IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

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| Rheinfrank, et al., | : | |
| | : | Case No. 1:13-cv-144 |
| Plaintiffs, | : | |
| | : | Judge Susan J. Dlott |
| v. | : | |
| | : | Order Granting in Part and Denying in |
| Abbott Laboratories, Inc., et al., | : | Part Defendants' Motion for Summary |
| | : | Judgment and Denying Plaintiffs' Motion |
| Defendants. | : | for Partial Summary Judgment |
| | : | |

This is a product liability case under Ohio law arising from Plaintiff Pamela Rheinfrank's ingestion of the antiepileptic drug, Depakote,[1] during her pregnancy with her daughter, M.B.D. Defendants Abbott Laboratories, Inc., Abbvie, Inc., and Abbott Laboratories[2] ("Defendants" or "Abbott") manufacture, market, and distribute Depakote. Plaintiffs allege that Rheinfrank's ingestion of Depakote during her pregnancy with M.B.D. caused injuries to her daughter, giving rise to this lawsuit.

This matter is before the Court on Defendants' Motion for Summary Judgment (Doc. 113) and Plaintiffs' Motion for Partial Summary Judgment (Doc. 112). Both motions are contested. Several motions regarding the expert witnesses to be presented at trial are also pending. For the reasons that follow, Defendants' Motion for Summary Judgment is **GRANTED IN PART AND DENIED IN PART**, and Plaintiffs' Motion for Partial Summary Judgment is **DENIED**.

[1] "Depakote" refers to Abbott's group of prescription drugs with the basic active ingredient valproic acid. Depakote is also sometimes referred to by the chemical names "valproic acid," "valproate," or "divalproex sodium." Depakote is an anti-epileptic drug that has been marketed by Abbott in the United States in some form since 1978.
[2] Effective January 2013, Abbott Laboratories separated into two publicly-traded health care companies: Abbott and AbbVie Inc. AbbVie Inc., the research-based pharmaceutical company, has responsibility for, among other things, the FDA-approved medicines Depakote, Depakote ER, Depakene, and Depacon.

## I. BACKGROUND[3]

### A. Facts

Plaintiff Pamela Rheinfrank was born September 11, 1974 and has suffered from epilepsy since childhood. Rheinfrank initially experienced seizures from infancy until age five. From age five to fourteen, Rheinfrank was seizure free; however, she began experiencing seizures again at age fourteen in 1988.

In 1988, Rheinfrank was prescribed both two antiepileptic drugs ("AEDs"), Depakote and Phenobarbital, to treat her seizures. Rheinfrank continued using Depakote and Phenobarbital during her pregnancy with four other children prior to M.B.D.'s birth; those children were born in 1990, 1992, 1994 and 2002. Rheinfrank became pregnant with M.B.D. in November or December of 2003. During her pregnancy, Rheinfrank's drug dosage was 500 milligrams of Depakote, three times per day, and 60 milligrams of Phenobarbital, two times per day. (Rheinfrank Dep. (July 1, 2014) at 7–8, Doc. 79 at PageID 1445.)

M.B.D. was born on July 25, 2004 and has been diagnosed with congenital malformations, facial dysmorphisms, cognitive impairment, developmental delay, and Fetal Valproate Syndrome ("FVS"). Plaintiffs attribute M.B.D.'s developmental delay and other physical and cognitive injuries to Rheinfrank's use of Depakote while pregnant with her from 2003-2004.

Although Rheinfrank has been treated by multiple doctors, the earliest medical records reflecting her treatment with Depakote are Walgreens Pharmacy records showing consistent prescriptions for Depakote from 2000 until 2008. These records indicate that Dr. Dagmar Lemus

[3] Except as otherwise indicated, background facts are drawn from Defendants' Proposed Statement of Undisputed Material Facts (Doc. 113-1 at PageID 13221–40) to the extent those facts are admitted in Plaintiffs' response thereto (Doc. 152-1 at PageID 19628–87) and Plaintiffs' Statement of Proposed Undisputed Facts (Doc. 112-1 at PageID 12593–609) to the extent those facts are admitted in Defendants' response thereto (Doc. 163-1 at PageID 21037–74). Where the parties do not explicitly agree on any statement of fact, the Court cites to the portion of the record providing support for the statement.

prescribed Depakote and Phenobarbital during Plaintiff Rheinfrank's pregnancy with M.B.D. At that time, Dr. Lemus was a resident of internal medicine at a clinic in Cincinnati's Good Samaritan Hospital. Dr. Lemus has no recollection of Rheinfrank and testified that she would not have been the originating prescriber of Rheinfrank's Depakote. (Lemus Dep. at 7, 10, 45, Doc.83 at PageID 3257–58, 3267.)

Depakote received Food and Drug Administration ("FDA") approval on or about March 3, 1983. (March 10, 1983 Letter from Department of Health and Human Services, Doc. 113-10 at PageID 13313–20.) As of 1988, Depakote was designated by the FDA as a Pregnancy Category D drug.

In 2003, a Black Box warning was included in the label, and the "Teratogenicity" Section of the Black Box warning read:

> **TERATOGENICITY:**
> VALPROATE CAN PRODUCE TERATOGENIC EFFECTS SUCH AS NEURAL TUBE DEFECTS (E.G., SPINA BIFIDA). ACCORDINGLY, THE USE OF DEPAKOTE TABLETS IN WOMEN OF CHILDBEARING POTENTIAL REQUIRES THAT THE BENEFITS OF ITS USE BE WEIGHED AGAINST THE RISK OF INJURY TO THE FETUS. THIS IS ESPECIALLY IMPORTANT WHEN THE TREATMENT OF A SPONTANEOUSLY REVERSIBLE CONDITION NOT ORDINARILY ASSOCIATED WITH PERMANENT INJURY OR RISK OF DEATH (E.G., MIGRAINE) IS CONTEMPLATED. SEE WARNINGS, INFORMATION FOR PATIENTS. AN INFORMATION SHEET DESCRIBING THE TERATOGENIC POTENTIAL OF VALPROATE IS AVAILABLE FOR PATIENTS.

(2000 Package Insert, Doc. 113-14 at PageID 13347; 2003 Package Insert, Doc. 113-15 at PageID 13367; 2001 PDR, Doc. 113-16 at PageID 13387; 2003 PDR, Doc. 113-17 at PageID 13397.)

The label also included the following language in the "Usage and Pregnancy" Section of the label:

**Usage in Pregnancy**

ACCORDING TO PUBLISHED AND UNPUBLISHED REPORTS, VALPROIC ACID MAY PRODUCE TERATOGENIC EFFECTS IN THE OFFPSRING OF HUMAN FEMALES RECEIVING THE DRUG DURING PREGNANCY. THERE ARE MULTIPLE REPORTS IN THE CLINICAL LITERATURE WHICH INDICATE THAT THE USE OF ANTIEPILEPTIC DRUGS DURING PREGNANCY RESULTS IN AN INCREASED INCIDENCE OF BIRTH DEFECTS IN THE OFFSPRING. ALTHOUGH DATA ARE MORE EXTENSIVE WITH RESPECT TO TRIMETHADIONE, PARAMETHADIONE, PHENYTOIN, AND PHENOBARBITAL, REPORTS INDICATE A POSSIBLE SIMILAR ASSOCIATION WITH THE USE OF OTHER ANTIEPILEPTIC DRUGS. THEREFORE, ANTIEPILEPSY DRUGS SHOULD BE ADMINISTERED TO WOMEN OF CHILDBEARING POTENTIAL ONLY IF THEY ARE CLEARLY SHOWN TO BE ESSENTIAL IN THE MANAGEMENT OF THEIR SEIZURES.

THE INCIDENCE OF NEURAL TUBE DEFECTS IN THE FETUS MAY BE INCREASED IN MOTHERS RECEIVING VALPROATE DURING THE FIRST TRIMESTER OF PREGNANCY. THE CENTERS FOR DISEASE CONTROL (CDC) HAS ESTIMATED THE RISK OF VALPROIC ACID EXPOSED WOMEN HAVING CHILDREN WITH SPINA BIFIDA TO BE APPROXIMATELY 1 TO 2%.

OTHER CONGENITAL ANOMALIES (E.G., CRANIOFACIAL DEFECTS, CARDIOVASCULAR MALFORMATIONS AND ANOMALIES INVOLVING VARIOUS BODY SYSTEMS), COMPATIBLE AND INCOMPATIBLE WITH LIFE, HAVE BEEN REPORTED. SUFFICENT DATA TO DETERMINE THE INCIDENCE OF THESE CONGENITAL ANOMALIES IS NOT AVAILABLE. THE HIGHER INCIDENCE OF CONGENITAL ANOMALIES IN ANTIEPILEPTIC DRUG-TREATED WOMEN WITH SEIZURE DISORDERS CANNOT BE REGARDED AS A CAUSE AND EFFECT RELATIONSHIP. THERE ARE INTRINSIC METHODOLOGIC PROBLEMS IN OBTAINING ADEQUATE DATA ON DRUG TERATOGENICITY IN HUMANS; GENETIC FACTORS OF THE EPILEPTIC CONDITION ITSELF, MAY BE MORE IMPORTANT THAN DRUG THERAPY IN CONTRIBUTING TO CONGENITAL ANOMALIES.

(Doc. 113-14 at PageID 13354; Doc. 113-15 at PageID 13374; Doc. 113-16 at PageID 13390; Doc. 113-17 at PageID 13399.)

**B. Procedural History**

Plaintiffs filed this action on February 28, 2013, and many related cases are pending throughout the country.[4] In their Amended Complaint, Plaintiffs assert statutory claims of strict liability under theories of design defect, inadequate warning, and nonconformance with representations under Ohio Rev. Code §§ 2307.75, 2307.76, and 2307.77, respectively; common law negligence; negligent misrepresentation and fraud; breach of express warranty and implied warranties of merchantability and fitness; unjust enrichment; and loss of consortium. Defendants have raised myriad defenses, including the learned intermediary doctrine and preemption.

On January 15, 2015, Plaintiffs filed two Motions for Partial Summary Judgment, and Defendants filed a Motion for Summary Judgment. For reasons explained on the record, the Court denied these Motions as moot subject to refiling. Subsequently, on January 28, 2015, Plaintiffs filed a Motion for Partial Summary Judgment on Defendants' Third Defense (Learned Intermediary) and Forty-Third Defense (Preemption) and Plaintiffs' Second Cause of Action for Failure to Warn. (Doc. 112.) Defendants filed a Motion for Summary Judgment as to all of Plaintiffs' claims. (Doc. 113.)

Thereafter, on February 17, 2015, the parties filed several *Daubert* Motions seeking to exclude or limit expert testimony. Plaintiffs filed a Motion to Exclude in Part Proffered Expert Opinions of Dr. Kwame Anyane-Yeboa, Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene (Doc. 136). The same day, Defendants filed a Motion to Exclude Testimony of C. Ralph Buncher, Sc.D (Doc. 153), Motion to Exclude Testimony of David Madigan, Ph.D. (Doc. 154), Motion to Exclude Testimony of Michael Privitera, M.D. (Doc. 155), Motion to Exclude Testimony of Suzanne Parisian, M.D. (Doc. 156), and Motion to Exclude Testimony of

[4] For example, approximately eighty-four cases are pending in the Southern District of Illinois on the docket of Judge Rosenstengel, in which numerous plaintiffs allege that they sustained personal injuries from the use of Abbott's prescription drug, Depakote.

Howard Saal, M.D. (Doc. 157). Although these Motions are fully ripe, the Court will defer ruling upon them unless they are necessary to the Court's summary judgment order.

## II. SUMMARY JUDGMENT STANDARD

Federal Rule of Civil Procedure 56 governs motions for summary judgment. Summary judgment is appropriate if "there is no genuine issue as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The movant has the burden of showing that no genuine issues of material fact are in dispute. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 585–87 (1986); *Provenzano v. LCI Holdings, Inc.*, 663 F.3d 806, 811 (6th Cir. 2011). The evidence, together with all inferences that can permissibly be drawn therefrom, must be read in the light most favorable to the nonmoving party. *See Matsushita Elec. Indus. Co., Ltd.*, 475 U.S. at 585–87; *Provenzano*, 663 F.3d at 811.

The movant may support a motion for summary judgment with affidavits or other proof or by exposing the lack of evidence on an issue for which the nonmoving party will bear the burden of proof at trial. *Celotex Corp. v. Catrett*, 477 U.S. 317, 322–24 (1986). In responding to a summary judgment motion, the nonmoving party may not rest upon the pleadings but must go beyond the pleadings and "present affirmative evidence in order to defeat a properly supported motion for summary judgment." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 257 (1986). The Court's task is not "to weigh the evidence and determine the truth of the matter but to determine whether there is a genuine issue for trial." *Liberty Lobby*, 477 U.S. at 249. A genuine issue for trial exists when there is sufficient "evidence on which the jury could reasonably find for the plaintiff." *Id.* at 252. "The court need consider only the cited materials, but it may consider other materials in the record." Fed. R. Civ. P. 56(c)(3).

"Where the parties have filed cross-motions for summary judgment, the court must consider each motion separately on its merits, since each party, as a movant for summary judgment, bears the burden to establish both the nonexistence of genuine issues of material fact and that party's entitlement to judgment as a matter of law." *In re Morgeson*, 371 B.R. 798, 800–01 (B.A.P. 6th Cir. 2007).

## III. ANALYSIS

Defendants moves for summary judgment on all claims, whereas Plaintiffs move for partial summary judgment. As briefly outlined below and more fully expounded upon throughout this Order, the Court will grant in part and deny in part Defendants' Motion for Summary Judgment and deny Plaintiffs' Motion for Partial Summary Judgment.

The Court will first consider the strict liability and negligence failure to warn claims. Defendants assert that Plaintiffs' claim that Defendants failed to warn of the risks of developmental delay is preempted. Defendants also contend that the Depakote label was adequate as a matter of law, Defendants were not required to provide language comparing Depakote to other drugs in its label, and the teratogenicity of Depakote is common knowledge. Defendants also assert they are entitled to summary judgment on the failure to warn claims because Plaintiffs cannot prove proximate cause. For the reasons discussed below, the Court will find that Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted. As to Plaintiffs' strict liability and negligence failure to warn claims, questions of fact as to the label's adequacy and causation preclude summary judgment for the Defendants. Finally, although Defendants contend a variety of other claims rise and fall with the failure to warn claims, the Court is not so persuaded.

Plaintiffs move for summary judgment on Defendants' strict liability failure to warn claim and on two of Defendants' defenses to the failure to warn claim: preemption and the learned intermediary defense. The Court will consider Plaintiffs' in support of their Motion for Partial Summary Judgment in conjunction with Defendants' Motion for Summary Judgment. For the reasons discussed below, the Court will deny Plaintiffs' Motion for Partial Summary Judgment in its entirety.

Following its analysis on the failure to warn claims, the Court will consecutively consider Defendants' arguments that it is entitled to summary judgment on Plaintiffs' remaining claims, which include: design defect, negligent misrepresentation and fraud, and unjust enrichment claim. Finding the Defendants' arguments persuasive, the Court will find Defendants entitled to summary judgment on each of these remaining claims.

Finally, Defendants assert Plaintiffs are unable to recover punitive damages in this action. The Court finds that Plaintiffs may pursue punitive damages for its common law claim, but not for its statutory failure to warn claim.

**A. Failure to Warn Claims**

The Court will first consider Defendants' Motion for Summary Judgment on Plaintiffs' failure to warn claims and Plaintiffs' Motion for Partial Summary Judgment on its statutory failure to warn claim and Defendants' defenses of preemption and the learned intermediary. Defendants move for summary judgment on all of Plaintiffs' claims that hinge upon the inadequate warning theory,[5] under which "a product is in a defective condition unreasonably dangerous when it is not accompanied by warnings sufficient to allow users to avoid risks inherent in the product." *In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d 791, 810 (N.D. Ohio

[5] Defendants argue that Plaintiffs' second, fifth, and sixth causes of action, and parts of the third, fourth, seventh, eighth, ninth, and tenth causes of action not predicated on an alleged design defect constitute the "failure to warn" claims. (Doc. 113 at PageID 13184, n.2.)

2004) (internal quotations removed).[6] Plaintiffs move for summary judgment on their second claim, strict liability for failure to warn under Ohio Rev. Code § 2307.76, as well as the defenses of preemption and the learned intermediary.

Plaintiffs base their products liability claims on theories of both strict liability and negligence. Strict products liability claims in Ohio are governed by Ohio Rev. Code §§ 2307.71–2307.80. Under Ohio statutory law, a manufacturer is subject to liability for compensatory damages based on a product liability claim if the Plaintiffs prove, by a preponderance of the evidence, that the label was defective due to inadequate warning or instruction and the defect was the proximate cause of M.B.D.'s injury. *McConnell v. Cosco, Inc.*, 238 F. Supp. 2d 970, 976 (S.D. Ohio 2003) (citing Ohio Rev. Code § 2307.73(A)). Under a negligent failure to warn claim, Plaintiffs "must show that the manufacturer had a duty to warn, that the duty was breached, and that [Plaintiffs'] injur[ies] proximately resulted from that breach of duty." *Id.* (citing *Hanlon v. Lane*, 648 N.E.2d 26, 28 (Ohio App. 1994)).

Plaintiffs allege Abbott failed to warn of the following: (1) the increased teratogenicity risk associated with higher doses of Depakote; (2) the increased risk of congenital malformations when Depakote is prescribed as part of polytherapy; (3) increased risk of impaired cognitive function and neurodevelopmental delay, caused by in utero exposure to Depakote; (4) increased risk of teratogenic effects to the developing fetus as compared to other antiepileptic drugs, which are safer for women of childbearing age; and (5) the greater risk to the fetus caused by Depakote usage than no treatment for seizure disorder. Defendants contend that Plaintiffs' failure to warn claim premised on the adequacy of Defendants' developmental delay warning is preempted, and that Plaintiffs cannot prove that any alleged inadequacy caused M.B.D.'s injuries.

[6] A federal court sitting in diversity must follow the law as declared by the legislature or the Supreme Court of the state whose law is applicable. *See Erie R. Co. v. Tompkins*, 304 U.S. 64 (1938). The parties agree Ohio law applies to this case.

### 1. Strict Liability and Negligence Standards for Failure to Warn

Under Ohio Rev. Code § 2307.76, a product is defective due to inadequate warning or instruction if either of the following applies:

> (1) It is defective due to inadequate warning or instruction at the time of marketing if, when it left the control of its manufacturer, both of the following applied:
> (a) The manufacturer knew or, in the exercise of reasonable care, should have known about a risk that is associated with the product and that allegedly caused harm for which the claimant seeks to recover compensatory damages;
> (b) The manufacturer failed to provide the warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm.
> (2) It is defective due to inadequate post-marketing warning or instruction if, at a relevant time after it left the control of its manufacturer, both of the following applied:
> (a) The manufacturer knew or, in the exercise of reasonable care, should have known about a risk that is associated with the product and that allegedly caused harm for which the claimant seeks to recover compensatory damages;
> (b) The manufacturer failed to provide the post-marketing warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm.

"A claim for negligent failure to warn has three basic elements: (1) a duty to warn against reasonably foreseeable risks; (3) breach of such a duty; and (3) injury that is proximately caused by the breach." *Reece v. Astrazeneca Pharm., L.P.*, 500 F. Supp. 2d 736, 751 (2007) (citing *Graham v. American Cyanamid Co.*, Nos. C-2-94-423, C-2-94-425, 2000 WL 1911431, at *10 (S.D. Ohio Dec. 21, 2000)). "The manufacturer must give suitable warning of a dangerous propensity that may result from use of the product." *Id.* (citing *Graham*, 2000 WL 1911431, at *11). "The warning necessary to satisfy the duty of ordinary care will vary based on the facts of each case." *Id.* (citing *Graham*, 2000 WL 1911431, at *11). "Because the standard for failure to warn requires that a manufacturer exercise reasonable care, the same standard applies for both

strict liability and negligence claims for inadequate warning." *McConnell v. Cosco, Inc.*, 238 F. Supp. 2d 970, 976 (2003) (citing *Crislip v. TCH Liquidating Co.*, 566 N.E.2d 1177, 1183 (Ohio 1990)). Accordingly, the Court will analyze the failure to warn claims jointly.

**a. Preemption**

Whether Plaintiffs' failure to warn claims are preempted is a threshold issue for both parties' motions. In their Motion for Partial Summary Judgment, Plaintiffs assert they are entitled to summary judgment on the defense of preemption, whereas Defendants contend that Plaintiffs' failure to warn of the risk of developmental delay is preempted. Defendants contend that it was impossible for Abbott to have given a warning regarding developmental delay prior to 2009. Abbott asserts that it sought the FDA's approval to add a developmental delay warning to its Depakote labeling in 2005 and 2007, and the FDA declined to approve the warning both times because, in its view, the scientific evidence was insufficient to support such a warning. Plaintiffs argue Defendants are unable to meet the high burden to establish preemption and that they are entitled to summary judgment on this defense.

Implied conflict preemption arises when "it is either impossible for a private party to comply with both state and federal requirements," *Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002) (citing *English v. General Elec. Co.*, 496 U.S. 72, 79 (1990)), "or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Id.* (citing *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941)). A failure to warn claim is preempted where the manufacturer of the drug proves that it was impossible to comply with state and federal law by submitting "clear evidence that the FDA would not have approved a change" to the drug's label. *Wyeth v. Levine*, 555 U.S. 555, 571 (2009).

Although the *Levine* Court articulated that the impossibility preemption defense is "demanding," it did not define the "clear evidence" standard, nor did it suggest the level of proof required. *Id*. at 571–573; *see Dobbs v. Wyeth Pharm.*, 797 F. Supp. 2d 1264, 1270 (W.D. Okla. 2011) (discussing the fact that lower courts are left to determine what satisfies the "clear evidence" standard in each case). Rather, the *Levine* Court found that the manufacturer offered no evidence that the FDA would have rejected the proffered warning. *Levine*, 555 U.S. at 571.

Before marketing a new drug, the manufacturer must submit a New Drug Application to the FDA, which demonstrates by "substantial evidence" that the medication is efficacious. *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 391 (7th Cir. 2010) (citing 21 U.S.C. § 355(d)(5)). "The FDA's approval is then conditioned on the manufacturer's use of the label it suggests." *Id*. (citing 21 C.F.R. § 314.105(b)). "Even after the medication is approved, the FDA continues to have authority over it and its label." *Id*. (citing 21 C.F.R. § 314.80–.81). Under FDA regulations:

> to change labeling (except for editorial and other minor revisions), the sponsor must submit a supplemental application fully explaining the basis for the change (§§ 314.70 and 601.12(f) (21 C.F.R. 314.70 and 601.12(f)))). The FDA permits two kinds of labeling supplements: (1) Prior approval supplements, which require FDA approval before a change is made (§§314.70(b) and 601.12(f)(1)); and (2) "changes being effected" (CBE) supplements, which may be implemented before FDA approval, but after FDA notification (§§ 314.70(c) and 601.12(f)(2)). While a sponsor is permitted to add risk information to the FPI without first obtaining FDA approval via a CBE supplement, FDA reviews all such submission and may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under section 502(a) of the act (21 U.S.C. 352). Thus, in practice, manufacturers typically consult with FDA prior to adding risk information to labeling.

Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922-01.[7] "The CBE regulation allows a manufacturer to modify a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction' . . . and to do so when it files its supplemental application, before the FDA has the opportunity to consider whether or not it will accept the change." *Mason*, 596 F.3d at 392 (citing 21 C.F.R. § 314.70(c)(6)(iii)(A), (C)).

**i. 2005 Attempt to Strengthen Label**

The FDA approved Depakote (divalproex sodium) in 1983. The drug was "indicated for use as sole and adjunctive therapy in the treatment of simple and complex absence seizures, including petit mal. Depakene may also be used adjunctively in patients with multiple seizure types which include absence seizures." (Doc. 114 at PageID 13813.)

On April 18, 2005, Abbott submitted a letter to Dr. Russell Katz of the FDA with the subject line "Supplement – Prior Approval Labeling."[8] (Doc. 113-31 at PageID 13536–63.) The purpose of the Supplement was to provide an update to the approved Depakote Tablets' label based on medical literature and a review of post-marketing safety data. Abbott asserted that "[t]he proposed labeling provides revised information related to teratogenicity and additional information for developmental delay and includes revisions to the **WARNINGS-Usage in Pregnancy** and the **Patient Information Leaflet** sections." (*Id*. at PageID 13536) (emphasis in original). With its Supplement, Abbott included "[a]n outline of safety-related changes for teratogenicity/developmental delay and DDI with topiramate" and "[n]ew information concerning the use of valproate in women of childbearing potential: teratogenicity and developmental delay." (*Id*. at 13537.)

[7] At the hearing on the pending motions for summary judgment, the parties clarified that they refer to CBE and CBE-0 interchangeably. (Transcript, Doc. 207 at PageID 26165, 26176.)
[8] This submission is also referred to as the 2005 Prior Approval Supplement (the "PAS") and/or the S-033.

Along with other modifications, the suggested label revision included adding the following language in the "Usage in Pregnancy" section of the label:

> *THERE ARE DATA THAT SUGGEST AN INCREASED INCIDENCE OF CONGENITAL MALFORMATIONS ASSOCIATED WITH THE USE OF VALPROIC ACID DURING PREGNANCY WHEN COMPARED WITH SOME OTHER ANTIEPILEPTIC DRUGS. THEREFORE, VALPROIC ACID SHOULD BE CONSIDERED FOR WOMEN OF CHILDBEARING POTENTIAL ONLY AFTER THE RISKS HAVE BEEN THOROUGHLY DISCUSSED WITH THE PATIENT AND WEIGHED AGAINST THE POTENTIAL BENEFITS OF TREATMENT.*
>
> . . .
>
> *THERE HAVE BEEN REPORTS OF DEVELOPMENTAL DELAY IN THE OFFSPRING OF WOMEN WHO HAVE RECEIVED VALPROIC ACID DURING PREGNANCY.*

(*Id*. at 13539–40.) Abbott also proposed adding the following language in its Patient Information Leaflet, under the section labeled, "Information For Women Who Could Become Pregnant:" "These medications have also been associated with other birth defects such as defects of the heart, the bones, and other parts of the body. Information suggests that birth defects may be more likely to occur with these medications than some other drugs that treat your medical condition. In addition, there have been reports of developmental delay in children born to women taking these medications." (*Id*. at 13542.) Abbott supported its submission with a White Paper labeled "New information concerning the use of valproate in women of childbearing potential: teratogenicity and developmental delay." (*Id.* at 13547.)

On February 7, 2006, the FDA responded by e-mail to Abbott's PAS and stated the proposed sentence referencing developmental delay should not be incorporated into labeling. (Doc. 113-33 at PageID 13582–83.) The e-mail stated:

> The sentence "There have been reports of developmental delay in the offspring of women who have received valproic acid during pregnancy" is based on two recent publications (Gaily E et al. Neurology 62(1):28-32, 2004 and Vinten J et al.

> Neurology 64(6):949-54, 2005) that attempted to correlate children's performance on IQ assessments with maternal prenatal use of valproate but which did not adequately control for maternal IQ and maternal educational attainment. Maternal IQ and maternal educational attainment are known to strongly correlate with children's performance on IQ assessments and thus would confound any attempt to draw a correlation to maternal prenatal valproate use. Given the studies' inability to establish this correlation, the proposed sentence should not be incorporated into labeling. A similar proposed sentence in the Patient Information Leaflet was removed in the Approval Letter for S-032 (January 11, 2006).

(*Id*. at 13582.)

**ii. 2007 General Correspondence with FDA**

On May 21, 2007, Abbott sent a letter to Dr. Katz of the FDA with the subject line "General Correspondence – Request for Advice regarding Developmental Labeling."[9] (Doc. 113-32 at PageID 13566–79.) The letter attached a White Paper labeled "Depakote Neurodevelopmental Delay White Paper" and stated that Abbott continued to monitor literature and spontaneous adverse drug events database for developmental delay associated with valproic acid. (*Id*.) The correspondence was intended to provide "an updated analysis of the occurrence of developmental delay in the attached white paper, which now includes more compelling data from the Neurodevelopment Effects of Antiepileptic Drugs (NEAD) study." (*Id.* at 13566.) The correspondence also stated the interim results from the NEAD study were "the first data with adequate control for maternal IQ using a standard IQ measure and show a significant developmental delay in 185 two-year-old children exposed to valproic acid during pregnancy." (*Id*. at 13566–67.) Abbott accordingly proposed that the following language be added to the "WARNINGS – Usage in Pregnancy" subsection of its label with consistent language added to the Patient Information Leaflet section of the label: "There have been reports of developmental delay in the offspring of women who have received valproate during pregnancy." (*Id.* at 13567.)

[9] This submission is also referred to as the 2007 Request for Advice ("RFA").

On March 3, 2008, the FDA Division of Neurology Products held a telephone conference with Abbott regarding the RFA. (Doc. 113-34 at PageID 13586.) Abbott's FDA Contact Report of the call states that "Dr. Katz stated they cannot approve this labeling change at this time," because the data was "not 'ripe 'for inclusion in labeling" as it was based on "interim data from Dr. K. Meador and the Neurodevelopment Effects of Antiepileptic Drugs (NEAD) Study group." (*Id*.) The Report further states:

> FDA feels that the sample size with VPA compared to other agents is small, some of the data for the 2 year old IQ evaluation was imputed, and there are too many confounding factors to believe the data is reliable at this timepoint in the study. Dr. Katz stated that they want to wait until the study is complete at the six-year time point. Dr. Embrescia then commented that there have been a number of cases of developmental delay reported through our post-marketing safety surveillance program, and asked whether that might not warrant the change in labeling. Dr. Katz asked for the number of cases we have, and Jim responded that at the time we submitted the proposed labeling change we had 240 reported cases, although many of those cases are confounded by other congenital abnormalities the patients have or other medications they were on. Dr. Katz indicated he thought these cases were probably too confounded to assess and that he believes this is the type of event where they want investigation in a formal setting to confirm.

(*Id*. at 13586–87.)

**iii. 2009 Correspondence**

On April 30, 2009, Abbott requested advice from the FDA about adding developmental delay warnings to the Depakote label. (Doc. 88-4 at PageID 5828–900.) Abbott's letter to the FDA states that since its requests on April 18, 2005 and May 21, 2007, Abbott monitored literature and post-marketing reports with respect to developmental delay and autism/autism spectrum disorder associated with in utero exposure to valproic acid. (*Id*. at 5828.) Abbott explained that since that time, "Dr. Meador *et al.* (2009) has released results of an interim analysis of 3-year IQ assessments from children with *in utero* AED exposure at an academic conference and published them recently in the *New England Journal of Medicine*." (*Id*.)

Additionally, "three (3) publications have recently been issued on the subject: Eriksson et al. (2005), Rasalam et al. (3005) and Nicolai et al. (2008)." (*Id*. at 5829.) Abbott requested the FDA to review the new information and "provide advice on the acceptability of these data for use to support an amendment to the current label regarding the risk of developmental delay and/or autism/autism spectrum disorder with intrauterine exposure to valproate." (*Id.*)

On September 18, 2009, the FDA held a teleconference with Abbott regarding Abbott's April 30, 2009 submission. (Doc. 88-4 at PageID 5825.) The FDA advised Abbott that it had requested data from Dr. Meador and planned to "independently review the data." (*Id*.) The FDA noted its statisticians "have raised concerns with [Dr. Meador's] study and the methodology for the collection of data." (*Id*.) "[B]efore taking regulatory actions with labeling, [the FDA] needed time to evaluate the data." (*Id*.) As a result, "[the FDA] stated that they were not ready to sign off on labeling language." (*Id*. at 5825–26.)

In response to Abbott's inquiry as to whether the FDA "would be open to [Abbott's] proposal for labeling language in the interim while the [FDA] completes its review[,]" the FDA advised that Abbott would be "well within [its] rights to submit a CBE but that [the FDA] would not take action until reviewing the data." (*Id*. at 5826.) Subsequently, on November 18, 2009, Abbott submitted a CBE-0 to add developmental delay warnings for Depakote. (Doc. 163-33 at PageID 22020–23.)

**iv. Failure to Warn of Developmental Delay Claim is Preempted**

Defendants argue that the FDA's 2006 and 2008 rejections of Defendants' attempt to add a developmental delay warning to the Depakote label constitute clear evidence that the FDA would have not have approved a developmental delay warning prior to M.B.D.'s injury in 2003-2004. Plaintiffs, on the other hand, contend that Defendants cannot meet the high burden

required to raise a preemption defense for three primary reasons: (1) the FDA did not approve Abbott's PAS because of Abbott's own omissions and failure to research the teratogenicity of Depakote, (2) Abbott failed to produce relevant documents, and (3) Abbott could have unilaterally added a warning with a CBE-0 at any time, but chose not to do so until 2009.

Preemption is warranted because there is clear evidence the FDA would not have approved a change to the Depakote label adding a developmental delay warning prior to M.B.D.'s injury. The Court finds the FDA's February 2006 decision that developmental delay warnings "should not be incorporated into [Depakote] labeling" and the FDA's 2008 belief that "the data do not provide sufficient evidence to support [Depakote] labeling changes at this time" constitute "clear evidence" that when confronted by the issue in 2003, the FDA would have rejected an attempt to add a developmental delay warning. (Doc. 113-33 at PageID 13582–83; Doc. 113-34 at PageID 13586–87.) *See Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 873 (7th Cir. 2010) (finding clear evidence that the FDA would not have approved a label change because the FDA did not approve "a reference to SJS/TEN on the label of over-the-counter drugs containing ibuprofen, when it had been asked to do so in the submission to which the agency was responding"); *Kaleta v. Abbott Laboratories, Inc*., No. 14-cv-847-NJR-SCW (S.D. Ill. Feb. 20, 2015) (order granting motion in limine to exclude evidence, testimony, and argument about preempted labeling issues) (examining the same FDA decisions at issue in this case and finding that the FDA's 2006 and 2008 rejections of Abbott's attempts to add a developmental delay warning constitute clear evidence the FDA would have rejected a similar change to the 1999 Depakote label); *In re Fosamax*, 951 F. Supp. 2d 695, 703 (D.N.J. 2013) (finding clear evidence the FDA would not have approved a label change prior to the plaintiff's injury where FDA had rejected prior attempts to strengthen the relevant label); *Dobbs v. Wyeth*

*Pharm.*, 797 F. Supp. 2d 1265, 1276–77 (W.D. Okla. 2011) (finding clear evidence that the FDA would have rejected an expanded warning for Effexor after the FDA rejected the warning added by the defendant). *See also Levine*, 555 U.S. at 571–72 (holding that Wyeth "failed to demonstrate that it was impossible for it to comply with both federal and state requirements" and reasoning that it "offered no such evidence" and never argued "that it attempted to give" a warning but "was prohibited from doing so by the FDA").

Although there have been a limited number of courts to rule on what constitutes clear evidence in determining whether a failure to warn claim is preempted, this Court is guided by Judge Rosenstengel's well-reasoned ruling on a motion in limine to exclude evidence, testimony, and argument about preempted labeling issues in *Kaleta*, No. 3:14-cv-847-NJR-SCW (ruling on motion in limine). In analyzing whether the motion should be granted, the *Kaleta* court examined the same 2006 and 2008 rejections to Abbott's attempts to add a developmental delay warning presently before this Court to determine whether those rejections constituted clear evidence the FDA would not have approved a 1999 developmental delay warning. Finding the evidence conclusive on the issue of preemption, the court held:

> The Court finds that there is clear evidence that the FDA would not have approved a change to the 1999 label to include a warning of developmental delay. As stated Above, Abbott tried, on various occasions, to secure approval of a developmental delay warning, and its requests were twice denied by the FDA (*See* Docs. 162-4; Doc. 162-5; Doc. 162-7; Doc. 162-8). In light of the fact that the FDA rejected the developmental delay warning in 2006 because it did not find that the available scientific evidence at that time supported the addition of such a warning, it is highly unlikely that the available scientific evidence, seven years prior to that date in 1999, would have supported the addition of such a warning. Notably, the FDA did not actually approve this developmental delay language until 2011.

*Id.* at *6–7. On this basis, the court granted the Abbott's motion in limine. Although the Court recognizes there are differences between the present case and the *Kaleta* case, the *Kaleta* court's ruling is persuasive.

The Court will briefly address the arguments raised by Plaintiffs, many of which were considered and rejected by the *Kaleta* court. First, Plaintiffs argue Abbott failed to conduct or sponsor published scientific research on Depakote and developmental delay, which constitutes deliberate inaction and a failure to press its position despite evidence to the contrary. Plaintiffs reason that if Abbott had funded or conducted studies that generated subsequently published data, those studies would have generated the same data sooner, and by 2003, the FDA would have allowed the developmental delay warnings based on that data. This reasoning is speculative. For example, in December 2004, Dr. Meador, who was a researcher running a pregnancy exposure registry to study multiple AEDs, including Depakote, presented interim registry data showing "possible developmental delay in some children exposed to VPA in utero." (Doc. 113-35 at PageID 13588–608.)[10] When the Meador data was available in 2009, Dr. Katz of the FDA was concerned about methodological issues with the data and wanted to independently review the results. (Doc. 88-4 at PageID 5825.) Thus, the FDA's 2006 and 2008 rejections of a developmental delay warning based on the then-available scientific evidence demonstrates it was highly unlikely that years prior, the scientific evidence would have supported such a warning and the FDA would have approved it in 2003-2004. *See Kaleta*, No. 3:14-cv-847-NJR-SCW, at *6–7.

[10] This data was taken from the NEAD study, a "prospective, observational investigation . . . [that studied] pregnant women with epilepsy who were receiving drug monotherapy (ie, carbamazepine, lamotrigine, phenytoin, or valproate) between October, 1999 and February, 2004, from 25 epilepsy centers in the UK and the USA." (Doc. 113-36 at PageID 13610–18.) This data was included in the White Paper submitted to the FDA on April 18, 2005 in support of Abbott's request to strengthen the Depakote label to include a developmental delay warning. As discussed *supra*, the FDA rejected Abbott's request in February 2006.

Plaintiffs also argue that Abbott submitted misleading or incomplete information with its 2005 and 2007 applications to the FDA. Plaintiffs support their position with proffered expert testimony of four experts who have reviewed and opined on allegedly misleading information in Abbott's White Papers submitted with Abbott's 2005, 2007, and 2009 correspondences with the FDA. Plaintiffs' argument that Abbott withheld certain information or misrepresented the results of studies in its 2005 and 2007 submissions to the FDA appears to be a fraud-on-the-FDA theory, which is preempted. *In re Fosamax*, MDL No. 2243, 2014 WL 1266994, at *17 (D.N.J. Mar. 26, 2014)[11] (citing *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 348 (2001)). As the Supreme Court held in *Buckman*, "state-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by, federal law." *Buckman*, 531 U.S. at 348.

Regardless, an expert's opinion that the FDA would have reacted differently if the submissions to the FDA in 2005 and 2007 had been supported by different evidence is speculative. Confronted with a similar argument in *In re Fosamax*, in which the court found that the plaintiff's claim against drug manufacturer Merck preempted, Judge Pisano reasoned:

> [W]hat Merck *could have* or *should have* done is immaterial because we know what Merck did. Similarly, *Wyeth v. Levine* provides for preemption where there is clear evidence that the FDA *would have* rejected a label change, and, again, we know that the FDA *did* reject it. Thus, any expert testimony relating to what

[11] Plaintiffs argue the *Fosamax* court applied the wrong legal standard and shifted the burden of proof of preemption to the plaintiffs, but the court's ruling was on an order to show cause. The *Fosamax* case is procedurally distinct. There, the Judicial Panel on Multidistrict Ligation centralized a number of related actions brought by plaintiffs who suffered femur fractures or similar bone injuries after taking Fosamax. The court ordered a process for selection of three of four early trial cases and the earliest of those, *Glynn*, was set for trial. The defendant moved for summary judgment in the *Glynn* case on federal preemption grounds, but, recognizing the large impact of its decision, the court reserved ruling on the issue. A jury trial took place, and the parties briefed the preemption issue three more times: a Rule 50(a) motion for judgment as a matter of law at the close of Plaintiffs' case, a renewed Rule 50(a) motion at the close of all evidence, and a Rule 50(b) motion for judgment as a matter of law. After considering the briefs, evidence, arguments, and trial record, the court granted the defendant's motion and found the plaintiff's state law claim for failure to warn was preempted, because clear evidence existed that the FDA would not have approved a stronger warning as of the date of the plaintiff's injury. Defendant then moved for an order to show cause as to why the claims of all other plaintiffs with injury dates prior to hers should not be dismissed pursuant to the court's preemption ruling, which was when the court ruled that the plaintiffs failed to show a genuine dispute of fact surrounding failure to warn claims, rendering them preempted and entitling defendant to judgment as a matter of law.

> Merck *could have* or *should have* done, and what the FDA *would* have done in response to the same is purely speculation and does not rise to the level of being a genuine fact dispute.

*In re Fosamax*, 2014 WL 1266994, at *9 (emphasis in original).

The same logic applies here. Testimony about what Abbott could have and should have researched or stated to the FDA in its applications is speculative, and does not serve as the basis for a genuine issue of material fact. Thus, as was the case in *In re Fosamax*, the Court finds that Plaintiffs' fraud-on-the-FDA theory is either preempted or based on speculation. *See In re Fosamax*, 2014 WL 1266994 at *17 (citing *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 348 (2001)). *See also In re Trasylol Products Liab. Litig.*, No. 08-MD-01928, 2010 WL 4259332, *12 (S.D. Fla. Oct. 21, 2010) ("[An expert] may not speculate as to what the FDA would have done in hypothetical circumstances."); *Webster v. Pacesetter, Inc.*, 259 F. Supp. 2d 27, 37 (D.D.C. 2003) ("Nor can plaintiffs create an issue of fact regarding their defective warning claim by speculating that *if* the FDA had known of the delayed perforation and tamponade incidents during the clinical trials and *if* defendant had investigated all the adverse incidents, the FDA would have either recalled the [product] or placed it on alert." (emphasis in original)).

Plaintiffs argue that the FDA's rejections of Abbott's PAS and RFA do not foreclose that the FDA would have accepted a CBE-0, had Abbott filed one. A CBE allows a manufacturer to immediately add a warning unilaterally, which is then subsequently reviewed by the FDA. 21 C.F.R. § 314.70(c). Plaintiffs argue that the FDA employs a different, more lenient standard for a CBE-0. Specifically, Plaintiffs point to Abbott's notes from a September 18, 2009 teleconference between Abbott and the FDA, during which the FDA advised Abbott that Abbott would be "well within [its] rights to submit a CBE but that [the FDA] would not take action until

reviewing the data" to argue this option was available at any time and that the changes to the label would have been accepted. (Doc. 88-4 at PageID 5826.)

Plaintiffs' argument that an earlier-filed CBE-0 could have been filed at any time to add a developmental delay warning is unpersuasive to demonstrate clear evidence that the FDA would have approved a developmental delay warning prior to M.B.D.'s injury. Although the option is available to submit a unilateral change through a CBE, the FDA must still ultimately approve and review that change. *Kaleta*, No. 3:14-cv-00847-NJP-SCW, at *8; 21 C.F.R. § 314.70(b)(3), (c)(4); 71 Fed. Reg. 3922 (The FDA reviews all such CBE submissions and "may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under section 502(a) of the act (21 U.S.C. 352)"); *see also Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 392 (7th Cir. 2010). Moreover, "[t]he FDA applies the same standards to evaluate both PAS and CBE supplements." *Kaleta*, No. 3:14-cv-00847, at *8. As the *Kaleta* court noted, the Seventh Circuit has held:

> The ability to make CBE labeling changes underscores a central premise of federal drug regulation: A 'manufacturer bears responsibility for the content of its label at all times.' *Levine*, 129 S. Ct. at 1197–98. While it is important for a manufacturer to warn of potential side effects, it is equally important that it not overwarn because overwarning can deter potentially beneficial uses of the drug by making it seem riskier than warranted and can dilute the effectiveness of valid warnings. Therefore, warnings may only be added when there is 'reasonable evidence of an association of a serious hazard with the drug.' 21 C.F.R. § 201.57 (2003). It is technically a violation of federal law to propose a CBE that is not based on reasonable evidence. 18 U.S.C. § 1001.

*Kaleta*, No. 3:14-cv-00847-NJP-SCW, * 8 (citing *Mason v. SmithKline Beecham Corp*., 596 F.3d 387, 392 (7th Cir. 2010)). In this case, Abbott has come forward with sufficient evidence that because the FDA rejected Abbott's 2005 PAS, it likely would have rejected an earlier-submitted CBE seeking to add the same language to the label that it eventually rejected in the PAS. *See Kaleta*, No. 3:14-cv-00847, at *8; *Fosamax*, 951 F. Supp. 2d at 704 ("Thus, since the

FDA rejected Defendant's PAS, it would not have approved a CBE seeking to add the same language to the label that it just rejected in the PAS.").

Finally, Plaintiffs argue that the FDA initially approved Abbott's proposed developmental delay warnings during a November 17, 2005 teleconference. This assertion arises from an internal Abbott FDA Contact Report regarding a November 2003 CBE application[12] to the FDA:

> [FDA's John Feeney] stated that FDA was in agreement with the latest wording provided to them regarding the multiorgan-hypersensitivity, teratogenicity and developmental delay, and the topiramate drug interaction. They noted that we had removed a sentence about developmental delay from the Patient Information Leaflet, and said that was OK. However, they wanted to know our rationale for removing it (ie. annotation to the removal).

(Doc. 114 at PageID 13919.) After Abbott submitted its 2005 PAS, the FDA advised Abbott that its S-032, which the FDA had not yet approved, was approvable, but asked Abbott to respond to various comments. (Doc. 163-18 at PageID 21638–42.) On July 1, 2005, Courtney Calder of the FDA advised Abbott to "pull the patient information leaflet changes from 033 and put it in 032 (state in the cover letter you are withdrawing it [sic] form 033)." (Doc. 163-27 at PageID 21944.) On July 21, 2005, Abbott submitted a letter to the FDA stating that it was removing the proposed text from the Patient Information Leaflet of Prior Approval Supplement to S-033, dated April 18, 2005. (Doc. 163-19 at PageID 21643–46.) Thus, this evidence makes clear that the FDA did not advise Abbott about or otherwise determine the acceptability of developmental delay warnings for the Depakote Prescribing Information before February 2006. (Doc. 163-24 at PageID 21934–35.) Plaintiffs' argument that the November 2005 FDA Contact Report therefore indicates that Abbott removed a developmental delay warning from its 2003 CBE application is inconsistent with the July correspondence between the FDA and Abbott. Thus, the argument that

[12] The 2003 CBE submission is also referred to as the S-032.

Abbott is either concealing documents or has a rationale document that could demonstrate Abbott advocated against its own request to add a developmental delay warning cuts against the evidence before the Court, which is that the FDA refused to include a developmental delay warning in 2006 and again, later, in 2008.

Thus, for these reasons, Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted.[13] Plaintiffs' motion for summary judgment on the defense of preemption is accordingly denied.

**b. Adequacy of Warning and Duty to Warn**

Having determined that Plaintiffs' allegation that Defendants failed to warn of the risk of developmental delay is preempted, the Court will next consider the parties' remaining arguments on the failure to warn claims. The Court will first turn to the Defendants' remaining three central arguments in moving for summary judgment: that the Depakote label was adequate as a matter of law, that Defendants were not required to provide language comparing the risks of Depakote to other AEDs in its label, and that the teratogenic risks of Depakote were common knowledge. The Court will next consider Plaintiffs' central argument in their Motion for Partial Summary Judgment that Defendants failed to adequately warn both Rheinfrank and her physician of the risks of Depakote, rendering the learned intermediary defense inapplicable. As expounded upon below, the Court finds questions of fact preclude summary judgment for either party on the failure to warn claims.

The Court will first consider whether the Depakote label was adequate as a matter of law. The parties dispute whether the warnings provided on the Depakote label were adequate in content and strength and whether they were required to be provided to Rheinfrank's physician or

[13] However, as discussed *infra*, summary judgment for the Defendants on the failure to warn claims is denied due to various questions of fact.

Rheinfrank directly. Generally, whether a particular warning is adequate is a question of fact for the jury. *In re Meridia Products Liability Litigation*, 328 F. Supp. 2d 791, 812 (N.D. Ohio 2004). "The fact finder may find a warning to be unreasonable, hence inadequate, in its factual content, its expression of the facts, or the method or form in which it is conveyed." *Seley v. G.D. Searle & Co.*, 423 N.E.2d 831, 837 (Ohio 1981). A warning's adequacy is measured by "what is stated" and "the manner in which it is stated." *Id.* "A reasonable warning not only conveys a fair indication of the nature of the dangers involved, but also warns with the degree of intensity demanded by the nature of the risk." *Id.* Thus, a warning may be found to be inadequate if it is "unduly delayed, reluctant in tone or lacking a sense of urgency," or where the "existence of a 'risk,' i.e., causal relationship between use of the product and resulting injury, has not been definitely established." *Id.*

Defendants argue their warnings are adequate as a matter of law. As of 1988, Depakote was designated by the FDA as a Pregnancy Category D drug.[14] Abbott also asserts it sent "Dear Doctor" letters in 1983 to the medical community to inform them of the risk of spina bifida among those exposed prenatally to valproic acid.[15] (Doc. 113-12 at PageID 13326–40.) In addition, Abbott incorporated a Black Box warning about teratogenicity in 1996. (Doc. 113-14; 113-15; 113-16; 113-17.)

Federal regulations do not limit drug manufacturers from strengthening their warnings to reflect new developments and comply with state laws. *Wyeth v. Levine*, 555 U.S. 555, 568–69 (2009) (citing 21 C.F.R. §§ 314.70(c)(6)(iii)(A), (C)). As the Supreme Court has explained, "it has remained a central premise of federal drug regulation that the manufacturer bears

[14] In 2003, Pregnancy Category D was assigned to a medication "[i]f 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[.]" 21 C.F.R. § 201.57 (April 1, 2003 ed.).

[15] Plaintiffs dispute that these letters were sent.

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. While the Pregnancy Category D and Black Box warning highlight important risks associated with the use of Depakote, they also direct the reader in some manner to consult additional sections of the warning label containing more information related to these risks in order to allow for a risk-benefit analysis, which Plaintiffs assert is inadequate.

In reviewing Plaintiffs' evidence offered in support of its contention that Abbott's 2003 label is inadequate, the Court finds summary judgment for Defendants is not warranted.[16] Thus, the Court is not persuaded that the mere fact that the label listed Depakote as a Pregnancy Category D drug and included a Black Box warning indicates that the label was adequate as a matter of law. *See Kaleta*, 3:14-cv-00847-NJR-SCW, at *11–12 (S.D. Ill. Feb. 14, 2015) (granting in part and denying in part Abbott's motion for summary judgment) (finding the mere fact that the label listed Depakote as a Category D drug and included a Black Box warning did not indicate that the label was adequate as a matter of law). Rather, there is a question of fact as to whether the 2003 Depakote warning was adequate. Plaintiffs have identified a number of alleged inadequacies in Abbott's warning, primarily through proffered testimony of multiple experts, the admissibility of which is disputed through *Daubert* motions.[17] For example, Dr. Michael D. Privitera, M.D. a tenured Professor of Neurology at the University of Cincinnati Medical Center, Director of the Epilepsy Center of the UC Neuroscience Institute and a clinician with University Neurology, Inc., opines that the Depakote label that existed in 2003 when

[16] The Court does not expressly rely upon the expert testimony of all experts brought forward by Plaintiffs in support of their argument that the 2003 Depakote label was inadequate. *C.f. J.B. by Lejune v. Abbott Laboratories*, No. 13-cv-326, 2014 WL 1464204, at *5 n.4 (S.D. Ill. April 14, 2014) (denying summary judgment on failure to warn claim and noting that the court did not expressly rely upon expert opinions, subject to pending but not yet ripe *Daubert* motions, in rendering its decision.)

[17] Although these motions are ripe, the Court defers ruling on the motions until after it can conduct a hearing on the matter. Rather, the Court will engage in a limited *Daubert* analysis only for purposes of this Order.

Rheinfrank became pregnant failed to provide adequate information to physicians and/or patients. (Doc. 109-1 at PageID 11711, 11718.) Such deficiencies include the label not stating that birth defects are greater with valproate than with other AEDs and the lack of warning that women of childbearing years should use contraception while taking valproate or not get pregnant while taking the drug. (*Id*. at 11718.)

**i. Admissibility of Dr. Privitera's Opinion**

Through a *Daubert* motion, Defendants argue Dr. Privitera is not qualified to testify about the adequacy of the Depakote label. (Doc. 155.) The Court will narrowly consider the admissibility of Dr. Privitera's opinion about the adequacy of the 2003 Depakote warning. Dr. Privitera is board certified by the American Board of Clinical Neurophysiology and American Board of Psychiatry and Neurology. (*Id*. at 11711.) He earned his B.A. in Biology from Johns Hopkins University and M.D. from State University of New York Medical Center. (*Id*.) Dr. Privitera is the author of numerous scientific peer-reviewed publications. (*Id*. at 11724–61.) The Court finds that Dr. Privitera is well-qualified based on this experience and education.

Defendants contend that Dr. Privitera's testimony regarding whether Defendants should have included additional or different warnings in the Depakote label and the adequacy of submissions to the FDA concern regulatory matters that are beyond the scope of Dr. Privitera's expertise. As Defendants point out, Dr. Privitera lacks specialized FDA product-labeling knowledge, skill, experience, training or education, and counsel admitted as much in his deposition. (*See* Doc. 109 at PageID 11625–26) (Ms. Abaray stating, "He's not a regulatory expert.")

Two cases are particularly instructive here. First, in *In re Gadolinium-Based Contrast Agents Prods. Liab. Litig*., MDL No. 1909, No. 1:08-GD-50000, 2010 WL 1796334, at *1 (N.D.

Ohio May 4, 2010), the court considered omnibus generic *Daubert* motions filed by the parties relating to the admissibility of experts in a products liability case in which plaintiffs alleged different agents in magnetic resonance scans caused a rare disease known as Nephrogenic Systemic Fibrosis ("NSF"). The court considered, among other issues, whether Dr. Fine, who was not a regulatory expert with expertise to opine on FDA regulations and the regulatory process or whether defendants complied with those regulations or processes, could, based on his "background as a nephrologist and his review of [defendants'] renal studies, internal documents and the published literature at the time" offer opinions about the adequacy of the defendants' warnings regarding the risks of the product at issue. *Id*. at *19. The court concluded that Dr. Fine was qualified to interpret and offer opinions about defendants' renal studies and therefore could offer opinions on whether the labeling information or Dear Doctor letters contained adequate information, or inaccuracies or omissions that could deprive or mislead physicians like himself who treat renally impaired patients about the risks associated with the administration of the product at issue. *Id.*

Second, in *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prods. Liab. Litig.*, No. MDL 1203, 2000 WL 876900, at *11 (E.D. Pa. June 20, 2000), the court considered whether the defendant pharmaceutical company adequately warned about the risks associated with the defendants' diet drugs. The defendants did not challenge the qualifications of the doctors to opine on their respective disciplines. *Id.* The court did not permit the doctors to testify as to regulatory requirements for labels or warnings, but did allow the experts to offer opinions concerning medical facts and science regarding the risks of the drugs in question, and to compare that knowledge with what was provided in the drug label and warning. *Id.* Specifically, the doctors were "qualified to render an opinion as to the labels' completeness,

accuracy, and —it follows from that—the extent to which any inaccuracies or omissions could either deprive a reader or mislead a reader of what the risks and benefits of the diet drugs in issue are or were at the time the labeling was published." *Id*.

The same is the case here. The parties do not dispute that Dr. Privitera is qualified as a neurologist, and his credentials establish his expertise in the field. However, Dr. Privitera is not qualified to opine on the regulatory aspects of the case, including whether Abbott was required to send a patient package leaflet directly to patients or whether Abbott's submissions to the FDA should have included certain materials. Similarly, testimony about what Defendants should have included in the label or what materials should have been submitted to the FDA falls outside the scope of his expertise, as it falls under the regulatory component and is speculative. Thus, Dr. Privitera also may not testify about whether Depakote should have been contraindicated for all women of childbearing years. On the other hand, testimony in which Dr. Privitera opines on the medical facts and science regarding the risks and benefits of Depakote and compares that knowledge with what was provided in the text of the labeling is admissible.[18]

**c. Comparative Label**

Having found that questions of fact exist as to the adequacy of Depakote's label's warnings, the Court will now consider Defendants' argument that they were not obligated under Ohio law to provide language in its label comparing the risks of Depakote to other AEDs.

[18] The parties also dispute whether Dr. Privitera's opinion regarding a developmental delay warning is admissible. For the reasons discussed *supra*, in which the Court concludes that Plaintiffs' claim that Defendants failed to warn of developmental delay is preempted, this testimony is not admissible. Defendants also argue Dr. Privitera's practice contradicts his opinions, but this argument goes to the weight of the evidence, not its admissibility. *Monroe v. Novartis Pharmaceuticals Corp*., 29 F.Supp.3d 1115, 1122 (S.D. Ohio 2014) (citing *McCullock v. H.B. Fuller Co.*, 61 F.3d 1038, 1044 (2d Cir. 1995) ("Disputes as to the strength of his credentials, faults in his use of differential etiology as a methodology, or lack of textual authority for his opinion, go to the weight, not the admissibility, of his testimony".) (citing *Daubert v. Merrell Dow Pharm., Inc*., 509 U.S. 579, 596, 113 S. Ct. 2786, 125 L.Ed.2d 469 (1993) ( "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.")). Thus, such issues of credibility are appropriate for the jury to resolve.

Specifically, Plaintiffs allege that Defendants' label was inadequate because it improperly compared Depakote to other AEDs, but the risks associated with Depakote were greater, including the increased risk of congenital malformations when Depakote is prescribed as part of polytherapy and the increased risk of teratogenic effects to the developing fetus as compared to other antiepileptic drugs, which are safer for women of childbearing age.

Defendants argue that Plaintiffs' allegation that its label failed to adequately warn of the increased risk of teratogenic effects to the developing fetus as compared to other antiepileptic drugs, which are safer for women of childbearing age, fails as a matter of law. Alternatively, Defendants argue that the voluntary duty rule, under which one who gratuitously undertakes a voluntary act assumes the duty to complete with due care under the circumstances, does not apply here. Finally, Defendants contest the evidence Plaintiffs rely upon for the proposition that Depakote was more harmful than other AEDs.

To support their argument that Defendants were under no obligation to provide a comparative warning, Defendants argue that the Sixth Circuit in *Ackley v. Wyeth Laboratories, Inc.,* has held that a manufacturer is "obligated to make a reasonable disclosure of all the risks inherent in its own drug," but "[i]t is not obligated to provide a comparison of its drug with others[']." 919 F.2d 397, 405 (6th Cir. 1990) (citing *Seley v. G.D. Searle & Co.,* 423 N.E.2d 831 (Ohio 1981)). Defendants contend that the portion of the label upon which Plaintiffs rely does not offer a comparison between Depakote and other AEDs.

Plaintiffs argue *Ackley* is distinguishable, and the Court agrees. As other courts have acknowledged, the *Ackley* case did not involve warnings that included comparative information. *See, e.g., J.B. v. Abbott Laboratories, Inc*., No. 13-cv-326-DRH-SCW, 2014 WL 1464204, at *5 (S.D. Ill. April 14, 2014) (distinguishing *Ackley* and other cases on the basis that they "do not

appear to involve warnings that included comparative information"); *Schedin v. Ortho-McNeil-Janseen Pharms., Inc.*, 776 F. Supp. 2d 907, 914 (D. Minn. 2011) (*Ackley* did not apply because information "on comparative drugs was germane to the particular condition at issue"). By contrast, in this case, Abbott compared Depakote's teratogenicity to the teratogenicity of other AEDs. Specifically, the 2003 label discusses teratogenicity and the fact that "reports indicate a possible similar association with the use of other antiepileptic drugs":

> THERE ARE MUTLIPLE REPORTS IN THE CLINICAL LITERATURE WHICH INDICATE THAT THE USE OF ANTIEPILEPTIC DRUGS DURING PREGNANCY RESULTS IN AN INCREASED INCIDENCE OF BIRTH DEFECTS IN THE OFFSPRING. ALTHOUGH DATA ARE MORE EXTENSIVE WITH RESPECT TO TRIMETHADIONE, PARAMETHADIONE, PHENYTOIN, AND PHENOBARBITAL, REPORTS INDICATE A POSSIBLE SIMILAR ASSOCIATION WITH THE USE OF OTHER ANTIEPILEPTIC DRUGS.

(Doc. 112-4 at PageID 12738.) The *Kaleta* court similarly found that the language that "reports indicate a possible similar association with the use of other antiepileptic drugs" from the 1999 Depakote label was comparative. *Kaleta v. Abbott Laboratories, Inc*., No. 14-CV-847-NJR-SCW, at *14 (S.D. Ill. Feb. 14, 2015) (granting in part and denying in part summary judgment for Abbott).

The Court will next turn to the question of whether the voluntary duty rule applies, as Plaintiffs contend. Under the voluntary duty doctrine, one who gratuitously undertakes a voluntary act assumes the duty to complete it with exercise of due care under the circumstances. *Seley*, 423 N.E.2d at 839 (citing *Briere v. Lathrop Co.*, 258 N.E.2d 597, 602 (Ohio 1970)). Defendants argue the voluntary duty rule does not apply to failure to adequately warn claims, because the doctrine "has no application to cases based on failure to provide adequate warnings with prescription drugs, whether grounded in negligence or strict liability." *Id.* The *Seley* case elaborates that the "voluntary duty" rule "has no application to cases based on failure to provide

adequate warnings with prescription drugs, whether grounded in negligence or strict liability[,]" as in this case. *Id.* This is so because "[i]t has become a well established rule in such cases that the manufacturer satisfies his duty to warn of dangers associated with use of the product by providing adequate warnings to the medical profession, and not the ultimate user" under the learned intermediary theory. *Id*. As previously discussed, whether it was adequate for Defendants to offer a comparative warning is a question of fact for the jury.

Defendants also argue Plaintiffs rely primarily on the fact that Abbott received preliminary unpublished data from the North American Anti-Epileptic Drug registry in August 2002 which suggested Depakote might be more teratogenic than other AEDs as the basis of its argument. (Doc. 83-2 at PageID 3410–25.) Citing other scholarly journals, Defendants contend the 2002 study results are hardly conclusive and did not represent the consensus of scientific thinking on the subject. For example, Defendants direct the Court to a 2004 article, which stated:

> While many studies have demonstrated an increased risk of fetal malformations (FMs) in women with epilepsy taking AEDs during pregnancy, there is still little solid data on the relative risk of the various AEDs or of different drug combinations and doses.

(Doc. 152-5 at PageID 19705 (Vajda, et al., Critical relationship between sodium valproate dose and human teratogenicity: results of the Australian register of anti-epileptic drugs in pregnancy, at 854 11(8) Journal of Clinical Neuroscience (2004)). The conflicting scientific evidence demonstrates there is a genuine issue of material question of fact for the jury to resolve as to whether there was sufficient evidence that Depakote was more teratogenic than other AEDs.

**d. Common Knowledge Defense**

The Court will next consider Defendants' argument in support of their Motion for Summary Judgment that they are not obligated to warn of risks that are common knowledge. A

product is not defective for inadequate warning if a manufacturer failed to instruct about "an open and obvious risk or a risk that is a matter of common knowledge." Ohio Rev. Code § 2307.76(B).

Defendants argue that the teratogenicity of Depakote increasing with higher doses and that the risk of congenital malformations increasing when Depakote is prescribed as a part of polytherapy were matters of common knowledge at the time of Rheinfrank's pregnancy with M.B.D. in 2003. Defendants contend the evidence demonstrates that higher doses of AEDs are riskier than lower doses and that AED polytherapy poses greater risks to a fetus than monotherapy were textbook medicine. To support their position, Defendants rely upon excerpts from published articles and textbook chapters that address AED polytherapy and dosing. (*See, e.g.*, Doc. 113-25 at PageID 13455–56 (Antonio V. Delgado-Escueta, M.D., and Dieter Janz, M.D., *Consensus guidelines: Preconception counseling, management, and care of the pregnant woman with epilepsy*, 42 NEUROLOGY (Suppl. 5), 149–160 (1992)); Doc. 113-29 at PageID 13518–24 (Martha J. Morrell, M.D., *Guidelines for the care of women with epilepsy*, 51 NEUROLOGY (Suppl. 4) S21–S27 (1998)); Doc. 113-30 at PageID 13526–33, (Samren, et al., *Antiepileptic Drug Regimens and Major Congenital Abnormalities in the Offspring*, ANNALS OF NEUROLOGY (Vol. 46, No. 5) (1999); Doc. 113-18 at PageID 13404–10 (CECIL TEXTBOOK OF MEDICINE (19th ed.)); Doc. 113-20 at PageID 13419–39 (HARRISON'S PRINCIPLES OF INTERNAL MEDICINE (14th ed., vol. 2))). Relying upon Dr. Lemus's deposition testimony, in which she agreed that both HARRISON'S and CECIL'S are standard reference books for internal medicine doctors, Defendants contend this information was readily accessible to general practitioners and specialists, including Dr. Lemus, Rheinfrank's prescribing physician in 2003. (Lemus Dep. at 47–48, Doc. 83 at PageID 3267.)

Although the cited exhibits generally discuss that polytherapy poses greater risks to a fetus than monotherapy, and that higher doses of AEDs are riskier than lower doses, the articles do not address polytherapy with valproate posing a significantly increased risk than polytherapy with other AEDs and the increased risk of higher dosages when women took Depakote, as opposed to other AEDs. For example, the 1996 edition of CECIL TEXTBOOK OF MEDICINE discusses that "use of two or more drugs" increases a risk of major fetal malformations, but does not address how the risk of polytherapy is changed or increased when Depakote is one of the drugs used:

> In the general population, *major fetal malformations* (cardiac defects, cleft lip or palate, neural tube defects, including spina bifida and anencephaly) occur in about 2% of pregnancies. This risk is increased 5 to 6% in infants born to women with epilepsy who have taken a single antiepileptic drug during pregnancy. Valproate increases the chance of neural tube defects by 1.5%, and carbamazepine polytherapy may also raise this specific risk by 0.5%, especially if there is a family history of neural tube defects. Use of two or more drugs carries a 10% risk of major fetal malformations.

(Doc. 83-2 at PageID 3401) (emphasis in original). Similarly, the 1998 edition of HARRISON'S PRINCIPLES OF INTERNAL MEDICINE states that the risk of fetal abnormalities increases with the number of AEDs used, but does not describe how Depakote increases teratogenicity:

> The overall incidence of fetal abnormalities in children born to mothers with epilepsy is 5 to 6 percent, compared to 2 to 3 percent in healthy women. Part of the higher incidence is due to teratogenic effects of antiepileptic drugs, and the risk increases with the number of medications used (e.g., 10 percent risk of malformations with three drugs).

(Doc. 113-20 at PageID 13436–37.) HARRISON'S also describes dosing and the preference for monotherapy when possible, but lacks a description about the increased risk of higher dosages of Depakote:

> Since the potential harm of uncontrolled seizures on the mother and fetus is considered greater than the teratogenic effects of antiepileptic drugs, it is currently recommended that pregnant women be maintained on effective drug therapy.

> When possible, it seems prudent to have the patient on monotherapy at the lowest effective dose, especially during the first trimester.

(*Id*. at 13437.)

Plaintiffs have demonstrated a genuine issue of material fact exists as to whether it was common knowledge at the time of Rheinfrank's pregnancy with M.B.D. in 2003 that the teratogenicity of Depakote increases with higher doses and that the risk of congenital malformations increases when Depakote is prescribed as a part of polytherapy. Because a question of fact exists, *Midwest Specialties, Inc. v. Crown Indus. Prods.* Co., 940 F. Supp. 1160, 1167 (N.D. Ohio 1996), which stands for the proposition that Abbott cannot be held liable for telling doctors what they already knew, is not dispositive. There, the Court found that it was evident from the pleadings and depositions that the risks associated with the product at issue were a matter of common knowledge in the salient industry. *Id.* By contrast, in this case, there is a question of material fact as to whether the aforementioned risks of Depakote were common knowledge in the salient industry.

**e. Learned Intermediary Defense**

Finally, the Court will consider Plaintiffs' argument that they are entitled to summary judgment on the learned intermediary defense. Defendants invoke the learned intermediary defense under both common law and Ohio Rev. Code § 2307.76(C) and claim they fulfilled their duty to warn of the risks of Depakote by warning Rheinfrank's physician. The learned intermediary defense applies if the "manufacturer provides otherwise adequate warning and instruction to the physician or other legally authorized person who prescribes or dispenses that ethical drug for a claimant in question and if the federal food and drug administration has not provided that warning or instruction relative to that ethical drug is to be given directly to the ultimate user of it." Ohio Rev. Code § 2307.76(C); *see Seley v. G.D. Searle & Co.*, 423 N.E.2d

831, 839–840 (Ohio 1981) (acknowledging the rule that the physician acts as a learned intermediary between manufacturer and patient). Defendants argue they adequately warned Rheinfrank's prescribing physician of the risks of Depakote and that the physician's testimony establishes she would not have changed her prescribing habits had she been warned differently.

In support of their Motion for Partial Summary Judgment on this defense, Plaintiffs argue the evidence establishes that the FDA required Abbott to create a stand-alone Patient Information Leaflet warning of the risks of teratogenicity as a condition of approval of Depakote for use for migraines in 1996. Plaintiffs assert that when Abbott voluntarily modified the language of the Patient Information Leaflet through a CBE-0 in 2003, Abbott was required to distribute the modified Patient Information Leaflets directly to all users, including Rheinfrank, but failed to do so. Plaintiffs argue this alleged failure to adequately warn Rheinfrank constitutes the proximate cause of M.B.D.'s injuries. Having reviewed the evidence, the Court finds Plaintiffs have failed to meet their burden in moving for summary judgment on this defense.

**i. Patient Information Leaflet as a Condition of Approval for Use for Migraine**

The following facts relating to the Patient Information Leaflet and communications between Abbott and the FDA are relevant to Plaintiffs' argument that the learned intermediary defense is inapplicable. The genesis of the Patient Information Leaflet was in 1994. At that time, Abbott submitted a supplemental new drug application to the FDA for an indication that Depakote could be used for prophylaxis of migraine headaches. It is undisputed that the FDA required Abbott to comply with certain conditions in order to be approved for migraine use. On June 16, 1995, the FDA notified Abbott that its supplemental new drug application to add an indication for migraine prevention to its Depakote labeling was "approvable," based upon certain conditions, including the following:

> That there is in place, prior to the initial distribution of Depakote® Tablets as a treatment for migraine, a mechanism/system to ensure that migraineurs receiving prescriptions for Depakote® Tablets for migraine prophylaxis will be provided with an information sheet that provides, in language readily understandable to a lay person, i) a clear and unambiguous warning that valproate is a known human teratogen and, ii) an explication of the potential risks this property of the drug imposes upon women who elect to use the product during their childbearing years.

(Doc. 84-3 at PageID 3920.) The FDA explained its reasons for specific concern about the risk-benefit analysis for migraine patients as the basis for its requirement for the information sheet:

> We are mindful that valproate containing products have long been marketed for use in the management of epilepsy, and more recently for the management of acute mania, without a requirement for a patient information sheet that calls attention to the drug's teratogenic potential. Drug product labeling, however, must provide information critical to the prudent use of a product for each of the indications for which it is recommended. What constitutes critical information is not an isolated function of the properties of the drug product, but the characteristics of the illness the product is intended to treat, and the nature of the population who suffer from that illness.
>
> Epilepsy and acute mania are potentially life-endangering illnesses; immediate control of their manifestations is vital to the well being of the patient. In contrast, migraine, albeit a chronic, painful, life-disrupting illness, is neither life-threatening nor life-endangering. Moreover, several marketed drug products are available that can effectively and safely abort acute migrainous attacks.
>
> In short, the risk benefit considerations impinging upon the use of Depakote® Tablets in migraine prophylaxis differ substantively from those affecting its use in epilepsy and mania.

(*Id.* at 3920–21.)

Although Abbott resisted creating a patient information sheet, suggesting instead it could provide "educational information and guidance for the prescribing physician to assist him or her in informing female migraineurs of child-bearing age about the potential teratogenic effects of valproate," the FDA would not agree to approval of Depakote for migraine "without a patient package insert" or "a unit of use package that included the patient information." (Doc. 84-3 at PageID 3926, 3930.)

The requirement that Abbott create an information sheet about the risks of teratogenicity for migraine patients sparked negotiations between Abbott and the FDA about how the relevant information would be conveyed and distributed. Hence, on December 1, 1995, Abbott submitted what it referred to as a patient information sheet or Patient Information Leaflet for migraine patients to the FDA, along with a proposal for how it would be delivered to the migraine patients. Abbott stated "we would propose that this distribution take place at the level of the prescribing physician." (Doc. 163-8 at PageID at 21151.) The means of distribution were proposed as follows:

- A copy of the patient leaflet will be included in the announcement letter to all neurologists.
- Sales representatives will deliver pads of these patient leaflets on the initial sales call for promotion for Depakote in migraine prophylaxis. Subsequently, additional pads of patient leaflets will be provided upon request using a business reply card or a toll free (1-800) telephone number.
- A copy of the patient leaflet will be inserted to sample packages distributed in connection with the promotion of Depakote in migraine prophylaxis.

(*Id*. at 21151–52.)

On January 19, 1996, Abbott and the FDA attended a telephone conference regarding the patient information sheets, during which Dr. Leber of the FDA "stated that [Abbott's] proposed means of distribution of the patient information sheet is agreeable in principle, but this is conditional upon having the information also in the primary labeling." (Doc. 82-2 at PageID 2837.) Abbott's summary of the call states that the FDA was agreeable to Abbott including the text of the Patient Information Leaflet at the end of the labeling as part of the package insert, with a reference statement in the "Information for Patients" section of the "Precautions" section of the labeling. (Doc. 82-2 at PageID 2837.) According to Abbott's records, the FDA "reiterated that [Abbott's] proposed means of distributing the patient information leaflet (as

proposed in our December 1, 1995 submission) was acceptable, if [Abbott] [met] the previously specified condition." (*Id.*)

On January 24, 1996, Abbott submitted draft labeling which incorporated the required information for patients in the Depakote package insert. (Doc. 163-10 at PageID 21214.) Abbott stated:

> The approach we have taken is to include the key information in the "PRECAUTIONS- Information for Patients" section of the labeling (see page 13 of the enclosed draft), and then to note that patients should be advised to read the Patient Information Leaflet that is referenced to its location at the end of the package insert where it is reprinted in its entirety.

(*Id*. at 21215.)

On March 18, 1996, the FDA completed its review and approved Abbott's supplemental new drug application dated June 30, 1994, concluding that "adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling." (Doc. 163-12 at PageID 21252.) On April 12, 1996, Abbott submitted copies of the final printed labeling to the FDA, "including the patient information leaflet, that is identical in content to the draft labeling enclosed with the March 18, 1996 approval letter." (Doc. 163-13 at PageID 21256.) Abbott contends the Patient Information Leaflet was renewed at least through 2000, and "thereafter the contents of the PIL have remained as a separate Patient Information Leaflet section of the Prescribing Information for Depakote." (Doc. 163 at PageID 21013 (emphasis removed); *see* Doc. 163-7 at PageID 21143–47.)

**ii. 2003 CBE-0 Modification to Patient Information Leaflet Sections of the Package Insert**

On November 10, 2003, Abbott submitted a Final Printed Label as a Special Supplement – Changes Being Effected (CBE) for Depakote Tablets. The submission "includes changes to

the WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, and Patient Information Leaflet sections of the package insert (PI)." (Doc. 82-2 at PageID 2923) (emphasis removed). The letter outlined two changes related to the Patient Information Leaflet:

> 2. Provided below are changes for NDA 18-723 (Depakote Tablets) and NDA 21-168 (Depakote ER) to the **Information for Patients** section. The migraine specific reference has been deleted to make the information neutral to indication. These changes (in addition to the change in the **Patient Information Leaflet**) were based upon information communicated to pharmaceutical manufacturers earlier this year regarding continued review of the data obtained from the Antiepileptic Drug (AED) Pregnancy Registry at Massachusetts General Hospital in Boston. The AED Pregnancy Registry reported that analysis of the data suggest that the use of valproate during pregnancy may be an important risk factor for major birth defects. Therefore, because the risk of birth defects may be associated with the use of valproate, Abbott Laboratories has elected to remove the migraine specific reference from the **Information for Patients** and the **Patient Information Leaflet** sections of the Depakote and Depakote ER PIs. This action is taken to provide a balanced communication of the information to patients receiving valproate treatment regardless of indication. In addition, Abbott Laboratories has elected to incorporate the **Patient Information Leaflet** into the Depakene Capsules and Syrup, and Depakote Sprinkle Capsule PIs. (see Section III for specific labeling revisions)
>
> > **PRECAUTIONS**
> > **Information for Patients**
> > ~~Migraine Patients:~~ Since DEPAKOTE has been associated with certain types of birth defects, female patients of child-bearing age considering the use of DEPAKOTE ~~for the prevention of migraine~~ should be advised to read the Patient Information Leaflet, which appears as the last section of the labeling.
> >
> > Note: the PI for Depakote ER did not contain a subheading of "Migraine Patients:" in the approved labeling.
>
> . . .
>
> 5. **The Patient Information Leaflet** section has been modified to remove the migraine specific language from NDA 18-723 (Depakote Tablets) and NDA 21-168 (Depakote ER) to make the language indication neutral. The **Patient Information Leaflet** (as modified) has been added to NDA 18-081, 18-082, and NDA 19-680 PIs (see Section III for a complete description of the change). Please refer to Section 2 above for an explanation and rationale regarding this change.

(*Id*. at PageID 2924–26) (emphasis in original).

### iii. Plaintiffs Are Not Entitled to Summary Judgment on the Learned Intermediary Defense

Plaintiffs have failed to demonstrate that they are entitled to summary judgment on the learned intermediary defense. Plaintiffs' theory that Defendants' 2003 CBE-0 unilaterally expanded their obligations to directly warn of the risk of teratogenicity to all users of childbearing age directly is not supported by the evidence. It is undisputed that in 1996, the FDA required Abbott to distribute a Patient Information Leaflet warning of the risks of teratogenicity as a condition for approving Depakote use for migraine. The FDA ratified Abbott's proposed distribution plan for the Patient Information Leaflet, which was to "take place at the level of the prescribing physician." (Doc. 163-8 at PageID at 21151.) The three limited circumstances under which the stand-alone Patient Information Leaflet was to be distributed included: providing a copy in the announcement letter to all neurologists, sales representatives delivering pads of leaflets on initial sales call for the promotion of Depakote for migraine use and subsequently, those leaflets would be provided upon request, and inserting Patient Information Leaflets in sample packages to be distributed in connection with the promotion of Depakote in migraine prophylaxis. (*Id.* at 21151–52.) The content of the Patient Information Leaflets was also required to be printed at the end of the Depakote package insert.

When Abbott voluntarily chose to remove the migraine-specific language of the Patient Information Leaflet as printed at the end of the package insert in 2003, it does not logically follow that Abbott also voluntarily undertook or was required to not only distribute the leaflet as described in 1995-1996 for the promotion of Depakote use for migraine, but to all users of childbearing age. Initially, Abbott's CBE-0 in 2003 was clear that Abbott was submitting changes to the "Patient Information Leaflet sections of the package insert (PI)" only. (Doc. 82-2

at PageID 2923) (emphasis removed). Thus, the change did not affect the stand-alone Patient Information Leaflet. Plaintiffs' argument fails for this reason alone.[19]

Moreover, Plaintiffs have not identified any communication between Abbott and the FDA, absent the 1995-1996 communications discussing distribution of Patient Information Leaflet for Depakote use in migraine, to support their position that the FDA required a direct warning to all women of child-bearing age. The 1995-1996 communications do not support Plaintiffs' position.[20] Rather, those documents demonstrate that the distribution of the Patient Information Leaflet was limited to promotional activities upon approving the indication of Depakote for migraine use and grounded in particularized concern about the risk/benefit analysis for use of the drug for migraine, as opposed to a different illness, such as epilepsy.

Defendants also argue that expanding the Patient Information Leaflet section of the package insert was voluntary and intended to aid the doctor's communication with patients, and thus does not abrogate the learned intermediary rule, relying upon *Seley v. G.D. Searle & Co.*, 423 N.E.2d 831, 840 (Ohio 1981). In *Seley*, the Ohio Supreme Court recognized that a manufacturer satisfies the duty to warn of dangers associated with the product at issue by providing adequate warnings to the medical profession, not the ultimate user of the product. *Id.* The "voluntary duty" doctrine has no application to prescription drug failure to warn cases grounded in negligence or strict liability, because of the learned intermediary defense. *Id.* In

[19] Plaintiffs point to the fact that Defendants' 2003 CBE-0 included an attachment of a marked up, indication neutral, stand-alone Patient Information Leaflet for support for the position that Abbott undertook warning all women of childbearing age of Depakote's teratogenicity by a stand-alone Patient Information Leaflet. (*See* Doc. 82-2 at PageID 2941–42.) The Court declines finding that this document establishes that the FDA required an indication neutral, stand-alone leaflet to be distributed to all Depakote users of childbearing age.

[20] Nor does Plaintiffs' argument that the Black Box warning refers to an information sheet establish a stand-alone leaflet was required to be distributed to all women of child-bearing age in 2003. ("AN INFORMATION SHEET DESCRIBING THE TERATOGENIC POTENTIAL OF VALPROATE IS AVAILABLE FOR PATIENTS." (2003 Package Insert, Doc. 113-15 at PageID 13367.)) This is consistent with the availability of a Patient Information Leaflet printed at the end of the package insert.

*Seley*, the drug manufacturer voluntarily prepared pamphlets about oral contraceptives for direct distribution to patients. The court stated:

> Informational pamphlets, such as provided Dr. Froehlich by Searle for distribution to his patients in the exercise of the doctor's discretion, can aid in expanding the range of communications between doctor and patient. Similarly, they may contribute to the patient's informed use of the drug while under the doctor's supervision. Nevertheless, a direct relationship between the manufacturer and the patient does not arise as a result of the provision of such brochures. In this case Mrs. Seley did not receive the allegedly deficient informational material directly from the manufacturer, but from her doctor. Although we recognize that the intent of such brochures is to ultimately benefit the user, we do not believe that by preparing such brochures and distributing them to physicians, a prescription drug manufacturer undertakes to render a voluntary service so as to invoke the "voluntary duty" rule set forth in *Briere v. Lathrop*, supra, thereby extending the scope of its duty to warn.

*Id.* The Court agrees that in this case, Abbott's voluntary expansion of its patient information leaflet in its package insert did not abrogate the role of the learned intermediary; rather, it was intended to aid the learned intermediary. As noted *supra*, there is a question of fact as to whether the information communicated to the learned intermediary was sufficient.

Thus, construing all evidence in the light most favorable to the non-moving party, Defendants, Plaintiffs have not come forward with evidence that the FDA required a warning or instruction be given directly to all women of childbearing age using Depakote in 2003. Accordingly, Plaintiffs are not entitled to summary judgment on this defense. There remains a question of fact as to whether Rheinfrank's prescribing physician was adequately warned such that she can be considered a learned intermediary.

**f. Causation**

**i. Proximate Cause**

Defendants also argue they are entitled to summary judgment because Plaintiffs cannot prove proximate cause. Specifically, Defendants contend Plaintiffs cannot show causation because a different warning would not have changed Rheinfrank's prescribing doctor's

treatment. Plaintiffs argue that the heeding presumption applies and that Defendants have failed to rebut the presumption that the inadequate warnings, be it to Rheinfrank or the physician, caused M.B.D.'s injuries.

In *Seley v. G.D. Searle & Co.*, 423 N.E.2d 831, 838 (Ohio 1981), the Ohio Supreme Court explained that, in the context of a failure to warn claim, proximate cause involves two issues: "(1) whether lack of adequate warnings contributed to the plaintiff's ingestion of the drug, and (2) whether ingestion of the drug constitutes a proximate cause of the plaintiff's injury." Defendants initially argue that Plaintiffs cannot prove that the lack of an adequate warning contributed to Rheinfrank's use of Depakote. Under Ohio law, it is presumed that if an adequate warning is given, it will be read and heeded, a presumption that benefits the manufacturer. *Id.* But "where no warning is given, or where an inadequate warning is given, a rebuttable presumption arises, beneficial to the plaintiff, that the failure to adequately warn was a proximate cause of the plaintiff's ingestion of the drug." *Id.* The presumption may be rebutted by proof that "an adequate warning would have made no difference in the physician's decision as to whether to prescribe a drug or as to whether to monitor the patient thereafter." *Id.* "Where a treating physician unequivocally testifies that an adequate warning would not have altered the course of treatment, summary judgment is warranted. However, it is not warranted if the evidence does not affirmatively establish that the physician 'would not have behaved differently had he received a different warning.'" *Sheffer v. Novartis Pharmaceuticals Corp.*, No. 3:12-cv-238, 2013 WL 5276558, at *11 (S.D. Ohio Sept. 18, 2013) (citing *Miller v. ALZA Corp.*, 759 F. Supp. 2d 929, 936 (S.D. Ohio 2010)). If rebutted, "the required element of proximate cause between the warning and ingestion of the drug is lacking." *Seley*, 423 N.E2d at 838–39.

Defendants argue that even if their label was not adequate as a matter of law, they have successfully rebutted the presumption that a failure to adequately warn was a proximate cause of Rheinfrank's use of the drug. Defendants rely upon testimony by both Dr. Lemus and Rheinfrank to support their argument that a stronger warning would not have altered Dr. Lemus's course of action and prevented Rheinfrank from ingesting the drug. Dr. Lemus, a resident in internal medicine in 2003, testified that she has no memory of Rheinfrank and cannot remember any specific conversations she had with her. (Lemus Dep. at 19, Doc. 83 at PageID 3260.) When questioned about her familiarity of Depakote's Black Box warning, she testified:

> Q. Now, when you prescribed Depakote in 2003, I take it you were aware of this black box warning about birth defects with Depakote?
> A. It's difficult to answer that question because I didn't have – I don't remember having a sense of this is a very dangerous drug for someone that could potentially get pregnant.
>
> I can't remember this patient, so I – I'm not even sure that I started prescribing this medication because as an internal medicine physician, Depakote is something that's usually prescribed by neurologists for seizures, and what I could only assume is that I continued the medication.

(*Id*.) Dr. Lemus also testified that she does not currently prescribe antiepileptic medications and that it is obvious to her now that "it's important for a childbearing woman/patient that is taking any type of medication that would be a Category D to be informed." (*Id*. at 24, PageID 3261.) Based on this evidence, Defendants contend that the record reflects Dr. Lemus did not give an adequate warning to Rheinfrank about the potential for birth defects caused by taking Depakote, not because she considered them unimportant, but because she may not have been aware of the drug's Black Box warning. Relying upon *Daniel v. Fisons Corp.*, 740 N.E.2d 681, 685 (Ohio App. 2000) for the proposition that a doctor who ignores the dosaging instructions defeats the presumption that the allegedly inadequate warning was a proximate cause of the plaintiff's

injury, Defendants argue that the evidence Dr. Lemus did not read the Depakote warnings indicates that an additional or stronger warning would not have affected her prescribing decision.

According to Rheinfrank, if she had been warned Depakote might cause birth defects, she would have discontinued using it:

> Q When you got pregnant, did any doctor give you any advice about Depakote or phenobarbital concerning potential risks to your fetus?
> A No.

(Rheinfrank Dep. (May 30, 2014) at 79, Doc. 106 at PageID 8905.)

> Q If you had been told that Depakote might produce birth defects in your unborn child if you took it while you were pregnant, would that have caused you to choose not to take Depakote?
> A Yes.

(Rheinfrank Dep. (July 1, 2014) at 58, Doc. 79 at PageID 1458.)

> Q Did any doctor tell you that the medication was safe to take?
> A They didn't tell me it wasn't.
> Q Did any doctor tell you the medication posed no risk whatsoever to you or your fetus?
> A Repeat that.
> Q Did any doctor tell you that there was no risk to your fetus in taking the antiepileptic drugs that you were taking?
> A No, they didn't tell me there was any.
> Q I didn't ask that question. My question is: Did any doctor tell you there was no risk to your fetus from taking an antiepileptic drug?
> A They didn't tell me either way.

(*Id*. at 35, PageID 1452.) According to Defendants, this evidence establishes that it is obvious that a lack of a stronger warning in the label did not contribute to Rheinfrank's use of the drug, thereby rebutting the heeding presumption.

Plaintiffs maintain that this testimony is insufficient to rebut the heeding presumption. Plaintiffs argue that Abbott had a duty, pursuant to its November 10, 2003 CBE-0, to directly warn women through the Patient Information Leaflet about the increased risk of birth defects and

failed to do so.[21] Plaintiffs also argue that Dr. Lemus's testimony does not establish Dr. Lemus would not have changed Rheinfrank's prescription had she been adequately warned. Dr. Lemus testified that if an epileptic patient's seizures were not well-controlled, she would refer that patient to a neurologist. (Lemus Dep. at 37, Doc. 83 at PageID 3265.) Plaintiffs argue that Dr. Lemus's testimony that she did not "remember having a sense of this is a very dangerous drug for someone who could get pregnant" does not demonstrate Dr. Lemus was unfamiliar with the Black Box warning, but, rather, that the warning itself was inadequate. (*Id*. at 19, PageID 3260.) On the other hand, Plaintiffs contend the record does not support the assertion that Dr. Lemus's testimony establishes she would not have changed her prescribing habits had she been adequately warned of Depakote's dangers for someone who could become pregnant. The issue of whether a physician would have responded differently to an adequate warning is one of credibility, and, hence, a question for the jury. *Sheffer*, 2013 WL 5276558, at *12.

Although Defendants argue Dr. Lemus's testimony is akin to the physician's testimony in *Daniel*, Dr. Lemus's testimony does not affirmatively establish that a different warning would not have changed her prescribing habits. 740 N.E.2d at 684–85. In *Daniel*, the drug's package insert cautioned against symptoms of toxicity and stated that no patient was to be maintained on any dosage that was not tolerated. *Id.* at 684. The package insert also instructed that the dosage was to be reduced by ten percent when a patient's serum level exceeded the therapeutic range, regardless of whether adverse reactions had become manifest. *Id*. Despite these instructions, and despite manifestations of signs of toxicity, the plaintiff's doctors maintained her on the drug and failed to reduce her dosage even when the drug levels exceeded the therapeutic range. *Id.* Because the package insert cautioned that the plaintiff's fever presented an increased risk of

[21] The Court determined that there is a question of fact whether Dr. Lemus was adequately warned of the risks of Depakote sufficient to be a learned intermediary, *supra*.

toxicity, and that, despite this, her doctors failed to heed the package insert's clear instruction to reduce the dosage, it could not be said that the addition of a viral warning would have had any impact on the determination to continue administering the drug. *Id.* at 685. The evidence that the doctors ignored dosing instructions served to defeat the presumption that the allegedly inadequate warning was a proximate cause of the plaintiff's ingestion of the drug. *Id.*

Plaintiffs in this case assert that failure to warn of the risks of teratogenicity to women of childbearing potential, not just to pregnant women, is the proximate cause of M.B.D.'s injury. Notably, there is no affirmative evidence that Dr. Lemus would not have discussed the risks of Depakote with Rheinfrank had Abbott issued a stronger warning. *Monroe v. Novartis Pharmaceuticals Corp.*, 29 F. Supp. 3d 1115, 1126 (S.D. Ohio 2014) ("[W]here the treating physician unequivocally testifies that s/he would have prescribed the subject drug despite adequate warnings, judgment as a matter of law is appropriate.") (citing *Miller v. ALZA Corp.*, 759 F.Supp.2d 929, 936 (S.D. Ohio 2010)). Moreover, Rheinfrank's testimony is irrelevant absent proof that a different warning would have cause Dr. Lemus to warn her of the risks of Depakote. *See Sheffer*, 2013 WL 5276558, at *12 (finding plaintiff's testimony irrelevant to proximate cause analysis absent evidence a different warning would have caused plaintiff's physician to warn her of risks of drug at issue). As in *Sheffer*, where the record did not include affirmative evidence of how the physician would have responded to different, stronger warnings, and drawing all reasonable inferences in Plaintiffs' favor, the Court finds a genuine issue of material fact concerning whether an adequate warning would have altered the course of Rheinfrank's treatment. A reasonable jury could find that if Abbott had issued a different warning, Dr. Lemus would have disclosed the risks of Depakote to Rheinfrank, who would have refused to take Depakote or used contraception, thereby averting M.B.D.'s injury. Thus, a jury

will have to determine whether Abbott is able to successfully rebut a presumption that the alleged inadequate warning was the proximate cause of Rheinfrank's use of Depakote.

For the aforementioned reasons, Defendants' motion for summary judgment on Plaintiffs' strict liability and negligence failure to warn claims is denied. Defendants assert via footnote that many other claims rise and fall with the negligence and strict liability failure to warn claims. These claims include Plaintiffs' negligent misrepresentation claim, breach of express warranty, and, to the extent they do not rely upon an alleged design defect, the nonconformance with representations, negligence, breach of implied warranty of merchantability, breach of implied warranty of fitness, unjust enrichment, and loss of consortium claims. Initially, Defendants have offered no case law under which the Court could conclude that it is proper to analyze all of these claims together. With the exception of the negligent misrepresentation, fraud, and unjust enrichment claims, addressed *infra*, Defendants have failed to meet their burden in demonstrating that they are entitled to summary judgment on Plaintiffs' breach of express warranty, nonconformance with representations, breach of implied warranty of merchantability, breach of implied warranty of fitness, and loss of consortium claims. Accordingly, summary judgment on these claims is also inappropriate.

Finally, for the reasons expressed herein, summary judgment for Plaintiffs on the strict liability failure to warn claim is also denied. The Court notes that the party moving for summary judgment with the burden of proof faces a higher burden. *Haj-Hamed v. Rushing*, No. 4:09-cv-2668, 2010 WL 2650174, at *2 (N.D. Ohio July 2, 2010) (*relying upon Arnett v. Myers*, 281 F.3d 552, 561 (6th Cir. 2002)). "[W]here the moving party has the burden—the plaintiff on a claim for relief or the defendant on an affirmative defense—his showing must be sufficient for the court to hold that no reasonable trier of fact could find other than for the moving party."

*Calderone v. United States*, 799 F.2d 254, 259 (6th Cir. 1986) (emphasis removed). Thus, the party with the burden of proof "must show that the record contains evidence satisfying the burden of persuasion and that the evidence is so powerful that no reasonable jury would be free to disbelieve it." *Arnett*, 281 F.3d at 561. "Accordingly, summary judgment in favor of the party with the burden of persuasion 'is inappropriate when the evidence is susceptible to different interpretations or inferences by the trier of fact.'" *Green v. Tudor*, 685 F. Supp. 2d 678, 685 (W.D. Mich. 2010) (quoting *Hunt v. Cromartie*, 526 U.S. 541, 553 (1999)). Multiple questions of material fact preclude summary judgment in favor of the Plaintiffs.

**B. Strict Products Liability – Design Defect**

Having fully considered the failure to warn claims, the Court now turns to Defendants' argument that they are entitled to summary judgment on Plaintiffs' design defect claim. Specifically, Defendants assert that Plaintiffs fail to adequately support their design defect claim, because there is no evidence that the risks of Depakote per se outweigh the risks of treatment or a safer alternative drug existed that would have prevented M.B.D.'s injuries. Under Ohio law, a product is defective in design if either of the following applies:

If, at the time it left the control of its manufacturer, the foreseeable risks associated with its design or formulation as determined pursuant to division (B) of this section exceeded the benefits associated with that design or formulation as determined pursuant to division (C) of this section.

> (1) When it left the control of its manufacturer, the foreseeable risks associated with its design or formulation as determined pursuant to division (B) of this section exceeded the benefits associated with that design or formulation as determined pursuant to division (C) of this section;
> (2) It is more dangerous than an ordinary consumer would expect when used in an intended or reasonably foreseeable manner.

Ohio Rev. Code § 2307.75(A) (2001) (amended 2004). "This statute offers two alternative approaches for demonstrating a design defect: a risk-benefit test in subsection (A)(1), and a consumer-expectations test in subsection (A)(2)"; thus, a jury may consider either or both theories of liability. *Newell Rubbermaid, Inc. v. Raymond Corp.*, 676 F.3d 521, 529 (6th Cir. 2012) (citing *Perkins v. Wilkinson Sword, Inc.*, 700 N.E.2d 1247, 1248 (1998)). In addition to meeting at least one of the two design-defect theories, Plaintiffs must also show there was no "practical and technical feasible alternative design that . . . that would have prevented the harm for which the claimant seeks to recover . . ." Ohio Rev. Code §2307.75(F); *Monroe v. Novartis Pharm. Corp.*, 29 F. Supp. 3d 1115, 1124 (S.D. Ohio 2014) ("Although this subsection does not state that it is a plaintiff's burden to prove an alternative design, the Sixth Circuit has so held." (citing *McGrath v. Gen. Motors Corp.*, 26 Fed. App'x 506, 510 (6th Cir. 2002)).

Plaintiffs argue Rheinfrank's seizures were never adequately controlled by Depakote, as evidenced by her testimony and testimony of her ex-husband that she experienced break-through seizures. (*See* Rheinfrank Dep. (July 1, 2014) at 22–28, Doc. 79 at PageID 1449–50; Durham Dep. at 32–36, Doc. 126 at PageID 14901–02.) Rheinfrank testified that in 2008, she switched to a different antiepileptic drug, Keppra, and has been seizure free since then. (Rheinfrank Dep. (July 1, 2014) at 63–64, Doc. 79 at PageID 1459.) Thus, Plaintiffs argue that Keppra is an alternative AED that was available during her 2003-2004 pregnancy with M.B.D.

Defendants argue, and the Court agrees, that there is no evidentiary support for Plaintiffs' contention that there were alternative drugs that could have controlled Rheinfrank's grand mal tonic-clonic seizures as well as the Depakote/Phenobarbital combination that as prescribed for

her for over twenty years, including by neurologists at the UC Neurology Clinic.[22] None of Plaintiffs' experts have opined that Keppra, which Rheinfrank started taking in 2008, or any other AED, would have been a viable alternative for her in the period of time shortly before Rheinfrank became pregnant with M.B.D. Merely because some AEDs are considered less teratogenic than Depakote does not mean they would have been suitable for controlling Rheinfrank's seizures. Plaintiffs ask this Court to make an inferential leap by concluding that the fact that Rheinfrank now takes Keppra, a less teratogenic AED, and has been seizure free since, necessarily establishes that her taking Keppra, or another AED, would have controlled her seizures and prevented M.B.D.'s injuries. Absent expert testimony to support this proposition, the Court is unable to conclude Plaintiffs have met their burden to demonstrate an alternative design exists that would have prevented the harm for which they seek to recover. On this basis, summary judgment for the Defendants on this claim is appropriate. *See Monroe* 29 F. Supp. 3d at 1124.

**C. Negligent Misrepresentation and Fraud**

Defendants argue they are entitled to summary judgment on Plaintiffs' negligent misrepresentation and fraud claims, because Plaintiffs cannot identify what misrepresentations Abbott made to Rheinfrank and have failed to carry their burden by relying only upon the allegations in the Complaint. Under Ohio law, to establish a claim for common law fraud, a plaintiff must prove:

> (a) a representation or, where there is a duty to disclose, concealment of a fact, (b) which is material to the transaction at hand, (c) made falsely, with knowledge of its falsity, or with such utter disregard and recklessness as to whether it is true or false that knowledge may be inferred, (d) with intent of misleading another into

[22] The parties raise other arguments relating to the viability of Plaintiffs' design defect claim, but the Court's conclusion regarding evidence of an AED is dispositive; as such, the Court will not address the additional arguments.

> relying upon it, (e) justifiable reliance upon the representation or concealment, and (f) a resulting injury proximately caused by the reliance.

*Glassner v. R.J. Reynolds Tobacco Co.*, 223 F.3d 343, 352 (6th Cir. 2000) (citing *Burr v. Bd. of Cnty. Comm'rs of Stark Co.*, 491 N.E.2d 1101, 1105 (Ohio 1986) (quotation marks and citations omitted)). A claim for negligent misrepresentation is established where:

> One who, in the course of his business, * * * supplies false information for the guidance of others in their business transactions, is subject to liability for pecuniary loss caused to them by their justifiable reliance upon the information, if he fails to exercise reasonable care or competence in obtaining or communicating the information.

*Gutter v. Dow Jones, Inc.*, 490 N.E.2d 898, 900 (Ohio 1986). Thus, both fraud and negligent misrepresentation require reliance upon the asserted omission or misrepresentation. Defendants contend Plaintiffs have failed to come forward with evidence of reliance, and on this basis, the negligent misrepresentation and fraud claims fail.

Defendants argue the evidence demonstrates that M.B.D. could not have relied on alleged misrepresentations as she was not born, whereas Rheinfrank "has not identified any misrepresentations Abbott made to her at any time." (Doc. 113 at PageID 13216.) Defendants cite Plaintiffs' response to Interrogatory 10 in support of their argument. Interrogatory 10 requested that Rheinfrank identify persons who made misrepresentations to Plaintiffs' doctors, to which Rheinfrank responded that she had no information responsive to the request. Specifically, Interrogatory 10 and Rheinfrank's response are as follows:

> **INTERROGATORY NO. 10**: Identify (a) any Person who provided Warnings, representations, or warranties that Your Health Care Providers allegedly heard, read, received or otherwise learned concerning Depakote before the Minor Plaintiff's birth or (b) any natural Person who allegedly should have but did not, provide accurate, adequate, legally sufficient Warnings, representations, or warranties that Your Health Care Providers allegedly heard, read, received, or otherwise learned concerning Depakote before the Minor Plaintiff's birth.

**ANSWER TO INTERROGATORY NO. 10**:

> Plaintiff objects to this interrogatory on the ground that it is overbroad, so as to render the interrogatory unduly burdensome and oppressive. Plaintiff objects to this interrogatory to the extent that it calls for a legal conclusion. Without waiving such objection, Plaintiff states that she has no information responsive to this request.

(Doc. 115 at PageID 14126.) Defendants further argue that "even if Plaintiffs could recover for alleged misrepresentations to Dr. Lemus, she recalls nothing about her purported decision to prescribe Depakote for Ms. Rheinfrank, including anything that Abbott allegedly told her." (Doc. 113 at PageID 13216 (citing Doc. 83 at PageID 3260).)

In response, Plaintiffs argue that Plaintiffs' response to Interrogatory 10 demonstrates she had no personal knowledge about persons who made misrepresentations to Plaintiffs' doctors, and Abbott "had the opportunity to depose Ms. Rheinfrank's physicians and determine what misrepresentations were made to them and by whom." (Doc. 152 at PageID 19621.) Further, Dr. Lemus's testimony that she cannot remember whether she read the Depakote label does not demonstrate she failed to read the label, as discussed *supra* in the failure to warn proximate cause analysis. Plaintiffs also contend that Abbott owed a duty not merely to Dr. Lemus, but to the entire medical community. Because the evidence must be construed in the light most favorable to Plaintiffs, the non-moving party, Plaintiffs urge the Court to deny summary judgment for Defendants on these claims.

Where a party moving for summary judgment identifies an absence of evidence to support a claim for which the plaintiff has the burden of proof, the nonmoving party may not rest upon the pleadings but must go beyond the pleadings and "present affirmative evidence in order to defeat a properly supported motion for summary judgment." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 257 (1986). Plaintiffs have not done so in this case. Rather, Plaintiffs contend Defendants could have asked questions to determine the alleged misrepresentations and that the

duty was owed not only to Dr. Lemus, but to the entire medical profession. The cited evidence is insufficient to demonstrate that either Rheinfrank or Dr. Lemus relied upon the alleged misrepresentations and/or omissions. As such, summary judgment for the Defendants on these claims is appropriate.

**D. Unjust Enrichment**

In their Motion for Summary Judgment, Defendants argue Plaintiffs' unjust enrichment claim fails, because Plaintiffs have not identified a recoverable benefit conferred to Abbott. Under Ohio law, a plaintiff is required to demonstrate three elements to support a claim of unjust enrichment: "(1) a benefit conferred by the plaintiff upon the defendant; (2) knowledge by the defendant of the benefit; and (3) retention of the benefit by the defendant under circumstances where it would be unjust to do so without payment." *Delahunt v. Cytodyne Technologies*, 241 F. Supp. 2d 827, 836 (S.D. Ohio 2003) (citing *Reisenfeld & Co. v. Network Group, Inc*. 277 F.3d 856, 860 (6th Cir. 2002)).

Defendants argue that because Rheinfrank allegedly purchased Depakote from a pharmacy, and not from Abbott directly, she is unable to prevail on her unjust enrichment claim. *See Young v. Carrier Corp.*, No. 4:14-cv-0974, 2014 WL 6617650, at *7 (N.D. Ohio Nov. 21, 2014) ("unjust enrichment is not an available remedy when a plaintiff does not make her purchase directly from the manufacturer.") Although Plaintiffs argue that they need not purchase the drug directly from the manufacturer, as Defendants contend, the only Southern District of Ohio case Plaintiffs cite to support that argument is not applicable. *See Delahunt v. Cytodine Techs.*, 241 F. Supp. 2d 827, 836 (S.D. Ohio 2003). In *Delahunt*, the court denied defendants' motion to dismiss unjust enrichment claims brought by the plaintiffs on behalf of a purported class that included both consumers who purchased the product directly from the manufacturer and consumers who purchased the product from a retailer. *Id*. at 830–31. *Delahunt* is therefore

distinguishable from the facts of this case, as Plaintiffs do not allege or offer proof that they purchased Depakote directly from Defendants.

Regardless, Plaintiffs' assertion that Abbott received a substantial benefit from the marketing and sales of its drug and communicated internally about its sales strategies does not establish the required elements of unjust enrichment. *See Chamberlain v. Am. Tobacco Co.,* No. 1:96-CV-02005-PAG, 1999 WL 33994451, at *15 (N.D. Ohio Nov. 19, 1999) (finding plaintiffs' claim for unjust enrichment failed as a matter of law; a seller is not unjustly enriched simply because he derives a profit from the sale of a product). For these reasons, summary judgment for the Defendants is appropriate on this claim.

**E. Punitive Damages**

Lastly, Defendants argue Plaintiffs are unable to recover punitive damages in this action for two reasons. First, Defendants contend Plaintiffs cannot recover punitive damages for common law claims under the 2004 version of the Ohio Products Liability Act ("OPLA"). Second, Defendants argue that Plaintiffs may not recover for punitive damages for their statutory failure to warn claim under the current version of the OPLA, because there has not been a finding of fraud on the FDA. As discussed below, the Court will find that Plaintiffs may pursue punitive damages for their common law negligence claim but are precluded from pursuing punitive damages under the OPLA.

**a. Plaintiffs' Common Law Negligence Claim**

In 2005, the OPLA was amended, and one of the changes included an explicit abrogation of all common law product liability causes of action. Ohio Rev. Code § 2307.71(B). Prior to the 2005 amendments, Ohio Rev. Code § 2307.80 (2004) stated:

> (A) Subject to division (C) of this section, punitive or exemplary damages shall not be awarded against a manufacturer or supplier in question in connection

> with a product liability claim unless the claimant establishes, by clear and convincing evidence, that the harm for which the claimant is entitled to recover compensatory damages in accordance with section 2307.73 or 2307.78 of the Revised Code was the result of misconduct of the manufacturer or supplier in question that manifested a flagrant disregard of the safety of persons who might be harmed by the product in question. The fact by itself that a product is defective does not establish a flagrant disregard of the safety of persons who might be harmed by that product.
>
> . . .
>
> (C) If a claimant alleges in a product liability claim that a drug caused harm to the claimant, the manufacturer of the drug shall not be liable for punitive or exemplary damages in connection with that product liability claim if the drug that allegedly caused the harm was manufactured and labeled in relevant and material respects in accordance with the terms of an approval or license issued by the federal food and drug administration under the "Federal Food, Drug, and Cosmetic Act," 52 Stat. 1040 (1938), 21 U.S.C. 301-392, as amended, or the "Public Health Service Act," 58 Stat. 682 (1944), 42 U.S.C. 201-300cc-15, as amended, unless it is established by a preponderance of the evidence, that the manufacturer fraudulently and in violation of the applicable regulations of the food and drug administration withheld from the food and drug administration information known to be material and relevant to the harm that the claimant allegedly suffered or misrepresented to the food and drug administration information of that type.

Ohio Rev. Code § 2307.80 (2004) (West).[23] Under Ohio Rev. Code § 2307.71, "[a]s used in sections 2307.71 to 2307.80 of the Revised Code":

> (M) "Product liability claim" means a claim that is asserted in a civil action and that seeks to recover compensatory damages from a manufacturer or supplier for death, physical injury to person, emotional distress, or physical damage to property other than the product in question, that allegedly arose from any of the following:
> (1) The design, formulation, production, construction, creation, assembly, rebuilding, testing, or marketing of that product;
> (2) Any warning or instruction, or lack of warning or instruction, associated with that product;
> (3) Any failure of that product to conform to any relevant representation or warranty.

[23] Although Ohio Rev. Code § 2307.80 was amended on April 7, 2005, the statute is not retroactive. *Mastellone v. Lightning Rod Mut. Ins. Co.*, 884 N.E2d 1130, 1136 (Ohio Ct. App. 2008). The parties agree that the 2004 version of the statute controls, as Plaintiff M.B.D. was born on July 25, 2004.

Ohio Rev. Code § 2307.71 (2004).[24] Abbott argues that Plaintiffs may not recover punitive damages under the language of the then-existing statute, because the definition of "product liability claim" usurped common law claims of negligence.

Other than cite the definition of "products liability claim" under Ohio Rev. Code § 2307.80(M), Defendants offer no authority for the position that all negligence or other common law claims preclude a punitive damages award. Defendants also ignore Plaintiffs' argument that they may pursue punitive damages under Ohio Rev. Code § 2315.21 for its common law causes of action. Ohio Rev. Code § 2315.21 permits recovery for punitive or exemplary damages in a tort action if:

> The actions or omissions of that defendant demonstrate malice, aggravated or egregious fraud, oppression, or insult, or that the defendant as principal or master authorized, participated in, or ratified actions or omissions of an agent or servant that so demonstrate.
> (2) The plaintiff in question has adduced proof of actual damages that resulted from actions or omissions as described in division (B)(1) of this section.

Ohio Rev. Code § 2315.21 (A) (2004).

The definition of "product liability claim" under the 2004 version of Ohio Rev. Code § 2307.71(M) has been analyzed by the Ohio Supreme Court, which held: "[a]lthough couched in broad language, this definition does not mention or otherwise discuss the common-law action of negligent design. More important, there is no explicit statement that this definition was meant to abolish common-law actions sounding in negligence." *Carrel v. Allied Products Corp*., 677 N.E.2d 795, 799 (Ohio 1997), *superseded by statute,* Ohio Rev. Code § 2307.71(B); *see Cincinnati v. Beretta U.S.A. Corp.,* 768 N.E.2d 1136, 1147 (Ohio 2002) ("the common-law failure-to-warn claim survives the enactment of Ohio's Product Liability Act, R.C. 2307.71 *et*

[24] After the 2005 amendment, the statute defined a "product liability claim" as "a claim or cause of action" asserted in a civil action "pursuant to sections 2307.71 to 2307.80 of the Revised Code." Ohio Rev. Code § 2307.80.

*seq*.").  Thus, Defendants' argument that the definition of "products liability claim" applies to Plaintiffs' negligence claim is without merit and contravenes Ohio law.  Accordingly, under Ohio Rev. Code § 2315.21 (A), Plaintiffs may pursue punitive damages for their common law negligence claim.

**b. Punitive Damages for Statutory Product Liability Claim are Barred**

The parties dispute whether Plaintiffs may recover punitive damages for their statutory claims on the basis that Plaintiffs' recovery for punitive damages would amount to a preempted fraud-on-the-FDA claim.  Under the language of the statute, punitive damages are not recoverable unless Plaintiffs establish by "a preponderance of the evidence, that the manufacturer fraudulently and in violation of the applicable regulations of the food and drug administration withheld from the food and drug administration information known to be material and relevant to the harm that the claimant allegedly suffered or misrepresented to the food and drug administration information of that type."  Ohio Rev. Code § 2307.80 (2004).  Defendants contend that consistent with the holding in *Monroe v. Novartis Pharm. Corp*., 29 F. Supp. 3d 1115, 1130 (S.D. Ohio 2014), Plaintiffs are barred from recovering for punitive damages because the FDA has not made a finding of either fraud or misrepresentation.  The Court agrees that *Monroe* is nearly indistinguishable from this case and that its holding controls here.

In *Monroe*, the court succinctly traced how Sixth Circuit courts have applied and interpreted *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001), in which the Supreme Court held that "plaintiffs' state-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by, federal law."  *Id.* (citing *Buckman*, 531 U.S. at 348.)  The *Monroe* court explained that in *Garcia v. Wyeth-Ayerst Labs.*, 385 F.3d 961, 966 (6th Cir. 2004), "[t]he Sixth Circuit, looking at Michigan law with a framework similar to Ohio, found that the

difference between a common law claim of fraud on the FDA (as discussed in *Buckman*) and immunity under Michigan law unless fraud could be shown was 'immaterial in light of *Buckman*.'" *Id.* (interpreting *Garcia*, 385 F.3d at 966.). The Sixth Circuit in Garcia held that "**state tort remedies** requiring proof of fraud committed against the FDA are foreclosed since federal law preempts such claims." *Garcia*, 385 F.3d at 966 (emphasis added). In *Marsh v. Genentech, Inc.*, 693 F.3d 546, 551 (6th Cir. 2012), the Sixth Circuit extended this rule to "claims that the manufacturer misrepresented or withheld information about a drug from the FDA after the FDA had approved it." This Court, following the well-reasoned decision of *Monroe*, so too holds that "[b]ecause there has been no finding of fraud by the FDA here, no punitive damages claim [under the OPLA] is permissible." *Monroe*, 29 F. Supp. 2d 1115 at 1130.

Plaintiffs urge the Court to consider and adopt persuasive authority supporting their position that they have not asserted a fraud on the FDA claim but rather seek to introduce evidence of misrepresentation and/or fraud, thus rendering *Buckman* inapplicable. *See, e.g., Heinman v. Am. Home Prods. Corp.*, 13-cv-02070, 2014 U.S. Dist. LEXIS 124987, at *22 (D. Co., Sept. 8, 2014); *Schedin v. Ortho-McNeil-Janssen Pharms., Inc.*, 776 F. Supp. 2d 901, 915–16 (D. Minn. 2011); *In re Yasmin & Yaz (Drospirenone) Mktg., Sales Practices & Prods. Liab. Litig.*, 3:09-md-02100-DRH-PMF, MDL No. 2100, 2011 U.S. Dist. LEXIS 145593, at *63–64 (S.D. Ill. Dec. 16, 2011). The persuasive authority cited by Plaintiffs in support of their argument that they have not asserted a fraud on the FDA claim is distinguishable on the basis that those courts did not analyze the specific language of Ohio's statutory language, as the *Monroe* court did. Moreover, our sister court considered and rejected Plaintiffs' argument in *In re Gadolinium-Based Contrast Agents Products Liab. Litig.*, MDL No. 1909, 2013 WL 587655,

at *14 (N.D. Ohio Feb. 13, 2013), finding that "a punitive-damages claim for an FDA-approved drug is allowed under Ohio law *only if* the FDA has made a finding of either fraud or misrepresentation." Plaintiffs do not address the application of this case or *Monroe*.

Accordingly, finding *Monroe* controlling, because the FDA has not found that fraud or misrepresentation occurred, Defendants may not pursue punitive damages for their statutory failure to warn claim under the OPLA.

## IV. CONCLUSION

For the reasons discussed herein, Defendants' Motion for Summary Judgment (Doc. 113) is **GRANTED IN PART AND DENIED IN PART**. The Court finds that Plaintiffs' failure to warn claim predicated upon a failure to warn about the risks of developmental delay is preempted. Defendants' Motion for Summary Judgment on Plaintiffs' strict liability and negligence failure to warn claims, breach of express warranty, nonconformance with representations, breach of implied warranty of merchantability, breach of implied warranty of fitness, and loss of consortium claims is denied. Defendants' Motion for Summary Judgment on Plaintiffs' design defect, negligent misrepresentation, fraud, and unjust enrichment claims is granted. The Court finds that Plaintiffs may pursue punitive damages under their negligence theory in accordance with Ohio Rev. Code § 2315.21(A), but Plaintiffs are barred from pursuing punitive damages under statutory law, Ohio Rev. Code § 2307.80. Plaintiffs' Motion for Partial Summary Judgment (Doc. 112) is **DENIED**.

IT IS SO ORDERED.

S/Susan J. Dlott
Judge Susan J. Dlott
United States District Court