2019 PA Super 217

T.M. AND BRENDA TINKHAM APPELLANTS v. JANSSEN PHARMACEUTICALS INC.; JOHNSON & JOHNSON; JANSSEN RESEARCH & DEVELOPMENT, LLC; EXCERPTA MEDICA, INC.; AND ELSEVIER INC.,	:	IN THE SUPERIOR COURT OF PENNSYLVANIA No. 184 EDA 2018

Appeal from the Judgment Entered December 4, 2017
In the Court of Common Pleas of Philadelphia County Civil Division at
No(s): 1076 May Term, 2013

BEFORE: BOWES, J., STABILE, J., and McLAUGHLIN, J.

OPINION BY BOWES, J.: **FILED JULY 16, 2019**

T.M. and his mother, Brenda Tinkham, ("Plaintiffs") appeal from the December 4, 2017 judgment entered in favor of Janssen Pharmaceuticals, Inc., Johnson & Johnson, Janssen Research & Development, LLC ("Janssen"),[1] following entry of a compulsory nonsuit in their action seeking damages for the drug manufacturer's failure to adequately warn of the risk of gynecomastia

[1] Defendants Excerpta Medica, Inc. and Elsevier, Inc. were dismissed from the case earlier and are not involved in the instant appeal. "Janssen Pharmaceuticals, Inc. and Janssen Research & Development, LLC, are wholly owned companies of Johnson & Johnson." ***Pledger v. Janssen Pharms., Inc.***, 198 A.3d 1126, 1130 n.1 (Pa.Super. 2018).

associated with Risperdal use in children.[2] We vacate the judgment, reverse the order entering a compulsory nonsuit, and remand for a new trial.

We glean the following from the evidence offered by Plaintiffs at trial. In 2004, T.M. was seven years old and living with his family in Wichita Falls, Texas.[3] When he began acting out in school, his parents arranged for a mental health evaluation at the Rose Street Mental Health Clinic. Physician Assistant John Dewar diagnosed him with attention deficit hyperactivity disorder ("ADHD"), oppositional defiant disorder ("ODD"), and depression, and under the supervision of pediatric psychiatrists Harvey Martin, M.D. and Brian Wieck, M.D., prescribed Risperdal for T.M. Risperdal was not approved by the Food and Drug Administration ("FDA") for use in children, or for the indication for which it was prescribed. As approved, the drug was indicated only for adults with schizophrenia. Thus, Risperdal was prescribed for T.M. for an off-label

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[2] Gynecomastia is "a condition where female breast tissue grows in males." ***Murray v. Janssen Pharmaceuticals, Inc.***, 180 A.3d 1235, 1238 (Pa.Super. 2018). This case is one of more than five thousand cases coordinated in Philadelphia's Complex Litigation Center under the caption ***In re Risperdal Litigation***, involving males who allegedly developed gynecomastia as a result of taking the prescription drug Risperdal. ***Murray, supra*** at 1238.

[3] T.M. grew up in an Air Force family that moved from base to base throughout the United States. Although he was originally prescribed Risperdal in Texas, use of Risperdal continued when T.M. moved to the state of Washington. He was diagnosed with gynecomastia when he lived in Nebraska. The parties agree that Pennsylvania's procedural law governs this litigation, and that Texas's substantive law applies.

use.[4] At the time, Risperdal was known to cause increased prolactin levels associated with gynecomastia and other endocrine disorders. T.M. remained on Risperdal for three and one-half years. In 2006, T.M. developed breasts.

In May 2013, Plaintiffs filed the instant case against Janssen, the manufacturer and distributor of Risperdal, alleging negligent failure to provide adequate warnings of the known risk of gynecomastia associated with its drug,[5] and fraud. A jury trial commenced on November 28, 2016.

At trial, Plaintiffs offered the testimony of David Kessler, M.D, a physician specializing in pediatric medicine and public health, who served as the Commissioner of the FDA from 1990 through 1997, and who was formerly a biostatistics professor at the University of California and Dean of the Yale Medical School. Dr. Kessler provided expert testimony establishing that

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[4] "Off-label use" is the use of an FDA-approved drug for an unapproved use. Healthcare providers have the authority to prescribe a drug off-label, *i.e.*, for an indication for which it has not received FDA approval.

[5] Texas law recognizes a products liability cause of action for failure to warn in a pharmaceutical case. However, the Texas Products Liability Act ("TPLA") provides that there is a rebuttable presumption that defendants are not liable if the warnings or information accompanying the product are FDA approved. The presumption may be rebutted by proving that, *inter alia*, the defendant withheld or misrepresented material information to the FDA that was causally related to the injury, or the defendant promoted or advertised or recommended the product for an indication that was not FDA approved, it was used as promoted, and the claimant's injury was causally related to the promoted use of the product. ***See*** Tex. Civ. Prac. & Rem. Code § 82.007, effective September 1, 2003.

Janssen had a duty to warn of the known risks of gynecomastia with Risperdal use, and that it breached that duty. Dr. Kessler traced the history of Risperdal, explaining that it was a second-generation antipsychotic drug manufactured and marketed by Janssen. It was first approved by the FDA in 1993 for the treatment of adults with psychotic disorders such as schizophrenia. In 1996, Janssen asked the FDA for permission to include dosing information for children on the label as it was "aware that Risperdal was being utilized in children in adolescence" for off-label uses such as ADHD. Videotaped Deposition of David Kessler, M.D. 12/2/16, at 36.[6] The FDA refused the request, citing "inadequate support for the changes sought." ***Id***. at 40. Specifically, the FDA cited the "meager safety data" for Risperdal's pediatric use, and it feared that the proposed labeling would promote use in pediatric patients without justification. ***Id***. at 41-42; ***see also*** Plaintiffs' Exhibit 8 (letter from Paul Leber, M.D. to Janssen, 9/17/97).

Plaintiffs offered into evidence the 2002 package insert for Risperdal, often referred to as the "label." Plaintiffs' Exhibit 2. Dr. Kessler pointed to language therein that the drug's "[s]afety and effectiveness in children have not been established." ***Id***. Under "Precautions," the label listed "hyperprolactinemia," a condition in which one has higher than normal serum

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[6] The videotaped deposition of David Kessler, M.D., was taken on May 19 and 20, 2015, for use in the Risperdal litigation generally. It was played to the jury in this case commencing on December 2, 2016, and the page references are to the Designation Run Report.

levels of the hormone prolactin, the main function of which is to stimulate breast milk production after childbirth. The label also provided that "[a]s with other drugs that antagonize dopamine D receptors," elevated prolactin levels persisted "during chronic administration." ***Id***. at 42. The label acknowledged that although disturbances such as galactorrhea (the expression of breast milk), amenorrhea (absence of menstrual period), impotence, and gynecomastia (feminization of the male breast) had been reported with prolactin-elevating compounds, it stated that, "the clinical significance of elevated prolactin levels is unknown for most patients." ***Id***. at 18, 21. The contents of the Risperdal label remained the same until 2006.

Dr. Kessler testified that, in 2004, when Risperdal was prescribed off-label for T.M., Janssen was actively marketing the drug to physicians for off-label use in children. Janssen's July 29, 2002 business plan listed strategic initiatives associated with gaining acceptance of the usage of antipsychotics in child and adolescent psychology. Plaintiffs' Exhibit 19. This included "establishing Risperdal as having a favorable risk/benefit ratio" and "neutraliz[ing] safety and tolerability concerns." ***Id***.; Videotaped Deposition of David Kessler, M.D., ***supra*** at 82.

In 2006, the Risperdal label was changed. Pediatric use fell under the "Precautions" section of the 2006 label. The label indicated that Risperdal was approved by the FDA for use in children to treat irritability associated with autism, and that its safety and efficacy in treating children with schizophrenia

and bipolar mania had not been established. It reported that Risperdal's safety and efficacy had been established in short-term clinical trials in autistic children ages five to sixteen; longer term studies in autistic children; and other short-term and long-term studies of children with other psychiatric disorders. For the first time, the label disclosed that Risperdal was associated with higher prolactin levels than other antipsychotic drugs in the same class. Again, it warned of hyperprolactinemia, and the conditions associated with it, including gynecomastia, but stated that the risk of such side effects was "rare."[7] Plaintiffs' Exhibit 3 (2006 Label). In 2007, the label was updated to warn that the incidence of gynecomastia with the use of Risperdal was 2.3 percent.

Dr. Kessler then surveyed the studies and clinical trials Janssen had undertaken to test the safety and efficacy of Risperdal in young children and adolescents. Janssen carried out two short-term double-blind studies of children and adolescents ages five to seventeen years of age, completed in 2000, which demonstrated that forty-nine percent of the children who received Risperdal had elevated prolactin levels as compared to two percent of children who received a placebo. From the foregoing, the expert concluded that the results showed a statistically significant association between ingestion

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[7] "Rare" was defined on the label as events "occurring in fewer than one in a thousand patients." Plaintiffs' Exhibits 2 and 3. "Infrequent" was defined as "occurring in more than one in a hundred patients, but less than one in one thousand patients. ***Id***. "Frequent" meant that the risk occurred in at least one in one hundred patients. ***Id***.

of Risperdal and higher prolactin levels and, further, that higher prolactin levels were known to be associated with certain conditions, including gynecomastia.

Dr. Kessler explained that, in 2000, Janssen initiated an international study known as RIS-INT-41, which was intended to pay special attention to gynecomastia in boys and other prolactin-related events in children taking Risperdal. Risperdal was administered in two different doses to children with various levels of mental retardation and conduct disorder. The interim results showed that of the 266 males, ten were diagnosed with gynecomastia, an incidence rate of 3.75 percent. Sixteen of 319 patients had a prolactin-related adverse effect, a rate of 5 percent. In Dr. Kessler's opinion, this finding was a "red flag." Videotaped Deposition of David Kessler, M.D., ***supra*** at 56.

The RIS-INT-41 study continued for another year. As of August 2001, there were twenty-six documented cases of prolactin-related adverse events in 504 children, an incidence of 5.15 percent. Twenty-four of the twenty-six children with prolactin-related adverse events had gynecomastia, and twenty-three of them were male. Dr. Kessler opined that there was an obligation on the part of Janssen "certainly by July 2001" to convey this information to physicians who were prescribing the drug off-label to children. ***Id***. at 65.

Janssen initiated a second study, RIS-INT-70, which was an extension of RIS-INT-41. Dr. Kessler reported that there were four additional cases of gynecomastia in children who participated in both studies, a risk of 8.3

percent. The children who participated only in RIS-INT-70 had an incidence of gynecomastia of 12.5 percent.[8] ***Id***. at 70.

During the early 2000s, Janssen conducted eighteen clinical studies with pediatric patients, some of which were double-blind, *i.e.*, involved a placebo, and others that were open-lab studies. Six of the studies lasted up to six months. RIS-INT-41 and RIS-INT-70 were the only long-term studies, and the only studies that paid special attention to prolactin-related adverse events such as gynecomastia. The eighteen studies encompassed 1,885 subjects from five to eighteen years of age. In the double-blind studies, no children who received a placebo were diagnosed with gynecomastia. Eight of nine cases of gynecomastia reported were related to the long-term studies. Dr. Kessler testified that the studies indicated that gynecomastia was manifested over time after exposure and that short-term studies did not capture the actual number of related cases. ***Id***. at 72-79; Plaintiffs' Exhibit 17. Dr. Kessler informed the jury that, in January 2002, Janssen's own studies showed a significant association of 4.4% between hyperprolactinemia and gynecomastia in young males.

In May 2002, Janssen conducted a *post hoc* analysis of data from five of the eighteen earlier studies. RIS-INT-41 data was included; RIS-INT-70

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[8] Dr. Kessler testified that, although the RIS-INT-70 results were known to Janssen in September 2002, they were not published in the Journal of Child and Adolescent Psychopharmacology until November 3, 2006. Videotaped Deposition of David Kessler, M.D., ***supra*** at 72.

data was not. Dr. Kessler opined that Janssen was attempting to prove that Risperdal was not related to elevated prolactin levels, but the data proved otherwise. Analysis of the data showed a rate of 4.4% of gynecomastia. Plaintiffs' Exhibit 22. More importantly, he focused on one particular item of Janssen's supporting documentation, Table 21, which revealed that there were more prolactin-related side effects in Risperdal patients whose prolactin levels were higher. Dr. Kessler explained that Table 21 demonstrated a causal correlation between high prolactin levels and "prolactin related adverse effects," called PRAE, one of which was gynecomastia. He opined that the correlation was statistically significant, as there was a 98.5% likelihood that the side effects did not occur randomly. Internal Janssen emails confirmed, according to Dr. Kessler, that Janssen was aware of the significance of the findings. Based on the foregoing evidence of a causal connection between Risperdal and elevated levels of prolactin, and higher levels of prolactin and gynecomastia, Dr. Kessler opined that Janssen had a duty to warn physicians who were prescribing the drug off-label to children and to notify the FDA. ***Id***. at 121.

According to Dr. Kessler, Janssen breached its duty to disclose Table 21 to the FDA, and withheld data showing the correlation between elevated prolactin levels and prolactin related adverse effects such as gynecomastia from its own endocrinologist and psychiatrist consultants. The expert demonstrated how Janssen manipulated the study data in such a way as to

reduce the statistical significance of the association between Risperdal and boys with gynecomastia, and alleged that Janssen funded the publishing of a misleading article in the Journal of Clinical Psychiatry.[9] ***Id***. at 149.

Plaintiffs also offered the expert testimony of Mark Solomon, M.D., a plastic surgeon with expertise in gynecomastia and diseases of the breast. He examined T.M., who was at the time was twenty-one years of age, and confirmed that T.M. suffered from true gynecomastia. After reviewing the medical literature about Risperdal, T.M.'s family history, his medical records, and ruling out other possible causes of T.M.'s gynecomastia, Dr. Solomon concluded, with a reasonable degree of medical certainty, that Risperdal was the cause of T.M.'s gynecomastia. N.T. Trial (Jury), 12/7/16, at 71. He explained that, although T.M.'s family physician in Nebraska only diagnosed him with gynecomastia on May 19, 2010, his breasts had started to develop in 2006. Dr. Solomon opined that the timing was consistent with the development of breast tissue generally, and that T.M.'s early breast development could be seen in photographs from 2007.

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[9] Dr. Kessler testified that Janssen manipulated the data by removing boys who were less than ten years of age from the figures on gynecomastia, but failed to make a commensurate reduction in the number of overall subjects in the study. ***Id***. at 123. Consequently, when Janssen ran the numbers again in September 2002, instead of a 95 percent statistical significance, the smaller numbers resulted in only a 90 percent statistical significance. Videotaped Deposition of David Kessler, M.D., ***supra*** at 125-26.

When Plaintiffs attempted to elicit additional testimony from Dr. Solomon about two studies he had reviewed and relied upon in reaching his opinions, Janssen objected to the testimony on the ground that Dr. Solomon had not identified them in his expert report.[10] N.T. Trial (Jury), 12/7/16, at 53. Janssen maintained that it lacked fair notice of Dr. Solomon's testimony in this regard. Plaintiffs countered that since Janssen had cross-examined Dr. Solomon in other trials and depositions regarding the same articles, there was no surprise and no prejudice. Moreover, Plaintiffs argued that Janssen had been afforded the opportunity to depose Dr. Solomon in this case, but had declined. The trial court sustained Janssen's objection under Pa.R.C.P. 4003.5, finding that the expert's testimony regarding the literature and studies he relied upon was beyond the fair scope of his expert report, and precluded the expert's testimony in this regard. However, on cross-examination, Dr. Solomon testified that his opinion that Risperdal caused elevated prolactin levels was informed by his review of the literature, the package inserts, and Janssen's documents. N.T. Trial (Jury), 12/7/16, at 91.

In addition to the foregoing proof regarding the inadequacy of the Risperdal label, Janssen's failure to accurately report the drug's role in

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[10] The court would not allow Dr. Solomon to discuss any of the Risperdal labels, even though they were exhibits entered into evidence, because he did not state in his report that he had reviewed them. The court ruled that it was improper for the expert to "comment on something he never indicates that he reviewed, never indicates that he relies upon[.]" N.T. Trial (Jury), 12/7/16, at 137.

elevating prolactin levels and gynecomastia, and ingestion of Risperdal as the cause of T.M.'s gynecomastia, Plaintiffs offered the following proof to rebut the presumption under the TPLA that the label was adequate. The prescribed use in T.M., a child, was off-label and not approved by the FDA. Furthermore, it was not FDA-approved for ADHD or conduct disorders. Dr. Martin, Dr. Wieck, and Physician Assistant Dewar testified that Janssen had actively promoted the use of Risperdal in children, and that the marketing had influenced them to prescribe Risperdal for T.M. for an off-label use. Dr. Wieck, the psychiatrist who supervised the prescribing of Risperdal for T.M., attended a Janssen meeting, all expenses paid, in Miami Beach. In addition, just days before Dr. Wieck prescribed Risperdal for T.M., he had a visit from a Janssen representative, who talked about the use of Risperdal to treat younger children with agitation and anxiety and conduct disorders generally. The prescribers testified that if they had been aware that the real risk of gynecomastia with Risperdal was frequent rather than rare, and that Risperdal was linked to a greater elevation of prolactin levels than other antipsychotic drugs in the same class, they would have prescribed another medication instead. Brenda Tinkham testified that she was not told of the risk of gynecomastia or breast development when Risperdal was recommended for T.M. N.T. Trial (Jury), 12/8/16, at 60. Had she known, she stated she would not have agreed to its administration to T.M. ***Id***. at 44, 60.

On December 9, 2016, at the close of Plaintiffs' case, Janssen orally moved for a nonsuit. It alleged first that Plaintiffs failed to produce sufficient evidence to rebut the presumption under the TPLA that the FDA-approved warning was adequate. Specifically, Janssen maintained that Plaintiffs failed to prove that Janssen promoted or advertised Risperdal for an indication not approved by the FDA, or that plaintiff used it for an off-label use, and that Janssen's off-label promotion caused the prescriber to prescribe it for the off-label use.

Second, Janssen argued that Dr. Solomon's opinions did not meet the general or specific causation requirements for scientific reliability under Texas law, including proof of two epidemiological studies demonstrating a statistically significant doubling of the relative risk. Janssen maintained that the 2007 photographs of T.M. that Dr. Solomon testified showed budding breasts could not overcome the fact that T.M. stopped the medication in 2008 and was first diagnosed with gynecomastia in 2010. Finally, Janssen argued that there was a complete failure of proof as to fraud.[11]

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[11] After orally moving for a compulsory nonsuit, Janssen filed a written motion for compulsory nonsuit in which it advanced additional bases for nonsuit: (1) that Plaintiffs failed to establish that the warnings were inadequate and that the inadequate warnings were the proximate cause of T.M.'s injury; (2) that federal law preempted Plaintiffs' failure to warn claim; and (3) that Plaintiffs failed to introduce any evidence that Johnson & Johnson and Janssen Research & Development, LLC, were manufacturers or sellers under the Texas Products Liability Act.

Plaintiffs countered that they could maintain the action as they had rebutted the presumption under Texas's Products Liability Act that the warnings were adequate by introducing proof that Janssen promoted Risperdal for an indication that was not approved by the FDA; that the drug was used as promoted; and that T.M.'s gynecomastia was causally related to the promoted off-label use of Risperdal. ***See*** Tex. Civ. Prac. & Rem. Code § 82.007(b)(3)(A-C).

Plaintiffs argued that Texas law did not require proof of epidemiological studies to prove general or specific causation. Furthermore, they maintained that Texas's standards governing the reliability of scientific evidence of general or specific causation under Texas law were not substantive. They maintained that Pennsylvania adheres to ***Frye v. United States***, 293 F. 1013 (D.C. Cir. 1923), and that the issue was one of procedure and not a question governed by Texas substantive law.

The trial court granted the nonsuit, finding that Texas law as enunciated in ***Merrell Dow Pharm. v. Havner***, 953 S.W.2d 706 (Tex. 1997), and ***Merck & Co. v. Garza***, 347 S.W.3d 256, 266 (Tex. 2011), governed the issue of the sufficiency of expert scientific testimony regarding medical causation. It then construed ***Havner*** and ***Garza*** as strictly requiring Plaintiffs to introduce the

following proof of causation: 1) two epidemiological studies[12] proving general causation, *i.e.*, that exposure to a particular agent causes or increases the risk of the injury sustained; 2) that those studies demonstrated a doubling of the relative risk; and 3) that the plaintiff is similarly situated to the study participants. The trial court ruled that Dr. Solomon failed to introduce at least two epidemiological studies demonstrating a doubling of the risk for purposes of general causation and testify that T.M.'s circumstances were similar to those of the study subjects. The court reasoned that Plaintiffs could not rely upon Janssen's clinical trials, RIS-INT-41 and RIS-INT-70, to meet the requirement set forth in ***Havner*** because the studies did not show a doubling of the risk for gynecomastia or demonstrate that the subjects of those studies were similar to T.M. Thus, the court concluded that Plaintiffs' evidence was insufficient under Texas law to make out a *prima facie* failure to warn claim

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[12] Epidemiology is defined as "[t]he study of the relationships between the various factors that determine the frequency and distribution of diseases in human and other animal population." Stedman's Medical Dictionary (26th ed.). Epidemiological studies are one type of scientific research used to evaluate whether there is a correlation or causal relationship between exposure to a substance and adverse health effects. Cohort and case-control studies are just two examples of types of epidemiological studies. ***See*** *https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section7.html.*

In addition to epidemiological studies, there are various types of clinical research and trials calculated to measure and test new medications. ***See*** *https://www.fda.gov/forpatients/clinicaltrials/types/default.htm.* Meta-analysis is "a quantitative statistical analysis of several separate but similar experiments or studies in order to test the pooled data for statistical significance." Merriam-Webster Dictionary, ***see*** *https://www.merriam-webster.com/dictionary/meta-analysis.*

as it lacked the scientific reliability to prove that exposure to Risperdal caused gynecomastia, and that T.M. developed gynecomastia due to his ingestion of Risperdal.

Plaintiffs filed a post-trial motion, which the trial court denied. Plaintiffs appealed, both Plaintiffs and the trial court complied with Pa.R.A.P. 1925, and the matter is ripe for our review.

1. Did the trial court improperly enter nonsuit given the evidence introduced at trial concerning causation?

2. Did the trial court err by precluding Plaintiffs' causation expert from testifying about specific epidemiology studies under a "fair scope" of the expert report analysis?

Appellants' brief at 4.

Pennsylvania law is well settled that entry of a compulsory nonsuit is proper upon the motion of a defendant where, at the close of the plaintiff's case, the plaintiff has not introduced sufficient evidence to establish the necessary elements to maintain a cause of action. ***Gigus v. Giles & Ransome, Inc.***, 868 A.2d 459 (Pa.Super. 2005). On appeal, we review the evidence to determine whether the trial court abused its discretion or made an error of law. ***Baird v. Smiley***, 169 A.3d 120 (Pa.Super. 2017). Further, in making this determination, we must give the Plaintiffs the benefit of every fact and all reasonable inferences arising from the evidence and resolve all conflicts in the evidence in Plaintiffs' favor. ***Id.*** We will affirm the grant of compulsory nonsuit "only if no liability exists based on the relevant facts and

circumstances." ***Id***. at 121. Otherwise, the compulsory nonsuit is removed and the matter remanded for a new trial. ***Id***.

The threshold issue before us is whether the trial court correctly applied Texas law in ruling on the sufficiency of Plaintiffs' expert scientific evidence for purposes of the compulsory nonsuit. The trial court held that ***Havner*** required proof of two epidemiological studies showing a statistically significant doubling of the risk, evidence that T.M. was similarly situated to the patients in those studies, and that these requirements were "not merely procedural guideposts," but substantive under Texas law. Trial Court Opinion, 10/19/17, at 4. The court relied on ***Garza***, ***supra*** at 266, in concluding that since Plaintiffs failed to meet that threshold, the case could not go to the jury. As this is a question of law, our standard of review is *de novo* and our scope of review is plenary.

Plaintiffs contend first that the reliability and sufficiency of causation evidence is a question of procedure and that Pennsylvania law governs. Plaintiffs rely upon this Court's recent decision in ***Stange v. Janssen Pharm., Inc.,*** 179 A.3d 45, 53 (Pa.Super. 2018), in support of their assertion that "[e]vidence is procedural law as are the standards for reviewing and deciding dispositive motions." Plaintiffs' brief at 37. Plaintiffs maintain that the court erroneously applied Texas law to an issue that was procedural and governed by Pennsylvania law, specifically, ***Frye*** rather than ***Daubert v. Merrell Dow Pharm., Inc.***, 509 U.S. 579 (1993). Under Pennsylvania law, they argue that

the evidence was admissible, reliable, and legally sufficient to go to the jury. Plaintiffs point out that Janssen could have challenged the admissibility of Dr. Solomon's testimony by filing a pretrial ***Frye*** motion pursuant to Pa.R.E. 702, as it did in ***Stange***, ***supra***, but it elected not to do so. Instead, Janssen successfully objected to Dr. Solomon testifying about studies that he reviewed and relied upon, waited for Plaintiffs to rest, and then moved for compulsory nonsuit, citing Dr. Solomon's failure to introduce two epidemiological studies supporting his opinion.

Janssen contends that medical causation, both general and specific, is an essential element of Plaintiffs' failure to warn claim under Texas substantive law. It argues that in order to present a question of fact, Plaintiffs were compelled to provide the proof of causation required by ***Havner***. Appellees' brief at 12. It cites ***Havner*** and ***Garza*** as imposing a black-letter requirement under Texas law that a plaintiff introduce at least two epidemiological studies showing a statistically significant doubling of the risk, and evidence that the plaintiff is similar to the subjects of the studies, in order present a question of fact for the jury in a failure-to-warn case.[13] According

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[13] Janssen relies upon ***Freeman v. AMF, Inc.*** (***In re Asbestos Prods. Liab. Litigation***), 2012 U.S. Dist. LEXIS 31650 (E.D. Pa. 2012), for the proposition that ***Havner***'s standard for the reliability of epidemiological evidence is substantive. In that case, however, the parties agreed to apply Texas substantive law, and merely treated the issue as one governed by Texas law. We observe, however, that the trial court noted therein that no epidemiological studies were required under Texas law to prove general

to Janssen, since Dr. Solomon, Plaintiffs' only "causation" expert, neglected to cite any medical literature or studies to support his opinions, Plaintiffs could not meet their burden of proof, and thus, the entry of a compulsory nonsuit was warranted. ***Id***. at 16-17.

Whether the sufficiency of causation evidence is a procedural or substantive issue governed by Pennsylvania or Texas law is critical to the disposition of this appeal. Under Pennsylvania law, experts who are qualified by their "scientific, technical or other specialized knowledge beyond that possessed by a layperson" routinely provide causation evidence. Pa.R.E. 702. Whether the expert witness is qualified is a determination left to the sound discretion of the trial court. ***Daniel v. Wyeth***, 15 A.3d 909, 926 (Pa.Super. 2011). A qualified expert's causation testimony, rendered to a reasonable degree of medical certainty and adequately based in fact, is generally sufficient to make out a *prima facie* case of failure to warn. ***See Snizavich v. Rohm & Haas, Co.***, 83 A.3d 191, 195 (Pa.Super. 2013) (holding that an expert's testimony must be "based on more than mere personal belief," and "must be supported by reference to facts, testimony or empirical data").

Where, however, a party seeks to introduce novel scientific evidence through the conclusions of an expert, Pennsylvania follows the standard set forth in ***Frye***. Before novel science enters the courtroom, a party seeking to

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causation, and that ***Havner*** merely established the threshold for the scientific reliability of such evidence when it was relied upon.

introduce it must demonstrate "that the relevant scientific community has reached general acceptance of the principles and methodology employed by the expert witness before the court will allow the expert witness to testify as to his conclusions." ***Reading Radio, Inc. v. Fink***, 833 A.2d 199, 208 (Pa.Super. 2003) (citing ***Trach v. Fellin***, 817 A.2d 1102, 1108-09 (Pa.Super. 2003) (*en banc*)). The expert's conclusions need not be generally accepted as long as they are derived from generally accepted principles and sound scientific research. Once the evidence crosses that threshold, Pennsylvania courts allow juries to assign to it whatever weight they feel is appropriate. The ***Frye*** rule has been incorporated into Pa.R.E. 702.

On the other hand, the federal courts, as well as some states, apply the rule espoused in ***Daubert***, ***supra***, when determining whether proffered scientific evidence is sufficiently reliable to be admissible. ***Daubert*** involves a judicial evaluation of the validity of the underlying data relied upon by experts. Texas adopted its version of ***Daubert*** in ***E.I. du Pont de Nemours & Co. v. Robinson***, 923 S.W.2d 549 (Tex. 1995). In determining whether scientific evidence was sufficiently reliable to be admissible, the ***Robinson*** court identified a non-exclusive list of factors, now known as the ***Robinson*** factors, which trial courts should consider in making a preliminary admissibility determination under Texas Rule of Evidence 702:

(1) The extent to which the theory has been or can be tested;

(2) The extent to which the technique relies upon the subjective interpretation of the expert;

(3) Whether the theory has been subjected to peer review and publication;

(4) the technique's potential rate of error;

(5) Whether the underlying theory or technique has been generally accepted as valid by the relevant scientific community; and

(6) The non-judicial uses that have been made of the theory or technique.

Havner, ***supra*** at 714 (quoting ***Robinson***, 923 S.W.2d at 557).

In ***Havner***, the Texas Supreme Court expanded the role of the ***Robinson*** factors. Instead of being employed solely to determine whether scientific evidence was reliable enough to be admissible, the court mandated that those factors be reweighed and re-evaluated by the court when it conducted its sufficiency review. In essence, a court would make a *sua sponte* second reliability determination of the scientific evidence in determining whether it was sufficient to sustain the verdict. Texas courts call this a "no-evidence" review. ***Havner***, ***supra*** at 721. Under Texas law, a court will find "no evidence" to sustain the verdict when "(a) there is complete absence of evidence of a vital fact, (b) the court is barred by rules of law or of evidence from giving effect to the only evidence offered to prove a vital fact, (c) the evidence offered to prove a vital fact is no more than a mere scintilla, or (d) the evidence conclusively establishes the opposite of the vital fact." ***Id***.

The facts in ***Havner*** are instructive. The Havners sued Merrell Dow for negligence, defective design, and defective marketing of its drug Bendectin, a

drug prescribed to pregnant women to relieve morning sickness. It was not a failure to warn case. They alleged that mother's ingestion of Bendectin caused limb defects in their daughter *in utero*.

At several stages of the litigation, Merrell Dow challenged the scientific reliability of the Havners' evidence that Bendectin ingested by pregnant women caused limb defects in their unborn children. Immediately prior to trial, Merrell Dow filed motions *in limine* seeking to exclude the Havners' causation testimony. Following a ***Robinson*** hearing, the motions were denied. At the close of the Havners' case, the court denied Merrell Dow's motion for a directed verdict. At the conclusion of trial, the jury returned a verdict in favor of the Havners and awarded both compensatory and punitive damages. On appeal, a divided court of appeals affirmed the compensatory damages, but reversed the award of punitive damages. The Supreme Court of Texas granted Merrell Dow's application for writ of error that challenged both the legal sufficiency and admissibility of the Havners' causation evidence.

The Texas Supreme Court reviewed the record and noted that thirty million women worldwide had taken Bendectin from 1957 to 1983. The FDA investigated a possible association between the drug and birth defects, but concluded that there was no increased risk shown.[14] More than thirty

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[14] The ***Havner*** court showed deference to the FDA's evaluation of a drug. It suggested that courts follow the lead of the FDA, which rejected "isolated case reports, random experience, and reports lacking the details which permit scientific evaluation," and promulgated regulations "that detail the

published and peer-reviewed studies on a possible association between Bendectin and birth defects failed to demonstrate an increased risk of limb defects. The ***Havner*** court observed that no plaintiff had ever prevailed in federal court in a Bendectin case, and that in some cases, causation evidence provided by the same experts who testified on behalf of the Havners had been held inadmissible or legally insufficient. The issue before Texas's highest court was "whether the Havners' evidence is scientifically reliable and thus some evidence to support the judgment in their favor." ***Havner***, ***supra*** at 711.

In making that determination, the court analyzed the epidemiological evidence to determine whether it was reliable. While it acknowledged that epidemiological studies may shed light on whether there is an association between a disease or condition and some drug or agent suspected of causing that disease or condition, it noted that such studies could not establish specific causation, *i.e.*, that a particular individual contracted the disease or condition due to exposure to the drug or agent. After examining how other courts had determined what evidence was admissible or, in some cases sufficient, to establish scientifically reliable causation, the ***Havner*** court concluded that "properly designed and executed epidemiological studies may be part of the evidence supporting causation in a toxic tort case," but that there must be a showing of more than a doubling of the risk. ***Havner***, ***supra*** at 717. The

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requirements for clinical investigations of the safety and effectiveness of drugs." ***Merrell Dow Pharm., Inc. v. Havner***, 953 S.W.2d 706, 721 (Tex. 1997) (citing 21 C.F.R. § 314.126(e) (1996)).

court explained that if a condition occurs in six out of 1,000 people who are not exposed to a certain drug, and studies show that nine out of 1,000 people who take the drug manifest the condition, it is still more likely than not that causes other than the drug were responsible. It reasoned that, in order to prove that a condition was statistically more likely than not caused by a drug, a study would have to show that at least twelve people out of 1,000 took the drug and developed the condition. This is a relative risk of two, and relevant in proving general causation, *i.e.*, "whether a substance is capable of causing a particular injury or condition in the general population." ***Id***. at 714. The court acknowledged that while such a study could shed some light on the association between the drug and the condition, it would not suffice to prove specific causation, *i.e.,* that "a substance caused a particular individual's injury." ***Id***. at 714. In most cases, the court concluded, expert medical testimony would be required to bridge that gap. ***Id***.

The ***Havner*** court ruled that, "[t]he use of [two] scientifically reliable epidemiological studies and the requirement of more than a doubling of the risk strikes a balance between the needs of our legal system and the limits of science." ***Id***. at 718.[15] In addition, the court held that to survive legal sufficiency review, a plaintiff must show that he is similar to those in the

[15] The ***Havner*** court expressly rejected the notion "that a relative risk of more than 2.0 is a litmus test" as, in some cases, "[t]here may be no causal relationship even if the relative risk is high." ***Id***.

studies, *i.e.*, exposed to similar levels of the same substance, and that the timing of onset is consistent with that experienced by others in the study, and introduce expert testimony ruling out other plausible causes.[16]

Thus, the court reaffirmed that medical causation evidence must be reliable as measured against the ***Robinson*** factors. For instance, the court made it clear that the bare opinion of a physician that, to a reasonable degree of medical certainty, the limb defect was caused by her mother's ingestion of Bendectin while pregnant, was not scientifically reliable. It approved, however, of evidence negating other plausible causes of the condition with reasonable certainty, *i.e.*, the differential diagnosis methodology employed by Dr. Solomon herein. It concluded that "courts must make a determination of reliability from all the evidence, . . . assuming it passes muster under ***Robinson***," in determining whether there is legally sufficient evidence to support a judgment. ***Id***. at 720. In addition, however, the court set forth an evidentiary standard for the reliability of epidemiological studies used to prove medical causation. Epidemiological proof that did not meet that standard was unreliable and no evidence at all.

After identifying "statistical shortcomings" in the Havners' epidemiological evidence, and noting that it had not been subjected to peer review or publication, both of which the court regarded as significant indicia

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[16] In ***Merck & Co. v. Garza***, 347 S.W.3d 256, 266 (Tex. 2011), the court acknowledged that usage in a study did not have to match the claimant's usage exactly. Rather, the conditions of the study only had to be substantially similar to the claimant's circumstances.

of reliability, the court disregarded that evidence when it conducted its no-evidence sufficiency determination. Since there was no scientifically reliable evidence of causation that would support the verdict, the court reversed the judgment.

The upshot of ***Havner*** is that, even if scientific evidence is held to be admissible, Texas courts will re-examine the scientific reliability of the evidence when subsequently making a sufficiency determination. Where the admitted scientific evidence is found lacking, Texas courts treat it as no evidence at all in determining whether the evidence is sufficient to support the verdict rendered by the jury.

More recently, in ***Garza***, following a jury verdict in favor of plaintiffs in a defective design/failure to warn death case involving the drug Vioxx, the Texas Supreme Court held, citing ***Havner***, that epidemiological evidence that did not show a doubling of the risk was not reliable proof of causation and could not be used to support the verdict. The court dismissed as unreliable Merck's own VIGOR study relied upon by the plaintiffs to show general causation, as it examined persons who took much larger doses of Vioxx for a substantially longer time than the decedent. Meta-analysis of cardiovascular data that combined results of many different studies, involved differing dosages, durations, and comparison drugs, was deemed unreliable as it showed a relative risk of only 1.19 percent when the VIGOR results were removed from the analysis. The APPROVe study relied upon by plaintiffs was not sufficiently similar as it only showed statistically significant differences in

the incidence of cardiovascular death after eighteen months of use, and decedent took Vioxx for only twenty-five days. Although the VICTOR study showed statistically significant results for confirmed "thrombotic events" with a relative risk exceeding 3.0, the court noted that it was only one study, not the required two studies. Thus, the ***Garza*** Court concluded "the totality of the evidence cannot prove general causation if it does not meet the standards for scientific reliability established by ***Havner***." ***Id***. at 268.

Havner reaffirmed the vitality of the ***Robinson*** factors in determining whether scientific evidence is relevant and reliable. In addition, the court defined what constitutes scientifically-reliable epidemiological evidence. However, under Texas law, epidemiological studies are not required to prove general causation. ***Havner*** and ***Garza*** stand for the proposition that where such studies are the only evidence of general causation, or relied upon by experts in support of their general causation opinions, unless there are at least two studies that reveal at least a doubling of the risk, the evidence is too speculative to permit a jury to find causation.[17] Thus, the issue is one of the scientific reliability of evidence.

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[17] In making its determination whether scientific evidence of causation is reliable enough to support the verdict, a Texas court looks at the totality of the evidence, including all evidence introduced by the defense as well as that of the plaintiff. ***See Centocor Inc. v. Hamilton***, 310 S.W.3d 476 (Tex. App. 2010), *rev'd on other grounds,* 372 S.W.3d 140 (Tex. 2012), (finding evidence of general and specific causation sufficient where: Centocor's own package

As noted above, the parties agree that, in this matter, Pennsylvania law governs procedure and Texas substantive law applies. However, under settled Pennsylvania law, the law of the forum governs the issue of **whether** a matter is substantive or procedural. ***Foley v. Pittsburgh-Des Moines Co.***, 68 A.2d 517 (Pa. 1949). In ***Sheard v. J.J. DeLuca Co., Inc.***, 92 A.3d 68, 76 (Pa.Super. 2014), this Court explained the difference between procedural and substantive law as follows: "Substantive law is the portion of the law which creates the rights and duties of the parties to a judicial proceeding, whereas procedural law is the set of rules which prescribe the steps by which the parties may have their respective rights and duties judicially enforced." Recently, in ***Hammons v. Ethicon, Inc.***, 190 A.3d 1248, 1285 (Pa.Super. 2018), we relied upon this language in ***Sheard*** in concluding that remittitur was procedural, and that Pennsylvania law, as the law of the forum, governed. ***See also Commonwealth v. Sanchez***, 716 A.2d 1221, 1223 (Pa. 1998) (holding that in conflicts cases involving matters of procedure, we apply our own procedural laws when we are the forum state); ***see also Murray***, ***supra***

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insert, approved by the FDA, described clinical trial findings prior to FDA approval that some patients may rarely suffer from lupus-like syndrome as a result of Remicade; Centocor's own witness testified that if a risk associated with a drug's treatment is included on the package insert, that risk is "reasonably associated" with the treatment; Centocor's expert testified that there was a 0.25% risk of the syndrome in women of child-bearing age, that recent Remicade trials showed a two to three percent increase in the incidence of the syndrome, and that lupus is a recognized complication of Remicade).

at 1252 (finding Maryland damages cap to be a substantive limitation governed by Maryland law).

Texas law similarly provides that the law of the forum governs the issue of whether a matter is substantive or procedural. ***See Penny v. Powell***, 347 S.W.2d 601, 602 (Tex. 1961) (applying Texas rules of construction to determine that Louisiana Direct Action Statute was procedural and unenforceable in Texas); ***see also PennWell Corp. v. Ken Assocs.***, 123 S.W.3d 756, 764 (Tex. App. 2003) (holding what is a matter of substance and what is a matter of procedure is determined by the law of the forum state); ***accord Brandon v. Ivie***, 2018 Tex. App. LEXIS 7417, *3 (Tex. App. 2018) (applying Texas statute of limitation as they are procedural under Texas law); ***Owens-Corning Fiberglas Corp. v. Martin***, 942 S.W.2d 712 (Tex. App. 1997) (declining to apply Alabama's unanimous-verdict rule upon finding it procedural under Texas law).

Questions of evidence are governed by the law of the forum. ***Greenwood v. Hildebrand***, 515 A.2d 963, 964 (Pa.Super. 1986). Whether evidence, once admitted, is sufficient to support a verdict or survive a nonsuit is similarly a procedural inquiry. Our Supreme Court held in ***Foley***, ***supra*** that "[t]he law of the forum also controls all questions as to burden of proof and whether there is sufficient evidence of negligence and proximate causation to entitle the plaintiff to have the case submitted to the jury." ***Id***. at 521 (citing ***Sudol v. Gorga***, 31 A.2d 119, 120 (Pa. 1943); Restatement

Conflict of Laws § 595, comments a and b); ***see also Ryan v. Adam Scheidt Brewing Co.***, 197 F.2d 614, 615 (3d Cir. 1952) (relying upon ***Foley***, ***supra***, in holding that "the issue as to the quantum of proof necessary to take the case to the jury is procedural rather than substantive, and therefore must be decided in accordance with the law of the forum"). The Restatement (Second) of Conflicts of Law § 135, provides that, with some exceptions not pertinent herein, "The local law of the forum determines whether a party has introduced sufficient evidence to warrant a finding in his favor on an issue of fact." Based on the foregoing, we conclude that whether the scientific evidence of causation was reliable enough to survive a compulsory nonsuit was a procedural inquiry that should have been governed by Pennsylvania law.[18]

We find that a compulsory nonsuit was improperly entered applying Pennsylvania procedural law. "A compulsory non-suit . . . may be entered only in cases where it is clear that the plaintiff has not established a cause of action[.]" ***Portside Investors, L.P. v. Northern Ins. Co.***, 41 A.3d 1, 14

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[18] We find misplaced Janssen's reliance upon ***Freeman v. AMF, Inc.*** (***In re Asbestos Prods. Liab. Litigation***), 2012 U.S. Dist. LEXIS 31650 (E.D. Pa. 2012), for the proposition that ***Havner***'s standard for the reliability of epidemiological evidence is substantive. In that case, the parties simply agreed to apply Texas substantive law, and then treated that issue as substantive without any discussion or analysis. We also observe, however, that the court noted that no epidemiological studies were required under Texas law to prove general causation, and that ***Havner*** merely established the threshold for the scientific reliability of epidemiological evidence when it was relied upon.

(Pa.Super. 2011) (quoting ***Reading Radio, Inc. v. Fink***, 833 A.2d 199, 209-210 (Pa.Super. 2003). In making that determination, the plaintiff is entitled to the "benefit of all reasonable inferences arising from the evidence." ***Id***. A non-suit is proper only if the plaintiff has not introduced sufficient evidence to establish the necessary elements to maintain a cause of action. ***Id***.[19] Viewing all of the evidence in the light most favorable to the Plaintiffs, we conclude the evidence was sufficient to make out a *prima facie* failure-to-warn case based on Texas substantive law.

Under Texas law, drug manufacturers are subject to liability for failure to warn. ***See Tex. Civ. Prac. & Rem. Code*** § 82.007; ***see also*** n.5 *supra*. However, there is a statutory presumption that the drug manufacturer is not liable if the "warnings or information that accompanied the product in its distribution were those approved by the Federal Drug Administration." ***Id***. at § 82.007(a)(1). That presumption may be rebutted by evidence that (1) "the defendant . . . withheld from or misrepresented to the [FDA] required information that was material and relevant to the performance of the product and was causally related to the claimant's injury[,]" or 2) "the defendant

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[19] Pennsylvania trial and appellate courts do not conduct anything akin to Texas's no-evidence review of the reliability of scientific evidence when ruling on whether evidence is sufficient to sustain a verdict. We do not re-examine, reweigh, or disregard properly-admitted scientific evidence. Rather, we consider all evidence that was actually received without consideration of whether the evidence was properly admissible. ***See Commonwealth v. Gray***, 867 A.2d 560, 567 (Pa.Super. 2005) (reaffirming that appellate sufficiency determination is not conducted on a diminished record).

recommended, promoted, or advertised the pharmaceutical product for an indication not approved" by the FDA, and the claimant used the product as recommended, promoted, or advertised, resulting in his injury. ***Id***. at § 82.007(b)(1), (3).

It is undisputed that the FDA approved the warning accompanying Risperdal. However, Plaintiffs offered evidence that Janssen promoted the use of Risperdal for two off-label uses: for use in children, when it was not FDA-approved for children; and for treating ADHD in children, when it was not approved for the treatment of ADHD. In addition, Plaintiffs' expert Dr. Kessler testified that Janssen withheld and/or misrepresented material information to the FDA that was causally related to the incidence of gynecomastia in children, especially young males. We find there was sufficient evidence adduced by Plaintiffs to rebut that presumption.

Furthermore, in any failure-to-warn case under Texas law, a plaintiff must show that the warning was defective and that it was the producing cause of the plaintiff's injury. ***Wyeth-Ayerst Lab. Co. v. Modrano***, 28 S.W.3d 87, 94-95 (Tex.App. 2000) (citing ***Rolen v. Burroughs Wellcome Co.***, 856 A.W.2d 607 (Tex.App. 1993). In situations involving a pharmaceutical product, the manufacturer fulfills its duty by providing an adequate warning to the learned intermediary who prescribes the drug, who then assumes the duty to pass the necessary warnings on to the end users. ***Centocor, Inc. v. Hamilton***, 372 S.W.3d 140 (Tex. 2012) (extending the learned intermediary

doctrine adopted in ***Alm v. Aluminum Co. of Am.***, 717 S.W.2d 588, 590-92 (Tex. 1986), to manufacturers of pharmaceutical products). If, however, the warning to the prescribing physician is inadequate or misleading, then the drug manufacturer remains liable for injuries sustained by the end user. ***Id***. at 157. In establishing causation, the plaintiff must prove that a proper warning would have changed the decision of the intermediary to prescribe the product.

We find there was sufficient evidence introduced by Plaintiffs to make out a *prima facie* failure-to-warn case against Janssen under Texas substantive law. Plaintiffs' scientific evidence, much of which was based on Janssen's own clinical trials and studies, the results of which were published in scientific journals and peer-reviewed, showed a statistically significant relationship between ingestion of Risperdal, elevated prolactin levels, and gynecomastia in young males like T.M.[20] Dr. Kessler pointed to these studies and others, and opined, based on his education, knowledge, and experience, that the precautions and warnings on both the 2002 and 2006 Risperdal labels were inadequate and misleading, as they understated the known risk of gynecomastia from Risperdal. Dr. Kessler specifically stated that the label reported the risk of gynecomastia as "rare" when Janssen's own test results

[20] Dr. Kessler stated that the FDA leaves it up to drug manufacturers to design and conduct studies on the safety and efficacy of their drugs. Those results are submitted to the FDA, in accordance with applicable regulations.

showed that it was "frequent;" and that its label misrepresented Janssen's knowledge of the risks of Risperdal in children and adolescents. Dr. Kessler also pointed out that Janssen resisted the suggestion that the label contain a recommendation that the prolactin levels of Risperdal patients be monitored, although its tests showed a correlation of a higher incidence of prolactin-related adverse effects in subjects with higher prolactin levels. In sum, Dr. Kessler opined that Janssen promoted the drug for off-label use in children and adolescents, misrepresented its safety, and did not adequately warn physicians of the risks.

T.M.'s prescribing psychiatrists testified that they would not have prescribed the drug for him had they known the true nature of the risk. Mrs. Tinkham told the jury that she did not know about the risk of gynecomastia, and that she would not have agreed to its administration to T.M. had she known. Dr. Solomon conducted a physical examination of T.M., and confirmed an earlier diagnosis of gynecomastia. After review of T.M.'s personal and family medical histories, his medical records, and ruling out other possible causes of gynecomastia, he rendered his opinion, to a reasonable degree of medical certainty, that Risperdal caused T.M.'s gynecomastia.

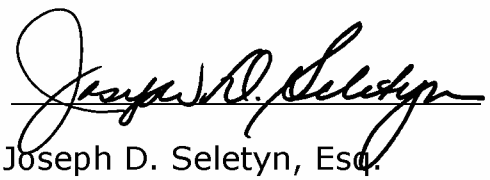
Viewing the foregoing evidence in the light most favorable to the Plaintiffs, we find it was legally sufficient under Pennsylvania law to make out a *prima facie* case for the jury under Texas substantive law governing failure

to warn. Accordingly, we find that a nonsuit was improperly entered, and remand for a new trial is warranted.

Based on our disposition, we do not reach Plaintiffs' second issue involving the propriety of the trial court's ruling precluding Dr. Solomon from testifying about the studies he relied upon in arriving at his expert causation opinions because he did not specifically reference those studies in his expert report.[21]

Judgment vacated. Order entering compulsory nonsuit reversed. Case remanded for a new trial. Jurisdiction relinquished.

Judgment Entered.



Joseph D. Seletyn, Esq.
Prothonotary

Date: 7/16/19

[21] We remind litigants, however, that where a ruling precludes evidence, the proponent of that evidence must make an offer of proof on the record to preserve the issue, unless the substance of the evidence is apparent from the record. ***See*** Pa.R.E. 103(a)(2) (providing that a party may claim error in a ruling to exclude evidence only if "the party informs the court of its substance by an offer of proof, unless the substance was apparent from the context").