensation.
>
> In making an award for pain and suffering, loss of enjoyment of life and/or permanent injury, you should exercise your authority with calm and reasonable judgment, and the damages you fix shall be just and reasonable in light of the evidence.

N.T. 6.30/16 a.m. at 173-76. After charging the jury on the law in the case, the jury deliberated. As mentioned above, the jury ultimately found in favor of the Plaintiffs and determined that they were entitled to a substantial award of damages. This Court did not invalidate the jury's verdict because the award was not unreasonable. *See Gillingham v. Consol Energy, Inc.*, 51 A.3d 841, 857 (Pa. Super. Ct. 2010) (recognizing that "[l]arge verdicts are not necessarily excessive verdicts."

Assessing damages in a case such as this is a difficult task. Per this Court's instructions, the jury was to consider economic and non-economic damages.

As Courts have explained, the "jury has wide latitude in assessing non-economic damages." *Meals ex rel. Meals*, 417 S.W.3d at 425. "We trust jurors to use their personal experiences and sensibilities to value the intangible harms such as pain, suffering, and the inability to engage in normal activities." *Id.* Additionally, Courts have recognized that "[d]amages for pain and suffering and for the loss of enjoyment of life are not easily quantified and do not lend themselves to easy valuation. Accordingly, determining the amount of these damages is appropriately left to the sound discretion of the jury or the judicial finder-of-fact." *Duran*, 271 S.W.3d at 210-11. Upon consideration of the evidence presented at trial and the damages sustained by Plaintiffs, this Court believes that the jury's finding should not be disturbed.

XIII. THE JURY RENDERED A VERDICT AS TO ALL DEFENDANTS

On appeal, Defendants claim that this Court should have entered judgment notwithstanding the verdict as to Johnson & Johnson and Janssen Research & Development, LLC because there was no evidence of wrongdoing as to either Defendant and the verdict form only asked the jury to render a verdict as to Janssen. Just as this Court found no merit in Defendants' claim at trial, it finds no merit in their claim on appeal.

At trial, defense counsel set forth the following argument in support of his claim that there was no evidence of wrongdoing by Defendants Johnson & Johnson and Janssen Research & Development, LLC:

> **MR. ABERNETHY:** Last issue, Your Honor, there's been no evidence whatsoever presented in this case that would establish any basis to show that two of the defendants, Johnson & Johnson or J&J PRD, made or sold the product, had any obligation to give warnings, or that there would be any obligation or any basis for liability. It's clear from the testimony that Janssen Pharmaceuticals sold the medication. But the parent company can't be held liable or an affiliate can't be held liable just because it's a parent or affiliate, and they've presented no evidence whatsoever to establish a claim against either of those companies.

N.T. 6/24/16 a.m. at 70-71. Plaintiffs' counsel disagreed with this argument:

> **MR. ITKIN:** Your Honor, we could go dig through the records and find some Johnson & Johnson stuff that has been presented through Dr. Kessler's testimony, but the way we have traditionally dealt with it is, you know, on the jury charge, calling it Janssen. We've been calling them Janssen throughout the case.

Id. This Court ultimately agreed with Plaintiffs. It was made clear throughout trial that Janssen Pharmaceuticals, Inc. and Janssen Research & Development, LLC, are wholly owned companies of Johnson & Johnson. While there was evidence that all Defendants were negligent in failing to warn of the risks associated with Risperdal, for ease of discussion and to avoid confusion at trial, Defendants were

collectively referred to as "Janssen." In keeping with that purpose, Janssen was listed on the verdict sheet. This did not mean that Johnson & Johnson and Janssen Research & Development, LLC were shielded from liability. Rather, it was understood that the jury's verdict would either impose liability on all the Defendants or none of the Defendants. As discussed above, the jury ultimately determined that the Defendants failed to adequately warn of the risk of gynecomastia associated with Risperdal use and that the Defendants' negligence was a cause of A.Y.'s gynecomastia.

Since liability was imposed on all Defendants, this claim should be dismissed. Defendants Johnson & Johnson and Janssen Research & Development, LLC were not entitled to judgment notwithstanding the verdict.

PLAINTIFFS' STATEMENT OF MATTERS COMPLAINED OF ON APPEAL:

The sole issue raised by Plaintiffs on appeal was previously addressed by the Honorable Arnold New in an Opinion dated October 22, 2015. *See In re: Risperdal Litigation*, March Term 2010, No. 296 attached hereto and marked as Exhibit "A"). This Court relies on that Opinion and incorporates by reference the arguments advanced therein.

CONCLUSION

For all the foregoing reasons, this Court respectfully requests that its judgment be affirmed in its entirety.

BY THE COURT:

[handwritten: signature]
PAULA PATRICK, J.

Appendix D

PENNSYLVANIA COURT OF COMMON PLEAS

No. 2094

A.Y., et al.,

Plaintiffs,

v.

JANSSEN PHARMACEUTICALS INC., et al.,

Defendants.

Filed: July, 5, 2016

Case Type: MASS TORT - RISPERDAL

Program: MASS TORT

TRIAL WORK SHEET

Trial Date:	Total Amount:	Number of Days	Disposit-ion Date:	Date Sheet Prepared
16-JUN-2016	☒ Jury ☐ Non-Jury Total Amount: $70,000,000.00	11	01-JUL-2016	05-JUL-2016

Full Description of Disposition (to be entered Verbatim on the Docket)

Jury verdict in favor of Plaintiff in the amount of $70 million

☐ Default Judgment/ Court Ordered	☒ Jury Verdict for Plaintiff
☐ Directed Verdict	☐ Jury Verdict for Defendant
☐ Transferred to binding arbitration	☐ Mistrial
☐ Finding for Defendant (Non-Jury)	☐ Hung Jury
☐ Finding for Plaintiff (Non-Jury)	☐ Non-Pros entered
☐ Damages Assessed	☐ Non-Suit entered
☐ Judgment entered by agreement	☐ Settled prior to assignment for trial (Team Leaders, only)

☐ Judgment entered

☐ Judgment satisfied

☐ Settled after assignment for trial

- ☐ prior to jury selection
- ☐ after jury sworn in

Appendix E

RELEVANT FEDERAL REGULATIONS

21 C.F.R. § 201.57 (2003). Specific requirements on content and format of labeling for human prescription drugs.

Each section heading listed in §201.56(d), if not omitted under § 201.56(d)(3), shall contain the following information in the following order:

(a) *Description.* (1) Under this section heading, the labeling shall contain:

(i) The proprietary name and the established name, if any, as defined in section 502(e)(2) of the act, of the drug;

(ii) The type of dosage form and the route of administration to which the labeling applies;

(iii) The same qualitative and/or quantitative ingredient information as required under § 201.100(b) for labels;

(iv) If the product is sterile, a statement of that fact;

(v) The pharmacological or therapeutic class of the drug;

(vi) The chemical name and structural formula of the drug;

(vii) If the product is radioactive, a statement of the important nuclear physical characteristics, such as the principal radiation emission data, external radiation, and physical decay characteristics.

(2) If appropriate, other important chemical or physical information, such as physical constants, or pH, shall be stated.

(b) *Clinical Pharmacology*. (1) Under this section heading, the labeling shall contain a concise factual summary of the clinical pharmacology and actions of the drug in humans. The summary may include information based on in vitro and/or animal data if the information is essential to a description of the biochemical and/or physiological mode of action of the drug or is otherwise pertinent to human therapeutics. Pharmacokinetic information that is important to safe and effective use of the drug is required, if known, e.g., degree and rate of absorption, pathways of biotransformation, percentage of dose as unchanged drug and metabolites, rate or half-time of elimination, concentration in body fluids associated with therapeutic and/or toxic effects, degree of binding to plasma proteins, degree of uptake by a particular organ or in the fetus, and passage across the blood brain barrier. Inclusion of pharmacokinetic information is restricted to that which relates to clinical use of the drug. If the pharmacological mode of action of the drug is unknown or if important metabolic or pharmacokinetic data in humans are unavailable, the labeling shall contain a statement about the lack of information.

(2) Data that demonstrate activity or effectiveness in in vitro or animal tests and that have not been shown by adequate and well-controlled clinical studies to be pertinent to clinical use may be included under this section of the labeling only under the following circumstances:

(i) In vitro data for anti-infective drugs may be included if the data are immediately preceded by the statement "The following in vitro data are available but their clinical significance is unknown."

(ii) For other classes of drugs, in vitro and animal data that have not been shown by adequate and well-controlled clinical studies, as defined in § 314.126(b) of this chapter, to be pertinent to clinical use may be used only if a waiver is granted under § 201.58 or § 314.126(b) of this chapter.

(c) *Indications and Usage.* (1) Under this section heading, the labeling shall state that:

(i) The drug is indicated in the treatment, prevention, or diagnosis of a recognized disease or condition, e.g., penicillin is indicated for the treatment of pneumonia due to susceptible pneumococci; and/or

(ii) The drug is indicated for the treatment, prevention, or diagnosis of an important manifestation of a disease or condition, e.g., chlorothiazide is indicated for the treatment of edema in patients with congestive heart failure; and/or

(iii) The drug is indicated for the relief of symptoms associated with a disease or syndrome, e.g., chlorpheniramine is indicated for the symptomatic relief of nasal congestion in patients with vasomotor rhinitis; and/or

(iv) The drug, if used for a particular indication only in conjuction with a primary mode of

therapy, e.g., diet, surgery, or some other drug, is an adjunct to the mode of therapy.

(2) All indications shall be supported by substantial evidence of effectiveness based on adequate and well-controlled studies as defined in § 314.126(b) of this chapter unless the requirement is waived under § 201.58 or § 314.126(b) of this chapter.

(3) This section of the labeling shall also contain the following additional information:

(i) If evidence is available to support the safety and effectiveness of the drug only in selected subgroups of the larger population with a disease, syndrome, or symptom under consideration, e.g., patients with mild disease or patients in a special age group, the labeling shall describe the available evidence and state the limitations of usefulness of the drug. The labeling shall also identify specific tests needed for selection or monitoring of the patients who need the drug, e.g., microbe susceptibility tests. Information on the approximate kind, degree, and duration of improvement to be anticipated shall be stated if available and shall be based on substantial evidence derived from adequate and well-controlled studies as defined in § 314.126(b) of this chapter unless the requirement is waived under § 201.58 or § 314.126(b) of this chapter. If the information is relevant to the recommended intervals between doses, the usual duration of treatment, or any modification of dosage, it shall be stated in the "Dosage and Administration" section of the labeling and referenced in this section.

(ii) If safety considerations are such that the drug should be reserved for certain situations, e.g., cases refractory to other drugs, this information shall be stated in this section.

(iii) If there are specific conditions that should be met before the drug is used on a long-term basis, e.g., demonstration of responsiveness to the drug in a short-term trial, the labeling shall identify the conditions; or, if the indications for long-term use are different from those for short-term use, the labeling shall identify the specific indications for each use.

(iv) If there is a common belief that the drug may be effective for a certain use or if there is a common use of the drug for a condition, but the preponderance of evidence related to the use or condition shows that the drug is ineffective, the Food and Drug Administration may require that the labeling state that there is a lack of evidence that the drug is effective for that use or condition.

(v) Any statements comparing the safety or effectiveness, either greater or less, of the drug with other agents for the same indication shall be supported by adequate and well-controlled studies as defined in § 314.126(b) of this chapter unless this requirement is waived under § 201.58 or § 314.126(b) of this chapter.

(d) *Contraindications.* Under this section heading, the labeling shall describe those situations in which the drug should not be used because the risk of use clearly outweighs any possible benefit. These situations include administration of the drug to patients known to have a hypersensitivity to it; use of

the drug in patients who, because of their particular age, sex, concomitant therapy, disease state, or other condition, have a substantial risk of being harmed by it; or continued use of the drug in the face of an unacceptably hazardous adverse reaction. Known hazards and not theoretical possibilities shall be listed, e.g., if hypersensitivity to the drug has not been demonstrated, it should not be listed as a contraindication. If no contraindications are known, this section of the labeling shall state "None known."

(e) *Warnings.* Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and Usage" section of the labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease or condition, and there is lack of substantial evidence of effectivenes for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these serious

adverse reactions and, if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective use of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

(f) *Precautions.* Under this section heading, the labeling shall contain the following subsections as appropriate for the drug:

(1) *General.* This subsection of the labeling shall contain information regarding any special care to be exercised by the practitioner for safe and effective use of the drug, e.g., precautions not required under any other specific section or subsection of the labeling.

(2) *Information for patients.* This subsection of the labeling shall contain information to be given to patients for safe and effective use of the drug, e.g., precautions concerning driving or the concomitant use of other substances that may have harmful additive effects. Any printed patient information or Medication Guide required under this chapter to be distributed to the patient shall be referred to under the "Precautions" section of the labeling and the full text of such patient information or Medication Guide shall be reprinted at the end of the labeling. The print size requirements for the Medication Guide set forth in § 208.20 of this chapter, however, do not apply to the Medication Guide that is reprinted in the professional labeling.

(3) *Laboratory tests.* This subsection of the labeling shall identify any laboratory tests that may be helpful in following the patient's response or in identifying possible adverse reactions. If appropriate, information shall be provided on such factors as the range of

normal and abnormal values expected in the particular situation and the recommended frequency with which tests should be done before, during, and after therapy.

(4)(i) *Drug interactions.* This subsection of the labeling shall contain specific practical guidance for the physician on preventing clinically significant drug/drug and drug/food interactions that may occur in vivo in patients taking the drug. Specific drugs or classes of drugs with which the drug to which the labeling applies may interact in vivo shall be identified, and the mechanism(s) of the interaction shall be briefly described. Information in this subsection of the labeling shall be limited to that pertaining to clinical use of the drug in patients. Drug interactions supported only by animal or in vitro experiments may not ordinarily be included, but animal or in vitro data may be used if shown to be clinically relevant. Drug incompatibilities, i.e., drug interactions that may occur when drugs are mixed in vitro, as in a solution for intravenous administration, shall be discussed under the "Dosage and Administration" section of the labeling rather than under this subsection of the labeling.

(ii) *Drug/laboratory test interactions.* This subsection of the labeling shall contain practical guidance on known interference of the drug with laboratory tests.

(5) *Carcinogenesis, mutagenesis, impairment of fertility.* This subsection of the labeling shall state whether long-term studies in animals have been

performed to evaluate carcinogenic potential and, if so, the species and results. If reproduction studies or other data in animals reveal a problem or potential problem concerning mutagenesis or impairment of fertility in either males or females, the information shall be described. Any precautionary statement on these topics shall include practical, relevant advice to the physician on the significance of these animal findings. If there is evidence from human data that the drug may be carcinogenic or mutagenic or that it impairs fertility, this information shall be included under the "Warnings" section of the labeling. Also, under "Precautions," the labeling shall state: "See 'Warnings' section for information on carcinogenesis, mutagenesis, and impairment of fertility."

(6) *Pregnancy*. This subsection of the labeling may be omitted only if the drug is not absorbed systemically and the drug is not known to have a potential for indirect harm to the fetus. For all other drugs, this subsection of the labeling shall contain the following information:

(i) *Teratogenic effects*. Under this heading the labeling shall identify one of the following categories that applies to the drug, and the labeling shall bear the statement required under the category:

(*a*) *Pregnancy category A.* If adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters), the labeling shall state: "Pregnancy Category A. Studies in pregnant women have not

shown that (*name of drug*) increases the risk of fetal abnormalities if administered during the first (*second, third, or all*) trimester(*s*) of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. Because studies cannot rule out the possibility of harm, however, (*name of drug*) should be used during pregnancy only if clearly needed." The labeling shall also contain a description of the human studies. If animal reproduction studies are available and they fail to demonstrate a risk to the fetus, the labeling shall also state: "Reproduction studies have been performed in (*kinds of animal*(*s*)) at doses up to (*x*) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to (*name of drug*)." The labeling shall also contain a description of available data on the effect of the drug on the later growth, development, and functional maturation of the child.

(*b*) *Pregnancy category B.* If animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women, the labeling shall state: "Pregnancy Category B. Reproduction studies have been performed in (*kind*(*s*) *of animal*(*s*)) at doses up to (*x*) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to (*name of drug*). There are, however, no adequate and well-controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed." If animal reproduction studies have shown an adverse effect (other than decrease in fertility), but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of a risk in later trimesters), the labeling shall state: "Pregnancy Category B. Reproduction studies in (*kind*(*s*) *of animal*(*s*)) have shown (*describe findings*) at (*x*) times the human dose. Studies in pregnant women, however, have not shown that (*name of drug*) increases the risk of abnormalities when administered during the first (*second, third, or all*) trimester(*s*) of pregnancy. Despite the animal findings, it would appear that the possibility of fetal harm is remote, if the drug is used during pregnancy. Nevertheless, because the studies in humans cannot rule out the possibility of harm, (*name of drug*) should be used during pregnancy only if clearly needed." The labeling shall also contain a description of the human studies and a description of available data on the effect of the drug on the later growth, development, and functional maturation of the child.

(*c*) *Pregnancy category C.* If animal reproduction studies have shown an adverse effect on the fetus, if there are no adequate and well-controlled studies in humans, and if

the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks, the labeling shall state: "Pregnancy Category C. (*Name of drug*) has been shown to be teratogenic (or to have an embryocidal effect or other adverse effect) in (*name*(*s*) *of species*) when given in doses (*x*) times the human dose. There are no adequate and well-controlled studies in pregnant women. (*Name of drug*) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus." The labeling shall contain a description of the animal studies. If there are no animal reproduction studies and no adequate and well-controlled studies in humans, the labeling shall state: "Pregnancy Category C. Animal reproduction studies have not been conducted with (*name of drug*). It is also not known whether (*name of drug*) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. (*Name of drug*) should be given to a pregnant woman only if clearly needed." The labeling shall contain a description of any available data on the effect of the drug on the later growth, development, and functional maturation of the child.

(*d*) *Pregnancy category D.* If there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable

despite its potential risks (for example, if the drug is needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective), the labeling shall state: "Pregnancy Category D. See 'Warnings' section." Under the "Warnings" section, the labeling states: "(*Name of drug*) can cause fetal harm when administered to a pregnant woman. (*Describe the human data and any pertinent animal data.*) If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus."

(*e*) *Pregnancy category X.* If studies in animals or humans have demonstrated fetal abnormalities or if there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both, and the risk of the use of the drug in a pregnant woman clearly outweighs any possible benefit (for example, safer drugs or other forms of therapy are available), the labeling shall state: "Pregnancy Category X. See 'Contraindications' section." Under "Contraindications," the labeling shall state: *"*(*Name of drug*) may (*can*) cause fetal harm when administered to a pregnant woman. (*Describe the human data and any pertinant animal data.*) (*Name of drug*) is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant

while taking this drug, the patient should be apprised of the potential hazard to the fetus."

(ii) *Nonteratogenic effects.* Under this heading the labeling shall contain other information on the drug's effects on reproduction and the drug's use during pregnancy that is not required specifically by one of the pregnancy categories, if the information is relevant to the safe and effective use of the drug. Information required under this heading shall include nonteratogenic effects in the fetus or newborn infant (for example, withdrawal symptoms or hypoglycemia) that may occur because of a pregnant woman's chronic use of the drug for a preexisting condition or disease.

(7) *Labor and delivery.* If the drug has a recognized use during labor or delivery (vaginal or abdominal delivery), whether or not the use is stated in the indications section of the labeling, this subsection of the labeling shall describe the available information about the effect of the drug on the mother and the fetus, on the duration of labor or delivery, on the possibility that forceps delivery or other intervention or resuscitation of the newborn will be necessary, and the effect of the drug on the later growth, development, and functional maturation of the child. If any information required under this subsection is unknown, this subsection of the labeling shall state that the information is unknown.

(8) *Nursing mothers.* (i) If a drug is absorbed systemically, this subsection of the labeling shall contain, if known, information about excretion of the drug in human milk and effects on the nursing

infant. Pertinent adverse effects observed in animal offspring shall be described.

(ii) If a drug is absorbed systemically and is known to be excreted in human milk, this subsection of the labeling shall contain one of the following statements, as appropriate. If the drug is associated with serious adverse reactions or if the drug has a known tumorigenic potential, the labeling shall state: "Because of the potential for serious adverse reactions in nursing infants from (*name of drug*) (or, "Because of the potential for tumorigenicity shown for (*name of drug*) in (*animal or human*) studies), a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother." If the drug is not associated with serious adverse reactions and does not have a known tumorigenic potential, the labeling shall state: "Caution should be exercised when (*name of drug*) is administered to a nursing woman."

(iii) If a drug is absorbed systemically and information on excretion in human milk is unknown, this subsection of the labeling shall contain one of the following statements, as appropriate. If the drug is associated with serious adverse reactions or has a known tumorigenic potential, the labeling shall state: "It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from (*name of drug*) (or, "Because of the potential for tumorigenicity

shown for (*name of drug*) in (*animal or human*) studies), a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother." If the drug is not associated with serious adverse reactions and does not have a known tumorigenic potential, the labeling shall state: "It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when (*name of drug*) is administered to a nursing woman."

(9) *Pediatric use.* (i) Pediatric population(s)/pediatric patient(s): For the purposes of paragraphs (f)(9)(ii) through (f)(9)(viii) of this setion, the terms *pediatric population(s)* and *pediatric patient(s)* are defined as the pediatric age group, from birth to 16 years, including age groups often called neonates, infants, children, and adolescents.

(ii) If there is a specific pediatric indication (i.e., an indication different from those approved for adults) that is supported by adequate and well-controlled studies in the pediatric population, it shall be described under the "Indications and Usage" section of the labeling, and appropriate pediatric dosage information shall be given under the "Dosage and Administration" section of the labeling. The "Pediatric use" subsection shall cite any limitations on the pediatric indication, need for specific monitoring, specific hazards associated with use of the drug in any subsets of the pediatric population (e.g., neonates),

differences between pediatric and adult responses to the drug, and other information related to the safe and effective pediatric use of the drug. Data summarized in this subsection of the labeling should be discussed in more detail, if appropriate, under the "Clinical Pharmacology" or "Clinical Studies" section. As appropriate, this information shall also be contained in the "Contraindications," "Warnings," and elsewhere in the "Precautions" sections.

(iii) If there are specific statements on pediatric use of the drug for an indication also approved for adults that are based on adequate and well-controlled studies in the pediatric population, they shall be summarized in the "Pediatric use" subsection of the labeling and discussed in more detail, if appropriate, under the "Clinical Pharmacology" and "Clinical Studies" sections. Appropriate pediatric dosage shall be given under the "Dosage and Administration" section of the labeling. The "Pediatric use" subsection of the labeling shall also cite any limitations on the pediatric use statement, need for specific monitoring, specific hazards associated with use of the drug in any subsets of the pediatric population (e.g., neonates), differences between pediatric and adult responses to the drug, and other information related to the safe and effective pediatric use of the drug. As appropriate, this information shall also be contained in the "Contraindications," "Warnings," and elsewhere in the "Precautions" sections.

(iv) FDA may approve a drug for pediatric use based on adequate and well-controlled studies in adults, with other information supporting pediatric use. In such cases, the agency will have concluded that the course of the disease and the effects of the drug, both beneficial and adverse, are sufficiently similar in the pediatric and adult populations to permit extrapolation from the adult efficacy data to pediatric patients. The additional information supporting pediatric use must ordinarily include data on the pharmacokinetics of the drug in the pediatric population for determination of appropriate dosage. Other information, such as data from pharmacodynamic studies of the drug in the pediatric population, data from other studies supporting the safety or effectiveness of the drug in pediatric patients, pertinent premarketing or postmarketing studies or experience, may be necessary to show that the drug can be used safely and effectively in pediatric patients. When a drug is approved for pediatric use based on adequate and well-controlled studies in adults with other information supporting pediatric use, the "Pediatric use" subsection of the labeling shall contain either the following statement, or a reasonable alternative: "The safety and effectiveness of (*drug name*) have been established in the age groups __ to __ (note any limitations, e.g., no data for pediatric patients under 2, or only applicable to certain indications approved in adults). Use of (*drug name*) in these age groups is supported by evidence from adequate and well-controlled studies of (*drug*

name) in adults with additional data (insert wording that accurately describes the data submitted to support a finding of substantial evidence of effectiveness in the pediatric population)." Data summarized in the preceding prescribed statement in this subsection of the labeling shall be discussed in more detail, if appropriate, under the "Clinical Pharmacology" or the "Clinical Studies" section. For example, pediatric pharmacokinetic or pharmacodynamic studies and dose-response information should be described in the "Clinical Pharmacology" section. Pediatric dosing instructions shall be included in the "Dosage and Administration" section of the labeling. Any differences between pediatric and adult responses, need for specific monitoring, dosing adjustments, and any other information related to safe and effective use of the drug in pediatric patients shall be cited briefly in the "Pediatric use" subsection and, as appropriate, in the "Contraindications," "Warnings," "Precautions," and "Dosage and Administration" sections.

(v) If the requirements for a finding of substantial evidence to support a pediatric indication or a pediatric use statement have not been met for a particular pediatric population, the "Pediatric use" subsection of the labeling shall contain an appropriate statement such as "Safety and effectiveness in pediatric patients below the age of (__) have not been established." If use of the drug in this pediatric population is associated with a specific hazard, the hazard shall be described in this subsection of the labeling, or, if

appropriate, the hazard shall be stated in the "Contraindications" or "Warnings" section of the labeling and this subsection shall refer to it.

(vi) If the requirements for a finding of substantial evidence to support a pediatric indication or a pediatric use statement have not been met for any pediatric population, this subsection of the labeling shall contain the following statement: "Safety and effectiveness in pediatric patients have not been established." If use of the drug in premature or neonatal infants, or other pediatric subgroups, is associated with a specific hazard, the hazard shall be described in this subsection of the labeling, or, if appropriate, the hazard shall be stated in the "Contraindications" or "Warnings" section of the labeling and this subsection shall refer to it.

(vii) If the sponsor believes that none of the statements described in paragraphs (f)(9)(ii) through (f)(9)(vi) of this section is appropriate or relevant to the labeling of a particular drug, the sponsor shall provide reasons for omission of the statements and may propose alternative statement(s). FDA may permit use of an alternative statement if FDA determines that no statement described in those paragraphs is appropriate or relevant to the drug's labeling and that the alternative statement is accurate and appropriate.

(viii) If the drug product contains one or more inactive ingredients that present an increased risk of toxic effects to neonates or other pediatric subgroups, a special note of this risk shall be

made, generally in the "Contraindications," "Warnings," or "Precautions" section.

(10) *Geriatric use.* (i) A specific geriatric indication, if any, that is supported by adequate and well-controlled studies in the geriatric population shall be described under the "Indications and Usage" section of the labeling, and appropriate geriatric dosage shall be stated under the "Dosage and Administration" section of the labeling. The "Geriatric use" subsection shall cite any limitations on the geriatric indication, need for specific monitoring, specific hazards associated with the geriatric indication, and other information related to the safe and effective use of the drug in the geriatric population. Unless otherwise noted, information contained in the "Geriatric use" subsection of the labeling shall pertain to use of the drug in persons 65 years of age and older. Data summarized in this subsection of the labeling shall be discussed in more detail, if appropriate, under "Clinical Pharmacology" or the "Clinical Studies" section. As appropriate, this information shall also be contained in "Contraindications," "Warnings," and elsewhere in "Precautions."

(ii) Specific statements on geriatric use of the drug for an indication approved for adults generally, as distinguished from a specific geriatric indication, shall be contained in the "Geriatric use" subsection and shall reflect all information available to the sponsor that is relevant to the appropriate use of the drug in elderly patients. This information includes

detailed results from controlled studies that are available to the sponsor and pertinent information from well-documented studies obtained from a literature search. Controlled studies include those that are part of the marketing application and other relevant studies available to the sponsor that have not been previously submitted in the investigational new drug application, new drug application, biological license application, or a supplement or amendment to one of these applications (e.g., postmarketing studies or adverse drug reaction reports). The "Geriatric use" subsection shall contain the following statement(s) or reasonable alternative, as applicable, taking into account available information:

(A) If clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether elderly subjects respond differently from younger subjects, and other reported clinical experience has not identified such differences, the "Geriatric use" subsection shall include the following statement:

"Clinical studies of (name of drug) did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose

> selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy."

(B) If clinical studies (including studies that are part of marketing applications and other relevant studies available to the sponsor that have not been submitted in the sponsor's applications) included enough elderly subjects to make it likely that differences in safety or effectiveness between elderly and younger subjects would have been detected, but no such differences (in safety or effectiveness) were observed, and other reported clinical experience has not identified such differences, the "Geriatric use" subsection shall contain the following statement:

> Of the total number of subjects in clinical studies of (name of drug), __ percent were 65 and over, while __ percent were 75 and over. (Alternatively, the labeling may state the total number of subjects included in the studies who were 65 and over and 75 and over.) No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience

has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

(C) If evidence from clinical studies and other reported clinical experience available to the sponsor indicates that use of the drug in elderly patients is associated with differences in safety or effectiveness, or requires specific monitoring or dosage adjustment, the "Geriatric use" subsection of the labeling shall contain a brief description of observed differences or specific monitoring or dosage requirements and, as appropriate, shall refer to more detailed discussions in the "Contraindications," "Warnings," "Dosage and Administration," or other sections of the labeling.

(iii)(A) If specific pharmacokinetic or pharmacodynamic studies have been carried out in the elderly, they shall be described briefly in the "Geriatric use" subsection of the labeling and in detail under the "Clinical Pharmacology" section. The "Clinical Pharmacology" section and "Drug interactions" subsection of the "Precautions" section ordinarily contain information on drug-disease and drug-drug interactions that is particularly relevant to the elderly, who are more likely to have concomitant illness and to utilize concomitant drugs.

(B) If a drug is known to be substantially excreted by the kidney, the "Geriatric use" subsection shall include the statement:

> "This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function."

(iv) If use of the drug in the elderly appears to cause a specific hazard, the hazard shall be described in the "Geriatric use" subsection of the labeling, or, if appropriate, the hazard shall be stated in the "Contraindications," "Warnings," or "Precautions" section of the labeling, and the "Geriatric use" subsection shall refer to those sections.

(v) Labeling under paragraphs (f)(10)(i) through (f)(10)(iii) of this section may include statements, if they would be useful in enhancing safe use of the drug, that reflect good clinical practice or past experience in a particular situation, e.g., for a sedating drug, it could be stated that:

> "Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of (name of drug) and observed closely."

(vi) If the sponsor believes that none of the requirements described in paragraphs (f)(10)(i) through (f)(10)(v) of this section is appropriate or relevant to the labeling of a particular drug, the sponsor shall provide reasons for omission of the statements and may propose an alternative statement. FDA may permit omission of the statements if FDA determines that no statement described in those paragraphs is appropriate or relevant to the drug's labeling. FDA may permit use of an alternative statement if the agency determines that such statement is accurate and appropriate.

(g) *Adverse Reactions.* An adverse reaction is an undesirable effect, reasonably associated with the use of the drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence.

(1) This section of the labeling shall list the adverse reactions that occur with the drug and with drugs in the same pharmacologically active and chemically related class, if applicable.

(2) In this listing, adverse reactions may be categorized by organ system, by severity of the reaction, by frequency, or by toxicological mechanism, or by a combination of these, as appropriate. If frequency information from adequate clinical studies is available, the categories and the adverse reactions within each category shall be listed in decreasing order of frequency. An adverse reaction that is significantly more severe than the other reactions listed in a category, however, shall be listed before those reactions, regardless of its frequency. If

frequency information from adequate clinical studies is not available, the categories and adverse reactions within each category shall be listed in decreasing order of severity. The approximate frequency of each adverse reaction shall be expressed in rough estimates or orders of magnitude essentially as follows: "The most frequent adverse reaction(s) to (*name of drug*) is (are) (*list reactions*). This (these) occur(s) in about (e.g., one-third of patients; one in 30 patients; less than one-tenth of patients). Less frequent adverse reactions are (*list reactions*), which occur in approximately (e.g., one in 100 patients). Other adverse reactions, which occur rarely, in approximately (e.g., one in 1,000 patients), are (*list reactions*)." Percent figures may not ordinarily be used unless they are documented by adequate and well-controlled studies as defined in § 314.126(b) of this chapter, they are shown to reflect general experience, and they do not falsely imply a greater degree of accuracy than actually exists.

(3) The "Warnings" section of the labeling or, if appropriate, the "Contraindications" section of the labeling shall identify any potentially fatal adverse reaction.

(4) Any claim comparing the drug to which the labeling applies with other drugs in terms of frequency, severity, or character of adverse reactions shall be based on adequate and well-controlled studies as defined in § 314.126(b) of this chapter unless this requirement is waived under § 201.58 or § 314.126(b) of this chapter.

(h) *Drug Abuse and Dependence.* Under this section heading, the labeling shall contain the following subsections, as appropriate for the drug:

(1) *Controlled Substance.* If the drug is controlled by the Drug Enforcement Administration, the schedule in which it is controlled shall be stated.

(2) *Abuse.* This subsection of the labeling shall be based primarily on human data and human experience, but pertinent animal data may also be used. This subsection shall state the types of abuse that can occur with the drug and the adverse reactions pertinent to them. Particularly susceptible patient populations shall be identified.

(3) *Dependence.* This subsection of the labeling shall describe characteristic effects resulting from both psychological and physical dependence that occur with the drug and shall identify the quantity of the drug over a period of time that may lead to tolerance or dependence, or both. Details shall be provided on the adverse effects of chronic abuse and the effects of abrupt withdrawal. Procedures necessary to diagnose the dependent state shall be provided, and the principles of treating the effects of abrupt withdrawal shall be described.

(i) *Overdosage.* Under this section heading, the labeling shall describe the signs, symptoms, and laboratory findings of acute overdosage and the general principles of treatment. This section shall be based on human data, when available. If human data are unavailable, appropriate animal and in vitro data may be used. Specific information shall be provided about the following:

(1) Signs, symptoms, and laboratory findings associated with an overdosage of the drug.

(2) Complications that can occur with the drug (for example, organ toxicity or delayed acidosis).

(3) Oral LD_{50} of the drug in animals; concentrations of the drug in biologic fluids associated with toxicity and/or death; physiologic variables influencing excretion of the drug, such as urine pH; and factors that influence the dose response relationship of the drug, such as tolerance. The pharmacokinetic data given in the "Clinical Pharmacology" section also may be referenced here, if applicable to overdoses.

(4) The amount of the drug in a single dose that is ordinarily associated with symptoms of overdosage and the amount of the drug in a single dose that is likely to be life-threatening.

(5) Whether the drug is dialyzable.

(6) Recommended general treatment procedures and specific measures for support of vital functions, such as proven antidotes, induced emesis, gastric lavage, and forced diuresis. Unqualified recommendations for which data are lacking with the specific drug or class of drugs, especially treatment using another drug (for example, central nervous system stimulants, respiratory stimulants) may not be stated unless specific data or

scientific rationale exists to support safe and effective use.

(j) *Dosage and Administration.* This section of the labeling shall state the recommended usual dose, the usual dosage range, and, if appropriate, an upper limit beyond which safety and effectiveness have not been established; dosages shall be stated for each indication when appropriate. This section shall also state the intervals recommended between doses, the optimal method of titrating dosage, the usual duration of treatment, and any modification of dosage needed in special patient populations, e.g., in children, in geriatric age groups, or in patients with renal or hepatic disease. Specific tables or monographs may be included to clarify dosage schedules. Radiation dosimetry information shall be stated for both the patient receiving a radioactive drug and the person administering it. This section shall also contain specific direction on dilution, preparation (including the strength of the final dosage solution, when prepared according to instructions, in terms of milligrams active ingredient per milliliter of reconstituted solution, unless another measure of the strength is more appropriate), and administration of the dosage form, if needed, e.g., the rate of administration of parenteral drug in milligrams per minute; storage conditions for stability of the drug or reconstituted drug, when important; essential information on drug incompatibilities if the drug is mixed in vitro with other drugs; and the following statement for parenterals: "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."

(k) *How Supplied.* This section of the labeling shall contain information on the available dosage forms to which the labeling applies and for which the manufacturer or distributor is responsible. The information shall ordinarily include:

(1) The strength of the dosage form, e.g., 10-milligram tablets, in metric system and, if the apothecary system is used, a statement of the strength is placed in parentheses after the metric designation;

(2) The units in which the dosage form is ordinarily available for prescribing by practitioners, e.g., bottles of 100;

(3) Appropriate information to facilitate identification of the dosage forms, such as shape, color, coating, scoring, and National Drug Code; and

(4) Special handling and storage conditions.

(*l*) *Animal Pharmacology and/or Animal Toxicology.* In most cases, the labeling need not include this section. Significant animal data necessary for safe and effective use of the drug in humans shall ordinarily be included in one or more of the other sections of the labeling, as appropriate. Commonly for a drug that has been marketed for a long time, and in rare cases for a new drug, chronic animal toxicity studies have not been performed or completed for a drug that is administered over prolonged periods or is implanted in the body. The unavailability of such data shall be stated in the appropriate section of the labeling for the drug. If the pertinent animal data cannot be appropriately incorporated into other sections of the labeling, this section may be used.

(m) *"Clinical Studies" and "References".* These sections may appear in labeling in the place of a detailed discussion of a subject that is of limited interest but nonetheless important. A reference to a specific important clinical study may be made in any section of the format required under §§ 201.56 and 201.57 if the study is essential to an understandable presentation of the available information. References may appear in sections of the labeling format, other than the "Clinical Studies" or "References" section, in rare circumstances only. A clinical study or reference may be cited in prescription drug labeling only under the following conditions:

(1) If the clinical study or reference is cited in the labeling in the place of a detailed discussion of data and information concerning an indication for use of the drug, the reference shall be based upon, or the clinical study shall constitute, an adequate and well-controlled clinical investigation under § 314.126(b) of this chapter.

(2) If the clinical study or reference is cited in the labeling in the place of a detailed discussion of data and information concerning a risk or risks from the use of the drug, the risk or risks shall also be identified or discussed in the appropriate section of the labeling for the drug.

21 C.F.R. § 314.70 (2003). Supplements and other changes to an approved application.

(a) *Changes to an approved application.* The applicant shall notify FDA about each change in each condition established in an approved application beyond the variations already provided for in the application. The notice is required to describe the

change fully. Depending on the type of change, the applicant shall notify FDA about it in a supplemental application under paragraph (b) or (c) of this section or by inclusion of the information in the annual report to the application under paragraph (d) of this section. Notwithstanding the requirements of paragraphs (b) and (c) of this section, an applicant shall make a change provided for in those paragraphs (for example, the deletion of an ingredient common to many drug products) in accordance with a notice, or regulation published in the FEDERAL REGISTER that provides for a less burdensome notification of the change (for example, by notification at the time a supplement is submitted or in the next annual report). Except for a supplemental application providing for a change in the labeling, the applicant, other than a foreign applicant, shall include in each supplemental application providing for a change under paragraph (b) or (c) of this section a statement certifying that a field copy of the supplement has been provided to the applicant's home FDA district office.

(b) *Supplements requiring FDA approval before the change is made.* An applicant shall submit a supplement, and obtain FDA approval of it, before making the changes listed below in the conditions in an approved application, unless the change is made to comply with an official compendium. An applicant may ask FDA to expedite its review of a supplement if a delay in making the change described in it would impose an extraordinary hardship on the applicant. Such a supplement and its mailing cover should be plainly marked: "Supplement—Expedited Review Requested."

(1) *Drug substance.* A change affecting the drug substance to accomplish any of the following:

(i) To relax the limits for a specification;

(ii) To establish a new regulatory analytical method;

(iii) To delete a specification or regulatory analytical method;

(iv) To change the synthesis of the drug substance, including a change in solvents and a change in the route of synthesis.

(v) To use a different facility or establishment to manufacture the drug substance, where: (*a*) the manufacturing process in the new facility or establishment differs materially from that in the former facility or establishment, or (*b*) the new facility or establishment has not received a satisfactory current good manufacturing practice (CGMP) inspection within the previous 2 years covering that manufacturing process.

(2) *Drug product.* A change affecting the drug product to accomplish any of the following:

(i) To add or delete an ingredient, or otherwise to change the composition of the drug product, other than deletion of an ingredient intended only to affect the color of the drug product;

(ii) To relax the limits for a specification;

(iii) To establish a new regulatory analytical method;

(iv) To delete a specification or regulatory analytical method;

(v) To change the method of manufacture of the drug product, including changing or relaxing an in-process control;

(vi) To use a different facility or establishment, including a different contract laboratory or labeler, to manufacture, process, or pack the drug product;

(vii) To change the container and closure system for the drug product (for example, glass to high density polyethylene (HDPE), or HDPE to polyvinyl chloride) or change a specification or regulatory analytical method for the container and closure system;

(viii) To change the size of the container, except for solid dosage forms, without a change in the container and closure system.

(ix) To extend the expiration date of the drug product based on data obtained under a new or revised stability testing protocol that has not been approved in the application.

(x) To establish a new procedure for reprocessing a batch of the drug product that fails to meet specifications.

(xi) To add a code imprint by printing with ink on a solid oral dosage form drug product.

(xii) To add a code imprint by embossing, debossing, or engraving on a modified release solid oral dosage form drug product.

(3) *Labeling.* (i) Any change in labeling, except one described in paragraphs (c)(2) or (d) of this section.

(ii) If applicable, any change to a Medication Guide required under part 208 of this chapter, except for changes in the information specified in § 208.20(b)(8)(iii) and (b)(8)(iv).

(c) *Supplements for changes that may be made before FDA approval.* An applicant shall submit a supplement at the time the applicant makes any kind of change listed below in the conditions in an approved application, unless the change is made to comply with an official compendium. A supplement under this paragraph is required to give a full explanation of the basis for the change, identify the date on which the change is made, and, if the change concerns labeling, include 12 copies of final printed labeling. The applicant shall promptly revise all promotional labeling and drug advertising to make it consistent with any change in the labeling. The supplement and its mailing cover should be plainly marked: "Special Supplement—Changes Being Effected."

(1) Adds a new specification or test method or changes in the methods, facilities (except a change to a new facility), or controls to provide increased assurance that the drug will have the characteristics of identity, strength, quality, and purity which it purports or is represented to possess;

(2) Changes labeling to accomplish any of the following:

(i) To add or strengthen a contraindication, warning, precaution, or adverse reaction;

(ii) To add or strengthen a statement about drug abuse, dependence, or over-dosage; or

(iii) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the product.

(iv) To delete false, misleading, or unsupported indications for use or claims for effectiveness.

(3) To use a different facility or establishment to manufacture the drug substance, where: (i) The manufacturing process in the new facility or establishment does not differ materially from that in the former facility or establishment, and (ii) the new facility or establishment has received a satisfactory current good manufacturing practice (CGMP) inspection within the previous 2 years covering that manufacturing process.

(d) *Changes described in the annual report.* An applicant shall not submit a supplement to make any change in the conditions in an approved application, unless otherwise required under paragraph (b) or (c) of this section, but shall describe the change in the next annual report required under § 314.81. Some examples of changes that can be described in the annual report are the following:

(1) Any change made to comply with an official compendium.

(2) A change in the labeling concerning the description of the drug product or in the information about how the drug product is supplied, that does not involve a change in the dosage strength or dosage form.

(3) An editorial or similar minor change in labeling.

(4) The deletion of an ingredient intended only to affect the color of the drug product.

(5) An extension of the expiration date based upon full shelf-life data obtained from a protocol approved in the application.

(6) A change within the container and closure system for the drug product (for example, a change from one high density polyethylene (HDPE) to another HDPE), except a change in container size for nonsolid dosage forms, based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium.

(7) The addition or deletion of an alternate analytical method.

(8) A change in the size of a container for a solid dosage form, without a change from one container and closure system to another.

(9) The addition by embossing, debossing, or engraving of a code imprint to a solid oral dosage form drug product other than a modified release dosage form, or a minor change in an existing code imprint.

(e) *Patent information.* The applicant shall comply with the patent information requirements under section 505(c)(2) of the act.

(f) *Claimed exclusivity.* If an applicant claims exclusivity under § 314.108 upon approval of a supplemental application for a change to its previously approved drug product, the applicant shall include with its supplemental application the information required under § 314.50(j).

(g) *Exception.* An applicant proposing to make a change of a type described in paragraphs (a), (b)(1), (b)(2), (c)(1), (c)(3), (d)(1), and (d)(4) through (d)(9) of this section affecting a recombinant DNA-derived

protein/polypeptide product or a complex or conjugate of a drug with a monoclonal antibody regulated under the Federal Food, Drug, and Cosmetic Act shall comply with the following:

(1) *Changes requiring supplement submission and approval prior to distribution of the product made using the change (major changes).* (i) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, or facilities that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(ii) These changes include, but are not limited to:

(A) Changes in the qualitative or quantitative formulation or other specifications as provided in the approved application or in the regulations;

(B) Changes requiring completion of an appropriate human study to demonstrate the equivalence of the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(C) Changes in the virus or adventitious agent removal or inactivation method(s);

(D) Changes in the source material or cell line;

(E) Establishment of a new master cell bank or seed; and

(F) Changes which may affect product sterility assurance, such as changes in

product or component sterilization method(s) or an addition, deletion, or substitution of steps in an aseptic processing operation.

(iii) The applicant must obtain approval of the supplement from FDA prior to distribution of the product made using the change. Except for submissions under paragraph (g)(4) of this section, the following shall be contained in the supplement:

(A) A detailed description of the proposed change;

(B) The product(s) involved;

(C) The manufacturing site(s) or area(s) affected;

(D) A description of the methods used and studies performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(E) The data derived from such studies;

(F) Relevant validation protocols and data; and

(G) A reference list of relevant standard operating procedures (SOP's).

(2) *Changes requiring supplement submission at least 30 days prior to distribution of the product made using the change.* (i) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, or facilities that has a moderate potential to have an adverse effect on the identity,

strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. The supplement shall be labeled "Supplement—Changes Being Effected in 30 Days" or, if applicable under paragraph (g)(2)(v) of this section, "Supplement—Changes Being Effected."

(ii) These changes include, but are not limited to:

(A) Change in the site of testing from one facility to another;

(B) An increase or decrease in production scale during finishing steps that involves new or different equipment; and

(C) Replacement of equipment with that of similar, but not identical, design and operating principle that does not affect the process methodology or process operating parameters.

(iii) Pending approval of the supplement by FDA, and except as provided in paragraph (g)(2)(v) of this section, distribution of the product made using the change may begin not less than 30 days after receipt of the supplement by FDA. The information listed in paragraph (g)(1)(iii)(A) through (g)(1)(iii)(G) of this section shall be contained in the supplement.

(iv) If within 30 days following FDA's receipt of the supplement, FDA informs the applicant that either:

(A) The change requires approval prior to distribution of the product in accordance with paragraph (g)(1) of this section; or

(B) Any of the information required under paragraph (g)(2)(iii) of this section is missing; the applicant shall not distribute the product made using the change until FDA determines that compliance with this section is achieved.

(v) In certain circumstances, FDA may determine that, based on experience with a particular type of change, the supplement for such change is usually complete and provides the proper information, and on particular assurances that the proposed change has been appropriately submitted, the product made using the change may be distributed immediately upon receipt of the supplement by FDA. These circumstances may include substantial similarity with a type of change regularly involving a "Supplement—Changes Being Effected" supplement, or a situation in which the applicant presents evidence that the proposed change has been validated in accordance with an approved protocol for such change under paragraph (g)(4) of this section.

(3) *Changes to be described in an annual report (minor changes).* (i) Changes in the product, production process, quality controls, equipment, or facilities that have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product shall be documented by the applicant in the next annual report in accordance with § 314.81(b)(2)(iv).

(ii) These changes include, but are not limited to:

(A) Any change made to comply with an official compendium that is consistent with FDA requirements;

(B) The deletion of an ingredient intended only to affect the color of the product;

(C) An extension of an expiration date based upon full shelf life data obtained from a protocol approved in the application;

(D) A change within the container and closure system for solid dosage forms, based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium;

(E) A change in the size of a container for a solid dosage form, without a change from one container and closure system to another;

(F) The addition by embossing, debossing, or engraving of a code imprint to a solid dosage form drug product other than a modified release dosage form, or a minor change in an existing code imprint; and

(G) The addition or deletion of an alternate analytical method.

(4) An applicant may submit one or more protocols describing the specific tests and validation studies and acceptable limits to be achieved to demonstrate the lack of adverse effect for specified types of manufacturing changes on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. Any such protocols, or change to a protocol, shall be

submitted as a supplement requiring approval from FDA prior to distribution of the product which, if approved, may justify a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect.