UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

Z.H. by and through KEVIN HUTCHENS and CHRISTIN HUTCHENS, individually, and as parents and next friends of Z.H.	)	**CASE NO.1:14CV176**
Plaintiffs,	)	**JUDGE CHRISTOPHER A. BOYKO**
Vs.	)	
ABBOTT LABORATORIES, INC. and ABBVIE, INC.	)	**ORDER**
Defendant.	)	

CHRISTOPHER A. BOYKO, J:

This matter is before the Court on Defendants' Motion to Exclude Certain Testimony From Plaintiffs' Designated Expert Witness, Godfrey Oakley, Jr. M.D. (ECF # 88). For the following reasons, the Court grants in part and denies in part Defendants' Motion.

Godfrey Oakley, Jr. M.D. is a physician, pediatrician, geneticist and epidemiologist with fifty years experience. He was chief of the Birth Defects Branch of the Centers for Disease Control and Prevention from 1981-1985 and Director of the Division of Birth Defects and Developmental Disabilities from 1985-1998. He has published over one hundred and fifty articles, abstracts, letters book chapters, editorials and comments and studies on topics relating to congenital malformations, epidemiology, genetic syndromes and birth defect surveillance.

Defendants move to exclude Dr. Oakley's opinions relating to: a hypothetical registry he claims Defendants should have set up in the 1980's; labeling; any testimony comparing the teratogenicity of Depakote to Accutane and Thalidomide; and any testimony that Depakote is the most dangerous anticonvulsant drug.

Rule 702 of the Federal Rules of Evidence states:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
> (b) the testimony is based on sufficient facts or data;
> (c) the testimony is the product of reliable principles and methods; and
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Rule 703 states:

> An expert may base an opinion on facts or data in the case that the expert has been made aware of or personally observed. If experts in the particular field would reasonably rely on those kinds of facts or data in forming an opinion on the subject, they need not be admissible for the opinion to be admitted. But if the facts or data would otherwise be inadmissible, the proponent of the opinion may disclose them to the jury only if their probative value in helping the jury evaluate the opinion substantially outweighs their prejudicial effect.

Under Federal Rules of Evidence, a trial judge must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, (1993). The objective of *Daubert's* "gatekeeping" function is to ensure the reliability and relevancy of expert testimony. *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999). The Supreme Court has held this "gatekeeping" obligation applies not only to scientific testimony, but to all expert testimony. *Id*. at 147. Courts

are not required to hold a formal hearing on *Daubert* challenges. *See Greenwell v. Boatwright,* 184 F.3d 492, 498 (6th Cir.1999). "[N]o matter how good" experts' "credentials" may be, they are "not permitted to speculate." *Tamraz v. Lincoln Elec. Co.,* 620 F.3d 665, 671 (6th Cir. 2010) quoting *Goebel v. Denver & Rio Grande W. R.R. Co.,* 215 F.3d 1083, 1088 (10th Cir.2000). "The party offering expert testimony bears the burden of establishing the foundational elements of admissibility by a preponderance of proof." *Jones v. Pramstaller,* 874 F. Supp. 2d 713, 718 (W.D. Mich. 2012) citing *Nelson v. Tennessee Gas Pipeline Co.,* 243 F.3d 244, 251 (6th Cir.2001). "Nevertheless, Rule 702's requirements are applied liberally, leaving '[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof [as] the traditional and appropriate means of attacking shaky but admissible evidence.'" *Jones,* 874 F.Supp.2d at 718 quoting *Daubert,* 509 U.S. at 596.

Pregnancy Registry

Dr. Oakley opines that Defendants were capable of establishing and should have established a pregnancy registry of women exposed to valproic acid at the time Depakote was first marketed in the early 1980's. Dr. Oakley opines that a pregnancy registry of women exposed to valproic acid would have collected data on the outcomes of these pregnancies to include the incidence and types of birth defects resulting from the exposure. Had Defendants conducted such a registry in the 1980's, Dr. Oakley opines that the teratogenic effects of Depakote and its relation to cognitive development would have been known a decade earlier.

According to Defendants, Dr. Oakley's opinions, relating to the creation of a pregnancy registry in the 1980's are irrelevant to the issues in this case. Defendants agree that they could have set up a registry in the 1980's. In fact, Defendants, acting in concert with other AED

manufacturers, established the North American Antiepileptic Drug Pregnancy Registry ("NAAED") in 1996. Preliminary data from the NAAED emerged in 2002 showing the teratogenic effects of Depakote when compared to other AEDs. The information was first published in a peer-reviewed journal in 2005.

The problem with Dr. Oakley's opinion on a pregnancy registry, as argued by Defendants, is that Dr. Oakley never indicates what the registry should have looked like. Dr. Oakley does not opine what pregnancies might have been registered, including Depakote exposures from monotherapy or polytherapy or whether it should have included pregnancies exposed to other AEDs and not Depakote. He fails to opine when such a registry would have enrolled enough pregnancies to produce statistically significant data. Also, Dr. Oakley does not opine whether a registry that included women exposed to AEDs other than Depakote should have included Lamictal-related results since Lamictal is the only potential alternative to Depakote under the facts of this case and it did not enter the market until 1994. Dr. Oakley did not do any predictive modeling, therefore, he does not and cannot opine on the kinds of information an earlier initiated registry would have reported. Without the above information or expert testimony on what information would have been uncovered and when it would have been uncovered, Dr. Oakley's opinion on a pregnancy registry amounts to nothing more than unsubstantiated speculation. In the absence of any evidence or testimony concerning what information about Depakote would have been learned and when it would have been learned arising from a pregnancy registry established in the 1980's, Defendants argue Dr. Oakley's opinion is not reliable and involves mere conjecture with no expert basis.

According to Plaintiffs, Dr. Oakley's opinions on the earlier establishment of a

pregnancy registry has been allowed in three other Depakote cases based on his experience overseeing birth defect registries and CDC-related research. His registry opinions are relevant as they relate directly to Defendants' duty to monitor the safety of Depakote and duty to warn. The Southern District of Illinois found Dr. Oakley's opinions on a pregnancy registry were not too speculative but would lead to a better understanding of the risks of Depakote use in women of child bearing age. Dr. Oakley opines that a pregnancy registry is simply a matter of gathering information on the women who took Depakote while pregnant and recording any adverse effects to the child. Dr. Oakley testified that exposure registries are plentiful and cited examples of exposure registries that could have served as models for a Depakote registry. Plaintiffs cite to the United States Supreme Court decision in *Wyeth v. Levine*, 555 U.S. 570-71 (2009) for the proposition that drug manufacturers have an ongoing duty to ensure that the warnings issued are adequate so long as the drug is on the market. Ohio law also imposes a duty on manufacturers to disclose all risks of which the manufacturer knew or should have known. Because Defendants knew of the birth defect risks of Depakote use in women of childbearing age in 1982, Dr. Oakley opines that, at a minimum, Defendants should have established a registry at that time.

The Court first notes that Defendants do not challenge Dr. Oakley's qualifications to opine on the issue of a pregnancy registry. Thus, there is no *Daubert* issue with his qualifications. Furthermore, the Court finds that Dr. Oakley's opinion that Defendants should have initiated a pregnancy registry in 1983 is relevant to what Defendants knew or should have known about the risks of birth defects at the time Christin was prescribed Depakote. Furthermore, Dr. Oakley may opine that had they initiated a registry earlier, Defendants would have known more about the risks of birth defects than they did in 2002. This conclusion follows

logically as it is axiomatic that the earlier one studies a drug the earlier one will learn of its effects. However, the Court agrees with Defendants that Dr. Oakley cannot opine that an earlier pregnancy registry would have elicited the same results or would have resulted in the same knowledge of the risks of Depakote use as found in the results from the 1996 registry. The Court is not convinced that it is scientifically reasonable to opine that the results obtained from the 1996 registry would have been obtained had the registry been implemented in 1983. Absent substantial foundation testimony and evidence on what the parameters should have been in a 1980's registry versus the parameters of the 1996 registry, including the difference in size of the populations to be studied, the number of participants needed to obtain significant results and what the registry in 1983 would have studied, it is simply too speculative to say what an unspecified 1980's registry would have uncovered regarding Depakote-related birth defects. Furthermore, its unclear to the Court how many women were even prescribed Depakote in 1983 given that it was newly marketed in the United States in 1983. The Court has no information on what other AEDs were available to women in 1983. Given these feasibility and study design issues, the Court does not find his opinions to be reliable and the Court grants Defendants' Motion in part, precluding Dr. Oakley from testifying as to what specific results could have been obtained had Defendants implemented a pregnancy registry prior to 1996.

Labeling Opinions

Defendants also seek to preclude Dr. Oakley from opining as to what teratogenic risk information should have been included on the 2002 Depakote label. Dr. Oakley is not a labeling expert, is not a neurologist, has never prescribed AEDs and has never been employed by the FDA. Plaintiffs concede Dr. Oakley is not a labeling expert. In the absence of his relevant

expertise in labeling and treating epileptic patients, Defendants seek to exclude the following opinions of Dr. Oakley:

> [A] Based on my own experience and scientific literature, valproic acid . . . should not be used by women of reproductive age unless there is no other drug or drug combination that can control her epilepsy. Such use should be rare.
>
> [B] It should not be the first drug used in women of reproductive age newly diagnosed with epilepsy.
>
> [C] I conclude that the 1982 Dear Doctor Letter and the valproic acid package insert should have included the 20.6 fold increased risk of spina bifida from first trimester exposure to valproic acid.
>
> [D] In my opinion, Abbott should have included the relative risk in its 1982 Dear Doctor Letter and in the package insert. I conclude that the risk is high enough and serious enough that
>
> [E] Abbott should have taken steps to limit the use of this drug to the absolute minimum number of women of reproductive age and
>
> [F] minimize pregnancies among women taking valproic acid by advising women taking valproic acid to be on effective birth control.

Plaintiffs acknowledge Dr. Oakley is not a labeling expert and that he is not offering labeling opinions. Plaintiffs response to Defendants' challenge to the above opinions is that Dr. Oakley should be permitted to opine that Depakote increased the odds of spina bifida by 20.6 times or 2,060 percent. This was knowledge Defendants had in 1982. According to Dr. Oakley, Defendants only warned prescribing physicians that Depakote posed a 1-2% estimated risk of spina bifida in children of women exposed to Depakote. This 1-2% figure was calculated by multiplying the incidence of spina bifida in the United States without exposure to Depakote by the 20.6 Depakote odds ratio. While the 1-2% figure is accurate it does not display, according to Plaintiffs, the full picture of the risk because physicians would not have known the incidence of spina bifida. Without the number, physicians would not have a clear picture of the scope of the

risk. Therefore, Dr. Oakley opines, Defendants should have included the odds ratio in the 1982 Dear Doctor Letter. Although he is not a labeling expert, Plaintiffs argue Dr. Oakley's experience as a physician, epidemiologist and teratologist qualifies him to opine on what warnings should have been presented to physicians. His testimony on the odds ratio will help the jury understand that simply conveying the absolute risk of 1-2% was an inadequate warning to physicians.

Because Plaintiffs do not oppose the Motion concerning opinions A,B,,D, E and F, the Court grants Defendants Motion and excludes Dr. Oakley's testimony on these issues.

Because Dr. Oakley is not a labeling expert, his opinion on what the Depakote insert warning should have included constitutes a labeling opinion, which must be excluded.

The Court holds that Dr. Oakley's opinion on what should have been included in the 1982 Dear Doctor Letter is irrelevant to the failure to warn claim because there is no evidence that an additional warning to physicians in 1982 would have influenced Dr. Foldvary's decision to prescribe Depakote in 2002. There is no evidence the 1982 Dear Doctor Letter was delivered to Dr. Foldvary nor was Dr. Foldvary even a physician in 1982. Thus, what should have been in the 1982 Dear Doctor Letter is not relevant to the facts in this case and the Court grants Defendants' Motion on the labeling issues.

Comparative Teratogenicity

Defendants seek to exclude Dr. Oakley's opinions that Depakote is the most dangerous of the modern anticonvulsant drugs and is in the top three drugs for causing life-altering serious birth defects among all drugs on the market in the United States.

Defendants contend Dr. Oakley's testimony concerns the present knowledge of

Depakote. His opinion states Depakote ***is*** the most dangerous. This is based on what is currently known about Depakote following years of research and study. He does not state that this was known by Defendants in 2002 and his opinion is not based on anything cited by Dr. Oakley predating Z.H.'s birth. In fact, at least with regard to Lamictal, it had not been on the market long enough to study its teratogenic risks as compared to Depakote. Thus, Defendants contend his opinion is not based on the knowledge of the comparative risks of Depakote versus other AEDs as of 2002 and must be excluded.

Similarly, Defendants seek to exclude Dr. Oakley's opinion that Depakote is among the top three teratogenic drugs on the market in the United States along with Thalidomide and Accutane. When asked the basis of this conclusion, Dr. Oakley relied on a list of human teratogens found in a textbook but on examination, Dr. Oakley was unable to state the congenital malformation rates of four randomly selected drugs on the list. According to Defendants, this establishes Dr. Oakley's lack of any scientifically valid basis for such an opinion. Furthermore, its prejudicial value far outweighs its probative value. Therefore, Defendants ask the Court to exclude such opinion testimony.

Plaintiffs argue that Dr. Oakley's "is the most dangerous of modern anticonvulsant drugs' opinion is clearly supported by evidence because it is currently printed on the Depakote label. Furthermore, although his opinion is a present sense opinion it is undisputed that the Depakote formulation has not changed since it was first marketed. Therefore, his opinion is relevant to today and 2002. This is also confirmed by the Holmes Report wherein the preliminary results were provided Defendants in 2002 and showed a higher risk of birth defects from Depakote use than other AEDs.

Because Dr. Oakley's opinion that Depakote is the most dangerous anticonvulsant drug is a present sense impression and he offers no opinion that it was the most dangerous anticonvulsant in 2002, it is irrelevant to the facts of this case. Dr. Oakley also fails to point to any supporting medical literature upon which he relied in arriving at this conclusion. Also, when read in the context of his Report, the statement seems directed at Depakote's dangers in causing spina bifida, a birth defect Z.H. does not suffer from. In light of the above, the Court grants Defendants Motion because Dr. Oakley's opinion is not relevant to what was known of the dangers of Depakote in 2002; it offers no reliable basis for support of the statement and is irrelevant to the facts in this case. This ruling is consistent with the Southern District of Illinois decision in *D.W.K. v. Abbott Laboratories*, No. 14CV847 2015 WL 4775868, (Feb. 13, 2015) wherein the court excluded Dr. Oakley's same opinion testimony because it did not provide a sufficient basis for the court to determine its reliability.

Lastly, Dr. Oakley's opinion that Depakote is among the top three teratogens must also be excluded because its relevance to the case as background information for the jury to comprehend the devastating effects of Depakote is outweighed by its prejudicial value. Its relevance is also questionable considering that it is a present sense conclusion by Dr. Oakley and does not relate to what was known in 2002. Lastly, Dr. Oakley offers no evidentiary basis for the conclusion other than it is based on his experience. However, it is a statement placing a numerical ranking on Depakote as among the top three teratogens, yet there is no supporting medical evidence upon which he bases this conclusion. Because he places a numerical ranking on its teratogenicity, in order to be admissible the Court believes it must be supported by some data. Because Dr. Oakley does not supply the basis, the Court finds it cannot examine its

reliability and therefore, excludes it as unreliable, irrelevant and its prejudicial value outweighs its probative value.

IT IS SO ORDERED.

s/ Christopher A. Boyko
CHRISTOPHER A. BOYKO
United States District Judge

Dated: January 13, 2017