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

Rheinfrank, et al.,	:	
	:	Case No. 1:13-cv-144
Plaintiffs,	:	
	:	Judge Susan J. Dlott
v.	:	
	:	Order Ruling on Motions *in Limine*
Abbott Laboratories, Inc., et al.,	:	
	:	
Defendants.	:	
	:	

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. Seventeen motions *in limine* filed by Defendants and two motions *in limine* filed by Plaintiffs are currently pending before the Court. The issues have been thoroughly briefed. Accordingly, the Court will consider these motions in turn.

I. LEGAL STANDARDS GOVERNING MOTIONS *IN LIMINE*

District courts have authority to adjudicate motions *in limine* pursuant to their "inherent authority to manage the course of trials." *Luce v. United States.*, 469 U.S. 38, 41 n.4 (1984). Courts should exclude evidence *in limine* "only when evidence is clearly inadmissible on all potential grounds." *Gresh v. Waste Servs. of Am., Inc.*, 738 F. Supp. 2d 702, 706 (E.D. Ky.

[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.

2010) (citation omitted). The Sixth Circuit has stated that the "better practice" is to address questions regarding the admissibility of broad categories of evidence "as they arise." *Sperberg v. Goodyear Tire & Rubber Co.*, 519 F.2d 708, 712 (6th Cir. 1975). "[A] court is almost always better situated during the actual trial to assess the value and utility of evidence." *Owner-Operator Independent Drivers Ass'n v. Comerica Bank*, No. 05–CV–0056, 2011 WL 4625359, at *1 (S.D. Ohio Oct. 3, 2011). Denial of a motion *in limine* does not necessarily mean that the evidence, which is the subject of the motion, will be admissible at trial. *Ind. Ins. Co. v. Gen. Elec. Co.*, 326 F. Supp. 2d 844, 846 (N.D. Ohio 2004).

II. DEFENDANTS' MOTIONS *IN LIMINE*

1. Defendants' Motion *in Limine* No. 1 to Exclude References About Preempted Labeling Issues (Doc. 228)

Defendants' Motion *in Limine* No. 1 is **GRANTED IN PART AND DENIED IN PART.** Defendants' Motion *in Limine* No. 1 asks the Court for an order excluding evidence, testimony, argument and other references about what they classify as two preempted labeling issues. First, Plaintiffs claim the Court should preclude evidence or argument that Abbott would have been able to implement a developmental delay warning prior to M.B.D.'s birth, because such a claim is preempted. Further, Plaintiffs argue the because that claim is preempted, the jury may not reach a verdict based upon a theory that Plaintiffs' injuries resulted from Abbott's failure to warn about developmental delay, and any argument suggesting otherwise should be precluded. Second, Plaintiffs ask the Court to bar evidence that Abbott should have unilaterally changed Depakote's Black Box Warnings.

As to the first issue, the Court found in its summary judgment order that Plaintiffs' claim that Defendants failed to warn of the risk of developmental delay is preempted. In is order, the

Court found that "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. 236 at PageID 27994) (citations removed). Thus, evidence and argument that Defendants should have or should have strengthened Depakote's warning to include a developmental delay warning prior to M.B.D.'s birth is irrelevant, because it is preempted. This evidence is therefore inadmissible. However, as stated by the Court on the record and again at the Final Pretrial Conference, the Court does not find that its summary judgment ruling precludes Plaintiffs from recovering for damages, including developmental delay, M.B.D. suffered as the result of Abbott's failure to warn of other risks, such as a failure to warn of the risks of the teratogenicity of Depakote to women of childbearing years.

As to the second issue, Defendants argue that the Court should bar any assertion that Abbott should have obtained a CBE to change the Black Box Warnings for Depakote, because the FDA dictates the existence and content of Black Box Warnings. Defendants argue a failure-to-warn claim based upon purported failure to change the Black Box Warning runs contrary to the FDA's legal control over Black Box Warnings, provides no grounds on which Plaintiffs could recover under Ohio law, and thus is irrelevant. Defendants also argue the evidence is inadmissible under Rule 403.

Plaintiffs argue that they have not offered testimony about unilateral changes to the Black Box warning but that they have marked deposition testimony and exhibits that Abbott negotiated with the FDA to weaken language contained in the Depakote Black Box warning about teratogenicity. Plaintiffs argue this testimony is relevant to Abbotts' claim that it gave the

strongest warning possible, the warning was drafted by the FDA, and that Abbott had no ability to influence the language in the Black Box.

Under 21 C.F.R. § 201.57(e)(2003):

> Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these serious adverse reactions and, if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective use of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

21 C.F.R. § 201.57(e)(2003). As described by the court in *Ray v. Allergan, Inc.*:

> Boxed warnings were created in 1979 by the FDA as a way to address special problems of the most serious nature—those that may lead to death or serious injury. . .
>
> During the comment period in 1979, the FDA was asked whether a manufacturer could include a boxed warning without first securing approval of the FDA and whether the FDA would consider the manufacturer's desires when specifying the location of boxed warnings. 44 Fed. Reg. 37,434, 37,448 (June 26, 1979). The FDA responded that "to ensure the significance of boxed warnings in drug labeling, they are permitted in labeling only when specifically required by the FDA. The labeler's desires about location and wording of boxed warnings, however, will be considered." *Id.; see also* Lars Noah, *The Imperative to Warn: Disentangling the 'Right to Know' from the 'Need to Know' about Consumer Product Hazards*, 11 Yale J. Reg. 293, 328 (1994) (quoting 44 Fed. Reg. 37,434, 37,448 (1979)).

863 F. Supp. 2d 552, 558–59 (E.D. Va. 2012) (granting Rule 59 motion for a new trial in a failure to warn case).

The Court agrees with Defendants that because Abbott has set forth clear evidence that a request to add a developmental delay warning prior to 2003 would have been futile, Plaintiffs may not introduce evidence that Abbott failed to request a Black Box Warning from the FDA regarding developmental delay. Plaintiffs may not argue, and indeed it appears consistent with

Plaintiffs' position, that Defendants could have unilaterally added a Black Box Warning. However, the Court will allow evidence that Defendants could have suggested stronger language for the Black Box Warning, aside from warning of developmental delay, as this evidence is relevant to the question of whether Defendants' warnings were adequate. The Court finds the probative value of this evidence outweighs any risk of unfair prejudice.

2. Defendants' Motion *in Limine* No. 2 to Exclude Evidence, Testimony, or Argument About Post-Conception Labeling and Regulatory Communications (Doc. 229)

Defendants' Motion *in Limine* No. 2 is **GRANTED IN PART AND TAKEN UNDER ADVISEMENT IN PART.** Defendants request the Court to exclude evidence of changes to the Depakote label made after M.B.D.'s conception and regulatory communications supporting that labeling to argue that the language in those labels should have been incorporated prior to M.B.D.'s conception. The Depakote label was changed subsequent to M.B.D.'s conception and birth in 2006, 2011, and 2013. Abbott argues all three labels should be excluded under Rule 401, 403, and/or 407.

Initially, the Court finds that these subsequent labels are irrelevant to the issue of whether the 2003-2003 label was adequate. Regardless, even if the subsequent labels were relevant, the Court finds that label changes made after M.B.D.'s conception and birth are inadmissible under Fed. R. Evid. 403, because the probative value of the subsequent labels is outweighed by the risk of unfair prejudice. The jury's role is to evaluate the adequacy of the Depakote label in 2003-2004. If the jury is presented with labels after this timeframe, the jury may conclude that Abbott's earlier labels were inadequate merely because the later labels include expanded warnings not present in the 2003-2004 version. Thus, the Court finds that the probative value of the subsequent labels is substantially outweighed by the danger of unfair prejudice. For this

reason, the subsequent labels are not admissible at trial. *See Giles v. Wyeth, Inc.*, 556 F.3d 596, 600 (7th Cir. 2009) (affirming district court's decision to exclude later warnings under Rule 403); *Kaleta v. Abbott Laboratories, Inc*., No. 14-cv-847-NJR-SCW, slip op. at *14 (S.D. Ill. Feb. 20, 2015) (order granting in part motion *in limine* to exclude subsequent labels).

As to Abbott's request to exclude "regulatory communications," the Court is unclear what the scope of those communications are and is therefore unable at this time to exclude such a broad category of evidence. As such, the Court takes the latter part of Defendants' motion relating to exclusion of regulatory communications under advisement.

3. Motion *in Limine* No. 3 to Exclude Evidence and Argument About Foreign Labeling (Doc. 224)

Defendants' Motion *in Limine* No. 3 is **DENIED**. Defendants request the Court to exclude foreign labeling for versions of Depakote sold around the world. Specifically, Defendants are concerned that Plaintiffs will seek to admit evidence and testimony regarding Epilim, the version of Depakote sold in the United Kingdom and elsewhere in Europe. Abbott argues that evidence concerning foreign labeling is not relevant to this case and is inadmissible. In addition, Defendants contend admission of such evidence is substantially outweighed by the risk of unfair prejudice, issue confusion, and wasting time.

Plaintiffs argue, and the Court agrees, that the content of foreign labeling is relevant and admissible. Such evidence is probative of the Defendants' knowledge during the relevant time period, prior to M.B.D.'s conception and birth, of Depakote. Defendants' knowledge of Depakote is probative of the adequacy of the warning and instruction for Depakote and the feasibility of alternative language. Under Ohio law, the adequacy of the label is measured by the

risks Abbott knew or should have known. Thus, labeling abroad, prior to M.B.D.'s conception and birth, is highly relevant to this inquiry.

The Court finds that evidence of the Epilim label is relevant to Abbott's knowledge of the risks of Depakote. The probative value of this evidence outweighs the risk of any prejudice to Abbott. *See Kaleta v. Abbott Laboratories, Inc*., No. 14-cv-847-NJR-SCW, slip op. at *15 (S.D. Ill. Feb. 20, 2015) (order denying in part motion in limine to exclude evidence of foreign labeling during relevant time period); *Mahaney ex rel. estate of Kyle v. Novartis Pharm. Corp.*, 835 F. Supp. 2d 299, 318 (W.D. Ky. 2011) (permitting evidence of foreign regulatory actions or package inserts in foreign countries in failure to warn case the evidence could bear on the manufacturer's knowledge and notice of the drug's side effects, but not permitting the evidence to show the manufacturer violated FDA's regulations).

4. Motion in Limine to Exclude Evidence, Testimony, and Argument Regarding May 2012 Plea Agreement, Civil Settlement, and Corporate Integrity Agreement (Doc. 217)

Defendants' Motion *in Limine* No. 4 is **GRANTED**. Abbott seeks to exclude evidence that on May 7, 2012, Abbott pleaded guilty to violating sections of the Federal Food, Drug and Cosmetic Act relating to the misbranding of Depakote, for at least two uses not approved by the FDA – control of agitation and aggression in elderly dementia patients from 1998 to 2006 and treatment of schizophrenia from 2002 to 2006. Abbott paid fines and forfeited assets totaling approximately $700 million to be paid to federal and state governmental organizations. Abbott also entered into a Civil Settlement Agreement with the Department of Justice in which it agreed to pay the federal government and Medicaid participating states $800 million to resolve further claims related to the off-label promotion of Depakote. Finally, Abbott entered into a Corporate

Integrity Agreement with the federal government. Plaintiffs argue this evidence is admissible to prove Defendants engaged in a nationwide scheme to sell Depakote for off-label purposes, including to sell Depakote off-label to Plaintiff for treatment of her tonic-clonic seizures when Depakote had not been approved for such an indication.

The Court agrees with Defendants that evidence of the guilty plea, settlement, and agreement reached in an entirely different case has no relevance in this case. *See Kaleta v. Abbott Laboratories, Inc*., No. 14-cv-847-NJR-SCW, slip op. at *4 (S.D. Ill. Feb. 20, 2015) (order excluding Abbott's 2012 plea and agreement). Further, the Court is not persuaded that evidence of over-promotion of Depakote for off-label uses not at issue (e.g., agitation and aggression in elderly dementia patients or treatment of schizophrenia) renders the evidence relevant to whether Defendants over-promoted Depakote for off-label uses in Plaintiff's case (generalized, tonic-clonic seizures). To that point, in *Dotegowski v. Abbott Labs, Inc.*, CGC-10-506794, slip op. at *12 (Superior Court Cal., Feb. 2, 2015) (excluding Abbott's plea and agreement), the court considered the admissibility of Abbott's plea, settlement, and agreement in the context of off-label usage, and similarly excluded the evidence on the basis that the corporate agreement and plea affected an entirely different population of individuals than was at issue. The Court agrees with the reasoning in *Dotegowski* and *Kaleta* and similarly finds the contested evidence to be irrelevant and inadmissible.

Even if the disputed evidence was relevant as Plaintiffs contend, the probative value of evidence of the guilty plea, settlement, and agreement is outweighed by the danger of unfair prejudice, confusing the issues, misleading the jury, undue delay, and wasting time. For example, the jury may assume that Abbott acted improperly merely because it entered into the plea, settlement, and agreement and paid significant fines, totaling approximately $1.5 billion.

The Court does not anticipate this evidence will be admissible for purposes of impeachment unless Abbott opens the door. Counsel are instructed to alert the Court during trial if they intend to offer this evidence or elicit testimony relating to it in any way.

5. **Motion *in Limine* No. 5 to Exclude Evidence, Testimony and References to Abbott's Alleged Off-Label Promotion of Depakote for Treatment of Any Condition Other Than Tonic-Clonic Seizures (Doc. 219)**

Defendants' Motion *in Limine* No. 5 is **GRANTED**. In its Motion, Defendants ask the Court to exclude testimony and evidence regarding Abbott's alleged off-label promotional/marketing activities and materials or any alleged off-label use of Depakote for any condition other than the one for which Plaintiff Rheinfrank was prescribed Depakote (generalized tonic-clonic seizures). As addressed in the Court's analysis in response to Defendants' Motion *in Limine* No. 4, evidence of Defendants' alleged off-label promotion and marketing of Depakote for conditions other than that for which are at issue here (generalized tonic-clonic seizures) is irrelevant.

Even if the disputed evidence was relevant, the probative value of such evidence is outweighed by the danger of unfair prejudice, confusing the issues, misleading the jury, undue delay, and wasting time.

6. **Motion *in Limine* No. 6 to Exclude References to Promotional Activities, Promotional Materials, and Sales and Marketing Practices (Doc. 214)**

Defendants' Motion in Limine No. 6 is **DENIED**. Defendants seek an order precluding Plaintiffs from presenting evidence of Abbott's promotional activities, distribution of promotional materials, and sales and marketing practices related to Depakote. Defendants argue this evidence is not relevant because Dr. Lemus, who prescribed Depakote during Plaintiff

Rheinfrank's pregnancy, does not recall any Abbott sales presentative or Depakote-related promotional activities.

Plaintiffs need not demonstrate reliance upon the promotional materials and marketing documents to in order for such evidence to be relevant in a failure to warn case. *Morales v. American Honda Motor Co., Inc.* 151 F.3d 500, 517 (6th Cir. 1998) (finding district court did not abuse its discretion in admitting advertisement into evidence despite the fact that there was no established reliance upon the advertisement). Regardless of whether Dr. Lemus can recall whether she relied upon promotional materials made by Abbott, evidence of promotional activities, distribution of promotional materials, and sales and marketing practices relating to Depakote are relevant to the issue of what Abbott knew about Depakote's risks and Depakote's proper use for women of childbearing years. The evidence may also be relevant to the content of the label itself. *See Kaleta v. Abbott Laboratories, Inc*., No. 14-cv-847-NJR-SCW, slip op at *18 (S.D. Ill. Feb. 20, 2015) (admitting evidence of promotional materials); *In re Yasmin & Yaz (Drospirenone) Mktg., Sales Practices & PMF Prods. Liab. Litig.*, 3:09-md-2100-DRH, 2011 WL 6740391, at *10 (S.D. Ill. Dec. 22, 2011) ("evidence about sales goals is certainly relevant particularly when it may impact decision making regarding labeling").

7. Motion *in Limine* No. 7 to Exclude Evidence, Testimony, or Argument that Abbott Should Have Created a Pregnancy Registry (Doc. 216)

Defendants' Motion *in Limine* No. 7 is **DENIED IN PART AND TAKEN UNDER ADVISEMENT IN PART**. Defendants ask the Court to preclude Plaintiffs from offering testimony that "Abbott should have conducted some undefined, post-market study, such as a pregnancy registry, to compare the safety and risks of Depakote against other competing anti-epileptic drugs." (Doc. 216 at PageID 26458) (emphasis removed). To the extent Defendants

are objecting to specific expert testimony, those concerns appear to have been fully briefed in Daubert motions and the Court anticipates its ruling on those motions will address those specific concerns. Accordingly, the Court will not rehash those arguments here.

Plaintiffs assert their position is not that Defendants had a duty to create a pregnancy registry, but that "a pregnancy registry is one of a myriad of options Defendants had at their disposal to fulfill their federal and state duties to warn of risks they should have known by M.B.D.'s birth." (Doc. 239 at PageID 28146.) The Court finds that the ways in which Defendants could have conducted post-marketing studies, including by creating a pregnancy registry, is relevant to the question of whether Defendants satisfied its continued duty to study Depakote and notify the medical professional of any additional safety information discovered from its use, and warn of the risks or dangers that it knew or should have known. However, it has not found that it is appropriate for Plaintiffs or her experts to opine that Defendants had a duty or was required to create a pregnancy registry. This ruling is consistent with *Kaleta*, in which the Court denied Abbott's motion *in limine* on this topic and permitted testimony concerning whether Abbott could have created a pregnancy registry. *Kaleta*, 3:14-cv-00847-NJR-SCW, slip. op. at *5 (S.D. Ill. Feb. 20, 2015) (denying in part and reserving ruling in part on motion to exclude evidence that defendant could have created a pregnancy registry). The Court agrees with the distinction drawn by the *Kaleta* court: "Plaintiffs' experts will not be permitted to opine that Abbott ***should have*** created a pregnancy registry. Rather, the experts may only opine that Abbott ***could have*** established a pregnancy registry, which may assist the jury in ultimately determining whether Abbott satisfied its duty to provide an adequate warning about the risks of Depakote." *Id*.

8. **Motion *in Limine* No. 9 to Exclude Evidence, Testimony, and Argument Related to Other Lawsuits, Claims, or Investigations (Doc. 220)**

Defendants' Motion *in Limine* No. 9 is **GRANTED IN PART AND TAKEN UNDER ADVISEMENT**. Defendants ask the Court for an order precluding Plaintiffs from entering into evidence information about other lawsuits, claims, or investigations against Abbott, regardless of whether they are related to Depakote. In response, Plaintiffs assert they do not anticipate offering such evidence at trial. However, Plaintiffs assert that the fact that other litigation exists will be unavoidably revealed to the jury, particularly when recorded deposition testimony is shown. Plaintiffs also assert that prior judicial admissions and discovery responses from other forums are admissible here. The Court finds that admission into evidence of other lawsuits, claims or investigations unrelated to this action is not admissible unless Defendants open the door. However, to the extent certain otherwise admissible evidence implies the existence of other lawsuits as Plaintiffs posit, the Court will need to make a ruling on a case-by-case basis. The parties are instructed to notify the Court of such evidence prior to attempting to enter it into evidence so the Court may consider its admissibility.

9. **Motion *in Limine* No. 10 to Exclude References to the Size and Resources of Law Firms and Cost of Defense; Golden Rule Arguments; and Evidence Regarding Discovery Disputes (Doc. 210)**

Defendants' Motion *in Limine* No. 10 is **GRANTED IN PART AND TAKEN UNDER ADVISEMENT**. Defendants move the Court to exclude evidence of the size and resources of the law firms representing Abbott and/or costs of defense, the "Golden Rule," or that the jury should put themselves in the position of the Plaintiffs, and discovery disputes.

As to the first issue, Plaintiffs represent this is a non-issue, and they have no intention of introducing evidence about the cost of defense or size of defense counsel's law firm. In any event, the Court notes that such evidence is irrelevant. As such, this aspect of Defendants' Motion is **GRANTED**.

With respect to whether Plaintiffs may use the "Golden Rule" argument, Plaintiffs assert they understand the bounds of this rule. Plaintiffs claim that while they are mindful of their limitations, they are within their rights to inform the jury to act as the conscience of the community or "send a message" when assessing punitive damages. Thus, the Court **GRANTS** Defendants' motion to exclude "Golden Rule" statements, but notes that there are certain appropriate and related exceptions upon which it may rule on a case-by-case basis, to the extent necessary.

Finally, as to discovery disputes, the Court notes that there are some outstanding discovery disputes. In particular, the Court anticipates ruling on deposition designations prior to trial, as discussed at the Final Pretrial Conference. The objections ruled upon should be omitted from the video and transcript testimony, to the extent possible. In addition, Plaintiffs have separately briefed the issue of whether a dispute about genetic testing may be raised at trial, which the Court has separately analyzed below in ruling on Plaintiffs' Motion *in Limine* No. 1. However, the Court finds that evidence or argument about discovery disputes would be irrelevant and unfairly prejudicial. *See Hinkle v. Ford Motor Co.*, No. 3:11-24-DCR, 2012 WL 4049477, at *6 (W.D. Ky. Sept. 13, 2012) (granting motion *in limine* to exclude evidence of discovery disputes as irrelevant and prejudicial, and noting that such disputes are properly for the Court to resolve).

10. Motion *in Limine* No. 11 to Exclude References to Scientific and Medical Data Post-Dating the Minor Plaintiff's July 2004 Birth (Doc. 230)

Defendants' Motion *in Limine* No. 11 is **DENIED**. Defendants ask the Court to exclude evidence regarding scientific and medical data, studies, treatises, and treatment guidelines relating to comparative teratogenicity of AEDs or other risks Abbott purportedly failed to disclose in its warnings and post-dating the July 2004 birth of M.B.D. as irrelevant, unfairly prejudicial, misleading, and a waste of time.

The Court is persuaded by the *Kaleta* ruling and reasoning denying a similar motion *in limine* that scientific and medical data issued after M.B.D.'s 2004 birth may be relevant and probative of data that could have and should have been known before M.B.D. was conceived. *Kaleta*, 3:14-cv-00847-NJR-SCW, slip. op. at *17 (S.D. Ill. Feb. 20, 2015) (denying motion *in limine* to exclude post-birth medical data). This evidence is also relevant to the issue of causation, because it is undisputed that Depakote's formulation has not changed since it was marketed in 1983. *Id.* As such, Plaintiffs will be allowed to introduce medical and scientific evidence, with proper foundation, if that evidence can be linked to the causation issues in the case.

11. Motion *in Limine* No. 13 to Exclude Evidence of the FDA's New Labeling Requirements (Doc. 231)

Defendants' Motion *in Limine* No. 13 is **GRANTED.** Defendants ask the Court to exclude evidence about the Final Rule issued on December 4, 2014 by the FDA regarding Content and Format of Labeling Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling.

Prescription drugs have been grouped into FDA use-in-pregnancy ratings and classified as Category A, B, C, D, or X. During the 2003-2004 timeframe, Depakote was listed as a Category D drug. The 2014 Final Rule requires removal of the use-in-pregnancy ratings from all prescription drugs. Instead, information and data regarding risks during pregnancy and lactation will be added to other sections of the product labeling. The new rule took effect in June 2015.

The new labeling regulation is irrelevant to the facts of this case, because during the time in question from 2003-2004, the use-in-pregnancy categories were required by the FDA. The FDA's subsequent decision to remove those categories does not have any bearing on the facts of this case. Even if such evidence were relevant, the danger of unfair prejudice, confusing the issues, and misleading the jury would outweigh any probative value. The Court is concerned that evidence of the FDA's changes approximately a decade later to pregnancy labeling requirements may lead the jury to assess the adequacy of the label based on requirements not in effect during the relevant time.

Plaintiffs note that one of Defendants' experts has written about the inadequacies of the pregnancy category system. Evidence of his article and critique of the pregnancy labeling system may come in on cross-examination. However, the fact that the FDA subsequently changed the pregnancy labeling in 2015 is irrelevant.

12. Motion *in Limine* No. 14 to Exclude References to or Evidence of Lawsuits Filed Against Defendants' Expert Witnesses (Doc. 211)

Defendants' Motion *in Limine* No. 14 is **TAKEN UNDER ADVISEMENT**. In their Motion, Defendants ask the Court to exclude references to or evidence of lawsuits filed against Defendants' expert witnesses. Defendants anticipate that Plaintiffs will question its experts

about malpractice lawsuits and argue this evidence is unrelated to the claims and the probative value is outweighed by risk of prejudice.

The Court agrees with Plaintiffs that evidence of prior lawsuits, particularly malpractice suits, is relevant and may be useful in helping the jury assess expert credibility and competency on cross-examination. However, the Court is mindful that extensive cross-examination on the topic could waste time and result in mini-trials. Accordingly, the Court will take this matter under advisement but finds that such evidence will generally be relevant and admissible.

13. Motion *in Limine* No. 15 to Exclude Evidence, Testimony, or Argument Related to Thalidomide, Accutane, Cylert or Other Drugs Unrelated to Depakote That Have Been Pulled From the Market (Doc. 213)

Defendants' Motion *in Limine* No. 15 is **DENIED**. Defendants ask the Court to exclude evidence relating to Thalidomide, Accutane, Cylert, or other drugs that have been pulled from the market. Defendants argue that evidence of pulled drugs is not relevant, and the probative value of this evidence is outweighed by the risk of unfair prejudice and misleading or confusing the jury. The Court notes at the onset of its analysis that there is a dispute of fact as to whether Thalidomide and Accutane remain on the market.

Plaintiffs argue that evidence about how the manufacturers of Accutane and Thalidomide acted proactively to create public awareness of the teratogenicity risks of their drugs is relevant. Plaintiffs argue this evidence is relevant to whether the Black Box Warning and Category D designation constituted adequate warnings and instruction for Depakote. In addition, Plaintiffs argue they may introduce evidence of how Abbott marketed Cylert, a drug it manufactured, with pre-printed informed consent forms which were made available to all physicians. This form

would be offered in juxtaposition to the "illusive Depakote Patient Information Leaflet" used for Depakote. (Doc. 242 at PageID 28756–57.)

The Court agrees with Plaintiffs that evidence of how manufacturers of Thalidomide or Accutane acted to create public awareness of the teratogenic effects of their drug or, in the case of Cylert, created a pre-printed inform consent form for physicians, is relevant to the issue of whether the warnings and instruction for Depakote were adequate. However, this evidence may not be used to show similarity among the drugs, as there are significant differences between Thalidomide, Accutane, and Cylert and Depakote. Thus, Plaintiffs may not use this evidence to argue that the drugs are the same as Depakote or have the same risk-benefit profile. However, examples of how other drugs warned about teratogenicity or other risks and/or communicated with patients is admissible to demonstrate a comparison of how manufacturers warned of risks of their drug.

The probative value of the example of how other warnings were conveyed to patients and/or physicians outweighs the risk of unfair prejudice, confusion, or misleading the jury. Although Defendants are concerned that mere mention of the name Thalidomide will inflame the jury, significant time has passed between when Thalidomide was first introduced on the market and its teratogenicity was discovered; thus, the Court is skeptical that the drug is even widely-known to have prejudicial effect upon mere mention of its name.

14. Defendants' Motion *in Limine* No. 16 to Exclude References to any Claim that Abbott Could be Liable for Allegedly Failing to Change Depakote's Pregnancy Category Rating (Doc. 218)

Defendants' Motion *in Limine* No. 16 is DENIED. Defendants' Motion asks the Court to exclude evidence that Abbott should have changed or could be liable for allegedly failing to

change Depakote's pregnancy category. Defendants contend such evidence should be barred, because the FDA has exclusive authority over pregnancy categories.

The Court agrees with Plaintiffs that Defendants have not cited any regulatory authority establishing that the FDA maintains exclusive control of pregnancy category designations. Abbott also has not provided evidence that it attempted to strengthen Depakote's pregnancy category and was prohibited by the FDA, as in the case of developmental delay warnings previously analyzed by the Court in its summary judgment order. Rather, evidence that Abbott could have taken steps to request to strengthen its pregnancy warning is relevant to the question of whether Abbott's warnings were adequate and admissible. The probative value of this evidence outweighs any risk of unfair prejudice.

15. Motion *in Limine* No. 17 to Exclude Evidence, Testimony and Argument Suggesting that Half-Siblings of Minor Plaintiff M.B.D. Have Birth Defects Caused by or Attributable to Pamela Rheinfrank's Ingestion of Depakote During Pregnancy (Doc. 212)

Defendants' Motion *in Limine* No. 17 is **GRANTED subject to its ruling on Plaintiff's Motion *in Limine* No. 1.** Defendants note in their Motion in Limine No. 17 that Plaintiff M.B.D. has four half-siblings, with whom she shares a biological mother. Defendants ask the Court to exclude evidence concerning birth defects or injuries purportedly suffered at birth by M.B.D.'s half siblings. Plaintiffs do not contest this request. The Court agrees that information concerning the health of M.B.D.'s siblings is irrelevant, because this case concerns only Plaintiff M.B.D.'s birth defects. The Court notes that additional arguments concerning admissibility of M.B.D.'s siblings were raised in response to Plaintiffs' Motion *in Limine* No. 1, and it has addressed those arguments in ruling on that motion.

16. Motion *in Limine* No. 18 to Exclude the Recitation of Exhibits as Evidence (Doc. 215)

Defendants' Motion *in Limine* No. 18, which asks the Court to exclude recitation of exhibits as evidence, is **TAKEN UNDER ADVISEMENT.** The Court will rule on objections on a case-by-case basis.

17. Motion *in Limine* No. 19 to Exclude Evidence or Argument Concerning Abbott's Alleged Promotion of Depakote for Off-Label Use in Treating Primary Generalized Tonic-Clonic Seizures, and its Efforts to Obtain FDA Approval for Depakote's Use in Treatment of Tonic-Clonic Seizures (Doc. 232)

Defendants' Motion *in Limine* No. 19 is **DENIED**. Defendants ask the Court to exclude Plaintiffs from presenting evidence about Abbott's alleged promotion or marketing of Depakote off-label for use in treating primary generalized tonic-clonic seizures and Abbott's unsuccessful efforts to obtain FDA approval for such an indication. Defendants argue that Depakote was prescribed off-label is irrelevant to any fact at issue, and the prejudice of introducing such evidence will mislead the jury.

As in *Krumpelbeck v. Breg, Inc.*, 491 Fed. App'x 713, 720 (6th Cir. 2012), the rejection by the FDA of Defendants' application for an indication for tonic-clonic seizures is probative of whether Abbott was or should have been on notice of the need to conduct testing of the safety of its product – in this case, Depakote for treatment of tonic-clonic seizures. Abbott's attempts at and denials of approval from the FDA to receive an indication for Depakote for the treatment of tonic-clonic seizures is relevant to the issues of Abbott's notice of the need to do further safety tests, its knowledge of risks, and whether its investigation into its drug was reasonable during the relevant timeframe. Abbott's promotion of Depakote for off-label use of treating tonic-clonic

seizures is also relevant to the issue of Abbott's knowledge and the feasibility of strengthening its label. The Court also finds that the probative value of this evidence outweighs the risk of prejudice, as whether Abbott's knowledge of the risks of its drug and/or the need for testing of its drug is central to the issue of whether the 2003-2004 Depakote label was adequate.

III. PLAINTIFFS' MOTIONS *IN LIMINE*

1. Plaintiffs' Motion in Limine No. 1 (Doc. 221)

Plaintiffs' Motion *in Limine* No. 1 is **GRANTED IN PART AND DENIED IN PART**. Plaintiffs move the Court to exclude evidence concerning (1) the effect of Plaintiff Rheinfrank's phenobarbital use to her pregnancy with M.B.D. or on M.B.D.'s health, (2) information regarding the health of Plaintiff Rheinfrank's older children and her pregnancies with them, (3) the fact that Plaintiff M.B.D. did not undergo additional genetic testing requested by Abbott, (4) certain personal aspects of Plaintiff Rheinfrank's life, and (5) circumstances under which Plaintiff Rheinfrank retained counsel. The Court will consider each of these arguments in turn.

Plaintiffs' request to exclude the effect of Plaintiff Rheinfrank's use of phenobarbital during her pregnancy with M.B.D. or on M.B.D.'s health is **DENIED.** Plaintiffs argue that because none of Defendants' experts opine that phenobarbital was the cause of Plaintiff Rheinfrank's injuries, no evidence about the effect of Rheinfrank's use of phenobarbital during her pregnancy with M.B.D. or on M.B.D's health is admissible. The Court finds that Abbott is free to cross-examine Plaintiffs' causation expert testimony about possible alternative causes of M.B.D.'s birth defects, including M.B.D.'s exposure to phenobarbital. "In Ohio, when testifying to proximate causation, an expert must testify that an event was the probable cause of the injury, that is, that it is more than fifty percent likely that the event caused the injury." *Freudeman v. Landing of Canton*, 702 F.3d 318, 325 n.3 (6th Cir. 2012) (relying upon *Stinson v. England*, 69

Ohio St. 3d 451, 455–56, 633 N.E.2d 532 (1994)). "If the expert cannot testify with this degree of certainty, he or she can still rebut the other side's expert testimony by identifying other possible causes." *Id*. (relying upon *Fritch v. The Univ. of Toledo Coll. Of Med*., No. 11AP-103, 2011 WL 3925697, at *4 (Ohio Ct. App. Sept. 8, 2011)). Accordingly, cross-examination/rebuttal regarding possible alternative causes is admissible.

Plaintiffs' request to exclude evidence of birth defects purportedly suffered at birth by M.B.D.'s half-siblings and Plaintiff Rheinfrank's pregnancies with M.B.D.'s half-siblings is **GRANTED IN PART AND DENIED IN PART**. The Court has already considered the admissibility of birth defects or injuries purportedly suffered at birth by M.B.D.'s half-siblings raised by Defendants' Motion *in Limine* No. 17, which is not admissible.

However, Defendants object to excluding all evidence concerning Plaintiff Rheinfrank's past pregnancies or her prescription history during those pregnancies. Defendants argue Plaintiff Rheinfrank's prescription and pregnancy history are evidence that bear on her knowledge of the risks of birth defects associated with Depakote, including whether she was warned about or aware of such risks prior to her pregnancy with M.B.D., particularly in light of the absence of medical records on the subject. The Court agrees that Plaintiff Rheinfrank's medical history, which spanned the course of four pregnancies prior to her birth with M.B.D., is relevant to her knowledge of the risks of Depakote, and the probative value of such evidence outweighs the risk of unfair prejudice.

Further, Abbott argues it should be permitted to introduce testimony concerning a seizure Plaintiff Rheinfrank's eldest child suffered after birth, which his doctors attributed to withdrawal from Depakote. The Court agrees that this evidence is probative of Plaintiff Rheinfrank's

knowledge of the risks of *in utero* exposure to Depakote. The Court finds that this evidence is relevant, and the probative value outweighs the risk of prejudice.

Plaintiffs' request to exclude evidence regarding Plaintiffs' "failure" to undergo genetic sequencing testing for Peter's Plus syndrome and full genome sequencing is **GRANTED**, consistent with the Court's ruling on Defendants' Motion *in Limine* No. 10 that evidence of discovery disputes is inadmissible. As Plaintiffs point out, the Court denied Abbott leave of court to perform these tests. (Doc. 74.) Defendants may cross-examine Plaintiffs' experts on their opinion regarding causation, but Defendants may not produce evidence of the discovery dispute regarding the genetic testing and full genome sequencing testing. The probative value of evidence of Plaintiffs' "failure" to undergo such testing – a request that was denied by the Court – would be outweighed by the risk of unfair prejudice and confusion of the jury.

Plaintiffs' request to exclude aspects of her personal life is **DENIED**. Plaintiffs seek to exclude evidence that Plaintiff Rheinfrank was the victim of domestic violence during her pregnancy with M.B.D. and that she smoked during her pregnancy with M.B.D. Plaintiffs argue that no expert has attributed M.B.D.'s birth defects to either domestic violence or smoking during pregnancy. Plaintiffs further argue that the evidence would be prejudicial. The Court finds that both issues are relevant to causation and would be appropriate to be raised during cross-examination of an expert witness. In addition, such evidence would be relevant on cross-examination of an expert witness as possible/alternative causes of M.B.D.'s injuries.

Plaintiffs' request to exclude evidence as to how Plaintiff Rheinfrank retained counsel is **GRANTED**. Plaintiffs argue this evidence is irrelevant. According to Plaintiffs, Plaintiff Rheinfrank testified in her deposition that she saw a Depakote commercial that informed her that Depakote was a bad drug, which lead her to retain counsel. Plaintiffs' counsel assert they did not

produce those commercials, nor had they advertised at all regarding Depakote. The Court does not find this evidence relevant to the issues of the case, or to Plaintiffs' knowledge of the risks of Depakote, as Defendants contend. Evidence about how Plaintiff retained counsel is irrelevant and therefore inadmissible.

2. Plaintiffs' Motion in Limine No. 2 (Doc. 223)

Plaintiffs' Motion *in Limine* seeks to "prohibit Defendants' counsel from presenting inadmissible, false, and/or unprovable evidence and argument throughout trial." (Doc. 223 at PageID 27093.) All counsel are bound by the Federal Rules of Civil Procedure, rules of ethics, local rules, and the undersigned's standing order. The Court, of course, intends not to allow false or inadmissible statements into evidence. The Court will **DENY** this motion, as it finds that it is more appropriate to respond to objections about inadmissibility of evidence or arguments on case-by-case objections by counsel.

IT IS SO ORDERED.

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