Control 150815005

IN THE COURT OF COMMON PLEAS
OF PHILADELPHIA COUNTY

CIVIL TRIAL DIVISION

ROBERT PORTER AND KATHERINE PORTER, INDIVIDUALLY, AND AS PARENTS AND NATURAL GUARDIANS OF ROBERT T. "BO" PORTER, A MINOR:	:	SEPTEMBER TERM, 2007 NO. 03275
Plaintiffs	:	
vs.	:	
SMITHKLINE BEECHAM CORPORATION, and PFIZER, INC.,	:	CONTROL NO.
Defendants	:	

MEMORANDUM OPINION

Plaintiff filed suit against Pfizer alleging that the ingestion of Zoloft by Katherine Porter during her pregnancy caused Minor plaintiff to be born with the serious birth defect omphalocele. On August 14, 2015 Defendant filed Frye Motions seeking to preclude the Expert Testimony of Dr. Freedman and Dr. Cabrera.[1] On august 26, 2015 Plaintiff filed a response. A two day hearing was held on September 16 and September 17, 2015. At that hearing the court heard from Dr. Freeman and Dr. Kimmel and received into evidence numerous documents including the written report of Dr. Cabrera.[2]

[1] A Third Frye motion as to Dr. Healy was withdrawn in Court upon the representation that he would not be called at trial

[2] Plaintiff bears the burden of proof that their proposed witness may testify. *Grady v. Frito-Lay*, 576 Pa. 546 839 A.2d 1038 (2003).

Minor Plaintiff Bo Porter was born with a giant omphalocele. A giant omphalocele is an abdominal wall birth defect in which an infant's intestine or other abdominal organs are outside of the body. During pregnancy Mrs. Porter took the anti-depressants Paxil and Zoloft for depression. Both these drugs are classified as SSRIs. Plaintiff proposes to call Dr. Freeman and Dr. Cabrera on the question of General and Specific causation The defendants claim the testimony of these experts fail to meet the consensus methodological requirements for the admissibility of scientific opinion testimony and should be precluded at trial.

The *Frye* test, adopted into Pennsylvania in the case of *Commonwealth v. Topa*,[3] has been clearly explained by the Supreme Court of Pennsylvania in *Grady v. Frito-Lay*,[4] and the Superior Court in *Trach v. Fellin*.[5]

The *Frye*[6] test is an evidentiary standard for determining whether the methodology employed by a proposed witness is considered scientific by others in a relevant scientific field. The *Frye* standard to determine whether scientific expert testimony will "help" the jury[7] is not applicable to all expert testimony. Although the proponent of evidence bears the burden of proving admissibility,[8] this admissibility standard applies only when "novel science" is proposed.[9] The *Frye* standard does not involve any Judicial finding of the accuracy of the ultimate opinion. It is only the methodology employed which is to be evaluated, not the conclusions reached.[10] The initial formulation of the *Frye* Court continues to be instructive:

> "Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential

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force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field in which it belongs."

The Pennsylvania *Frye* test for admissibility does not require this Court to independently determine the Judge's understanding of the science of epidemiology as applied to the facts of Bo Porter's birth defects. Unlike Courts which have adopted the *Daubert* [11] standard, this Court may not independently analyze or evaluate peer reviewed journal articles or other scientific material except as they relate to the methodology employed by the proposed expert witnesses in reaching conclusions. Thus as detailed by Justice Cappy in *Grady v. Frito-Lay*, the *Frye* test is comparable to other common Judicial functions.

Writing for the Court in *Grady v. Frito-Lay* Justice Cappy said:

> "One of the primary reasons we embraced the *Frye* test in *Topa* was its assurance that Judges would be guided by scientists when assessing the reliability of a scientific method."
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> "We believe now, as we did then, that requiring judges to pay deference to the conclusions of those who are in the best position to evaluate the merits of scientific theory and technique when ruling on the admissibility of scientific proof, as the *Frye* rule requires, is the better way of insuring that only reliable expert scientific evidence is admitted at trial."
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> "We also believe that the *Frye* test, which is premised on a rule-that of "general acceptance" –is more likely to yield uniform, objective, and predictable results among the courts, than is the application of the *Daubert* standard, which calls for a balancing of several factors. Moreover, the decisions of individual judges, whose backgrounds in science may vary widely, will be similarly guided by the consensus that exists in the scientific community on such matters."

Although both the *Frye* and *Daubert* standards relate to methodology and not conclusions, the differences are dramatic. Under the *Frye* standard this Court is required to

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perform fact finding only as to the synchronicity of proposed expert testimony with acceptable scientific investigation.[12] Pursuant to the *Daubert* standard scientific consensus does not per se permit opinion testimony. A scientific consensus that proper methodology was employed is only one of several nonexclusive criteria for determining whether the expert testimony will "assist" the jury. The *Daubert* standard requires the court to make an independent judicial scientific judgment whether the methodology is scientifically sound even if a scientific consensus of propriety exists. Judges with different understanding of scientific processes can make different rulings on the same opinion subject only to an abuse of discretion appellate review standard.[13] Pursuant to the *Frye* standard the Court need only determine whether an appropriate scientific community considers the methodology used to reach an opinion is scientifically sound. To be permissable for jury evaluation the methodology employed by the expert must be scientifically acceptable.[14] The Frye test recognizes that proper scientific methodology is not dependent upon the perspective of the court analyzing science or the jurisdiction involved in a case.

Real scientific knowledge is not and never has been static. Even using proper methodology scientists routinely disagree and even reach different conclusions while accepting the same underlying data as accurate. Through the interaction of differing but scientifically appropriate conclusions derived from commonly accepted data, knowledge progresses. Likewise different scientific disciplines may properly opine on the same questions using different but proper methodologies.

Thus, the trial court faces two primary questions in any *Frye* analysis:

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[12] Like preliminary rulings as to authenticity (Pa. R.E. 901 et. seq. or personal knowledge (Pa R.E. 602) the Court may not preclude opinion testimony because the Judge disagrees with the testimony. "Judges in jury trials should not exclude expert testimony simply because they disagree with the conclusions of the expert." *Betz v. Pneumo Abex, LLC,* 615 Pa. 504, 542-43, 44 A.3d 27, 51 (2012).

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1. Is the data and other underlying information relied upon the type of data properly relied upon in a scientific discipline appropriate to the question presented for jury determination? And;
2. Was this proper data analyzed in accord with a scientific discipline appropriate to the question presented for jury determination?

The Plaintiff seeks to have Robert M. Cabrera, Ph.D. to testify as to general and specific causation of the birth defects of Bo Porter. Within Dr. Cabrera's forty-seven page report, are five pages devoted to his training, education, and experience and twelve pages to animal studies concerning SSRIs and birth defects. The last animal study report referenced is from 1986, twenty-nine years old. Animal studies can be instructive in determining the teratogenicity of a pharmaceutical and indeed may possibly be the basis for a valid medical opinion in the absence of no human studies. However, animal studies are of limited utility where a significant body of studies in human populations exists in the literature. Dr. Cabrera does not acknowledge these limitations.

In his opinion concerning teratogencicity causation Dr. Cabrera relies on the Louik study, as did Dr. Freeman. He claims the Alwan and Freehus studies support this conclusion. His analysis suffers from many of the same methodological defect as Dr. Freeman's analysis.

Dr. Cabrera finds that the studies show that SSRIs significantly increase the risk of birth defects in human studies and opines that SSRIs are teratogenic. However, no where in his report does he specifically analyze SSRIs results excluding the known teratogen Paxil which has been identified as significantly different in effect from Zoloft and the other SSRIs.

Dr. Cabrera opines that the mechanism of action resulting in birth defects is the "alteration of serotonin signaling by sertraline, can impact embryonic development resulting in several different congenital malformations."

This opinion is nothing but speculation without support since Dr. Cabrera has no information as to the baseline level of serotonin causing signaling or the changed level of serotonin caused by Paxil, Zoloft or any other SSRI.

Additionally, Dr Cabrera needs a dose response analysis to draw a valid scientific conclusion that a medication causes a specific biological mechanism regards a base line dosage and the knowledge of the altered dose either of which is referred to by Dr. Cabrera.

There is no adequate discussion of the differences between Paxil and Zoloft.

For these reasons and the problems identified in the Memorandum Opinion granting the Frye motion as to Dr. Freeman, Dr. Cabrera is precluded from testifying.

BY THE COURT

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DATE MARK I. BERNSTEIN, J.

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1. Is the data and other underlying information relied upon the type of data properly relied upon in a scientific discipline appropriate to the question presented for jury determination? And;
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In this case the general causation methodology used by Dr. Freeman to conclude that Zoloft taken during pregnancy can be the cause of omphalocele is challenged as not scientifically proper. The defense also challenges Dr. Freeman's methodology used to conclude that Zoloft was the specific cause of Bo Porter's omphalocele. Plaintiff offers Dr. Freeman as an expert in epidemiology, forensic epidemiology, and medical science.

Dr. Freeman has an MD. From Sweden and a PhD. in Public Health. Dr. Freeman has taught for 10 years in the field of "Forensic Epidemiology." Dr. Freeman testified that "Forensic Epidemiology" is the use of epidemiology in a legal setting for evaluating causation.

THE COURT: Would you define forensic epidemiology for me, please?
THE WITNESS: Yes, it is the use of epidemiology in a legal setting for specifically the evaluation of causation. It differs somewhat from general epidemiology in that it has to do with evaluation of specific facts about a case and then take into account those facts in assessing what the epidemiologic evidence may apply or may not apply. [15]

Dr. Freeman testified that the methods used in the fields of Epidemiology and Forensic Epidemiology are identical but the applications are somewhat different.

THE COURT: Is there a difference between epidemiology for forensic purposes and epidemiology for any other purpose?

[15] Freeman, Hearing Transcript September 16. At Page 39: 2-4

THE WITNESS: The methods are identical between the two. The applications are somewhat different. [16]

Nonetheless, he believes improper epidemiological methodology can be proper forensic epidemiology methodology. In this conclusion he is wrong. There is no scientific discipline of "forensic." The term forensic is an adjective which describes the courtroom use of a scientific discipline such as epidemiology or teratology. There is no science of "forensic epidemiology" which is not totally dependent upon the methodology of the science of epidemiology.

Dr. Freeman does not describe any independent scientific method which governs "forensic"[17] epidemiology. However, he definitively believes a "reasonable degree of scientific certainty" is different in the scientific field of epidemiology from the "field" of forensic epidemiology. Dr. Freeman testified that the legal standard of "more probable than not' is his definition of "reasonable scientific certainty" and that this standard varies by jurisdiction.

THE COURT: Is that your standard or do you have a different standard?
THE WITNESS: Standards varies by jurisdiction, Your Honor.
THE COURT: By jurisdiction? What's a jurisdiction?
THE WITNESS: In my experience, different states have different standards for evidence in toxic tort.
THE COURT: So you're talking about a legal standard?
THE WITNESS: Yes.
THE COURT: So this is going back to the forensic part of forensic epidemiology?
THE WITNESS: That's correct.
THE COURT: Well, do you have a scientific standard or simply a jurisdictionally-based standard?
THE WITNESS: It would depend on the opinion I was being asked to give.
THE COURT: I'm really not following. Is there a scientific standard that's the same across state lines?
THE WITNESS: No, it is not.[18]

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[16] Id. at Line 15-17
[17] Black's Law Dictionary defines "forensic" as: "Belonging to courts of justice".
[18] Freeman, Hearing Transcript September 16. Page 179:1 – 180: 8.

Although Dr. Freeman believes the appropriate standard for a scientific conclusion in the field of "forensic" epidemiology depends on "jurisdiction," only a legal standard depends on jurisdiction and proper scientific methodology and conclusions do not vary whether testified to on the Pennsylvania side or the New Jersey side of the Benjamin Franklin Bridge.[19]

Proper epidemiological methodology begins with published study results which demonstrate an association between a drug and an unfortunate effect. Once an association has been found, a judgement as whether a real causal relationship between exposure to a drug and a particular birth defect really exists must be made. This judgment requires a critical analysis of the relevant literature applying proper epidemiologic principles and methods. It must be determined whether the observed results are due to a real association or merely the result of chance. Appropriate scientific studies must be analyzed for the possibility that the apparent associations were the result of chance, confounding or bias. It must also be considered whether the results have been replicated.

Proper methodology further requires that one not fall victim to the "Class Effect Fallacy" or the "Lumping Fallacy." A class effect cannot be assumed. The causation conclusion must be drug specific. Different birth defects should not be grouped together unless they a part of the same body system, share a common pathogenesis or there is a specific valid justification or necessity for an association[20] and chance, bias, and confounding have been eliminated. Even then, when generally accepted proper epidemiological methodology has found causation the Bradford-Hill Criteria must be considered. As the Bradford-Hill factors are properly considered, causality becomes a matter of the epidemiologist's professional judgment.

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[19] Indeed proper scientific epidemiological methodology is the same even in Romania

[20] See *Trach v. Fellin*, 2033 Pa. Super 53, 817 A.2d 1102 (2003).

Dr. Freeman claims to have based his analysis upon the same publicly available peer reviewed observational studies reported in the medical literature as that used by defense experts and defendant Pfizer itself in internal documents. In this he starts in accord with proper methodology. The parties agree on the relevant observational studies and to this extent Dr. Freeman's methodology is proper.[21]

However, Dr. Freeman's analysis improperly conflates three types of data: Zoloft and omphalocele, SSRI's generally and omphalocele, and SSRI's and gastrointestinal and abdominal malformations

Dr. Freeman correctly concedes that the studies reveal precious little specific data on Zoloft and omphalocele.[22] Dr. Freeman effectively solely relies on the Louik study as evidence of causation between Zoloft and the birth defect. The Louik study is the only study to report a statistically significant association between Zoloft and omphalocele. Reliance on this one study is questionable because of its limitations. Louik's confidence interval which ranges between 1.6 and 20.7 is exceptionally broad. Equally significant is the lack of power concerning the omphalocele results. The Louik study had only 3 exposed subjects who developed omphaocele thus limiting its statistical power. Studies that rely on a very small number of cases can present a random statistically unstable clustering pattern that may not replicate the reality of a larger population. The Louik authors were unable to rule out confounding or chance. The results have never been replicated concerning omphalocele. Dr. Freeman's testimony does not explain, or seemingly even consider these serious limitations.

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[21] The gold standard study is the randomized control trial in which the outcome of two comparable populations are identified and one is exposed to the medication. All agree that this kind of study cannot be ethically done concerning Zoloft in pregnant women. Thus, the only studies from which conclusions may be dawn are observational studies.

[22] Indeed Dr. Freeman has identified only three published studies which even find any association.

Dr. Freeman apparently exclusively relied on the study authors to take appropriate measures to control the issue of chance.

THE COURT: Before we move on bias, chance and confounding, was that considered in any way other than reading the studies and concluding that they have taken them all into account?
THE WITNESS: No, not exactly,Your Honor...[23]

While Dr. Freeman relies on this improperly broad assumption the Louik authors themselves expressed concern that they cannot distinguish true associations from random elevations of risk. The Louik authors were unable to rule out the possibility of chance:

> "The previously unreported associations we identified warrant particularly cautious interpretation. In the absence of preexisting hypotheses and the presence of multiple comparisons, distinguishing random variation from true elevations in risk is difficult. Despite the large size of our study overall, we had limited numbers to evaluate associations between rare outcomes and rare exposures. We included results based on small numbers of exposed subjects in order to allow other researchers to compare their observations with ours, but we caution that these estimates should not be interpreted as strong evidence of increased risks."[24]

Dr. Freeman ignores the issues specifically pointed out by the authors.

In addition to proper analysis of the appropriate literature, generally accepted methodology requires that the epidemiologist consider for the problem of confounding by indication. Women who are depressed and take SSRIs have been more likely to smoke, be older, have less education, have poor nutrition, use other drugs, and have chronic diseases such as diabetes and hypertension, than women who do not use SSRIs. These factors have been linked to an increased risk of birth defects.[25] Dr. Freeman does not properly analyze confounding.

Q You described looking at the methodological consideration in each of the studies cited in your report, right?
A With regard to confounding and bias and the role of chance; that is correct.

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[23] Freeman, Hearing Transcript September 16 at Page 76: 23 – 77: 4.
[24] Louik C. First Trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. N Engl J Med 2007, 356 (26) 2675-83 at 2680.
[25] *See, e.g.*, Huybrechts, K Antidepressant Use in Pregnancy and the Risk of Cardiac Defects. N Engl J Med 2014 370 2397-2407 at 2402-03.

Q By the way, that word "confounding" doesn't appear anywhere in your report, does it?
A I think you actually stated earlier that it's in a footnote in my report. But no, I cited specifically to the guidelines in the reference manual which is where that is discussed mostly.
Q My question is very simple, other than in a footnote because it is in the title of a study there, the word "confounding" appears nowhere in the 13 pages of your report, does it?
A I've already testified to that. I agreed with that.[26]

In his report Dr. Freeman cites Jimenes-Solem, Furu, and Huybrechts as three studies that also found statistically significant increased risk of congenital malformation associated with SSRI exposure.[27] All three of these studies acknowledged the problem of confounding, and discussed the problem in their analysis. Dr. Freeman does not address the authors conclusions about confounding.

Generally accepted methodology considers statistically significant replication of study results in different populations because apparent associations may reflect flaws in methodology. Dr. Freeman claims the Alwan and Reefhuis studies demonstrate replication. However, the population Alwan studied is only a subset of the Reefhuis population and therefore they are effectively the same. More significantly neither Reefhuis nor Alwan reported statistically significant associations between Zoloft and omphalocele. While non-significant results can be of some use, despite a multitude of subsequent studies which isolated omphalocele, there is no study which replicates or supports Dr. Freeman's conclusions.

Without significant independent scientific justification it is contrary to generally accepted methodology to assume the existence of a class effect. Dr. Freeman lumps all SSRI drug results together and assums a class effect.

Q Why did you look at other SSRIs and omphalocele, why did you look at the class of SSRIs?
A Other researchers have examined SSRIs as a class, they have considered them as a class.

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[26] Freeman Hearing Transcript. September 16, 2015 Page 172:11-173:2.
[27] Freeman Report Pages 8-9

That's one really important point. Another important point is I was unable to find any evidence that SSRIs, any convincing evidence that SSRIs necessarily have to be broken apart.[28]

Dr. Freeman relies on the Reefhuis Study. Yet Dr. Freeman concedes that the Reefhuis authors conclude that SSRI's should be looked at independantly.

Q Reefhuis, what does Reefhuis say about them looking at it as a class?
A Reefhuis says you should look at them individually because her results were different in between the drugs. I don't want to have a debate with someone who wrote a paper, but I don't necessarily agree with that. I think there's some issues with that.[29]

Dr. Freeman adopts the Class Effect fallacy as properly scientific. SSRI"s cannot be lumped together for all purposes. In fact the studies Dr. Freeman purports to rely on, definitively refute the class effect. These Studies have demonstrated the teratogenic effects of one SSRI, Paxil, without finding the same effect in other pharmaceuticals in the SSRI class. The Reefhuis study did not confirm links between Zoloft, the most often used SSRI, and omphalocele. Reefhuis however, did confirm the links between Paxil and omphalocele and between Prozac and omphalocele. Other studies specifically looked at omphaloce and SSRIs and could isolate no association.

Generally accepted causation criteria must be based on the data applicable to the specific birth defect at issue. Dr. Freeman improperly lumps together disparate birth defects.[30]

> "Grouping of defects—Human birth defects comprise many different developmental systems and structures, reflecting manifold differences in underlying pathogenesis and etiologies. Typically teratogenic exposures do not increase risks of all birth defects. Even specific groups of defects, e.g., heart defects, are heterogeneous in anatomy, development, and epidemiologic factors. Combining different birth defect types for analyses is a valid approach only if the defects being lumped have an underlying pathogenesis that is similar.'[31]

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[28] Freeman Hearing Transcript. September 16, 2015 Page 62:5-13. Dr. Freeman ignores the studies which demonstrate a much more likely causative effect between Paxil and birth defects
[29] Freeman Hearing Transcript. September 16, 2015 Page 62:24-63:6.
[30] Lumping Fallacy.
[31] Alwan S., Teratology Primer 2nd Edition (2010), at Page 11-31

Dr. Freeman, improperly lumps the omphalocele birth defect with digestive system defects and assumes medical literature concerning digestive system birth defects support his opinion. However, omphalocele is not a digestive system birth defect.[32]

Q When you collect data, Doctor, and you include a figure -- strike that. Doctor, when you are trying to analyze whether Zoloft causes omphalocele and you include a figure from a study from a category that does not include omphalocele and ignore the one that does, is that good scientific methodology?
A No, it's not good or bad scientific methodology. I mean, certainly errors are made –[33]

Q You told us this morning your methodology included looking at the studies of methodologies and relying on them, correct?
A Yes.
Q The EUROCAT is used in studies like Jimenez has findings for abdominal wall and had findings for digestive system, correct?
A Yes.
Q You put in your report the Jimenez-Solem findings for digestive system, correct?
A Yes.
Q You did not put a finding for abdominal wall which is the category that includes omphalocele, correct?
A That's correct.
Q That was a mistake, wasn't it?
A I think looking back at it and you asked me the question, yeah --
THE COURT: Wait. He's asking you one simple question, was that a mistake?
THE WITNESS: I would say on the balance of probability, it probably was. [34]

Dr. Freemen agrees that he must, and claims he has, applied the Bradford Hill Criteria to support his opinion. However, the starting procedure of any Bradford-Hill analysis is "an association between two variables" that is "perfectly clear-cut and beyond what we would care to attribute to the play of chance."[35] Dr. Freeman testified that generally accepted methodology requires a determination, first, that there's evidence of an association and, second, whether chance, bias and confounding have been accounted for, before application of the Bradford-Hill

[32] The EUROCAT classification system which groups birth defects classifies omphalocele as an abdominal wall defect.
[33] Freeman, Hearing Transcript September 16. At Page 145: 14-22.
[34] Freeman, Hearing Transcript September 16. At Page 156: 17 – 157: 15.
[35] Bradford-Hill (1965), 295.

criteria.[36] Because no such association has been properly demonstrated, the Bradford Hill criteria could not have been properly applied.

Dr. Freeman opines that it is biologically plausible that Zoloft can cause an infant to be born with omphalocele and lists a number of factors in support. However, Dr. Freeman does not explain why or how any of these factors support his opinion on biological plausiblity.

Dr. Freeman opines specifically that Bo Porter's giant omphalocele birth defect was caused by exposure to Zoloft in utero. However, Dr. Freeman is not a medical doctor and does not have a clinical medical degree.

Q You're not a medical doctor, are you, sir?
A I have a doctor of medicine degree. Technically that makes me a medical doctor. It is not an M.D. degree. It is not a clinical medical degree. It is more akin to a Ph.D in medicine.

THE COURT: I want to go to the answer to that question: Do you believe that you're permitted to treat people in Oregon?
THE WITNESS: I am permitted to treat people in Oregon, but under my original license as a chiropractor, Your Honor.
BY MR. HOOPER:
Q Are you allowed to provide medical treatment to people in Oregon?
A No, I'm not a licensed medical doctor.[37]

Medical Doctors may be permitted to give specific causation opinions when they base their opinion on their experience and clinical judgment. A physician must use clinical judgment and expertise to determine the possible cause of birth defects. This may be vital for the physician to properly advise their patients who may wish to consider another pregnancy. There is nothing novel or improper with clinical judgment testimony.[38] Dr. Freeman does not use clinical judgment, he relies upon "forensic" epidemiology to opine on specific causation.[39]

THE COURT: So, I understand your testimony is you agree that specific causation is beyond the domain of epidemiology, right?

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[36] Freeman, Hearing Transcript September 16. At Page 41: 22 – 42: 7.
[37] Freeman, Hearing Transcript September 16. At Page 30:6 – 31: 11.
[38] See *Haney v. Panonelli*, Pa. Super. 261, 830 A.2d 978 (2003).
[39] Freeman, Hearing Transcript September 16. At Page 93: 8 – 94: 10.

THE WITNESS: Epidemiologic studies.
THE COURT: Specific causation is beyond the domain of the science of epidemiology. Do you agree with that?
THE WITNESS: I do.
THE COURT: Okay. But it is not beyond the domain of forensic epidemiology; is that right?
THE WITNESS: That is correct.
THE COURT: Were your specific causation opinions in your capacity as an expert in epidemiology?
THE WITNESS: No, I would say that they came from my work and the science in the field of forensic epidemiology, which is directed at specific causation based on the epidemiologic conclusions from my general causation analysis.
THE COURT: And the science of epidemiology is not concerned or not capable of discussing specific causation, but forensic epidemiology is. Is that correct or incorrect?
THE WITNESS: It's not entirely correct.
THE COURT: What aspect is not correct?
THE WITNESS: Epidemiologic studies is used to evaluate causation, and it says that later in this chapter, two pages later it says, nonetheless epidemiologic studies are used to evaluate individual causation.
THE COURT: Okay, and when they are so used, that's forensic epidemiology.
THE WITNESS: Precisely.

The temporal relationship between the exposure and disease is also a factor which must be considered in assessing specific causation. For an exposure to be the cause of a disease the exposure must have occurred prior to the disease.[40] Dr. Freeman fails to address the temporal failure of exposure between Mrs. Porter's use of Zoloft and minor plaintiff's giant omphalocele. A Giant Omphalocele is the result of an incomplete folding of the abdominal wall during the third to fifth weeks of pregnancy. During the third to fifth weeks of her pregnancy Mrs. Porter was taking Peroxetine (a generic version of the known teratogene Paxil). Mrs. Porter did not begin taking Zoloft until her seventh week of pregnancy. While Dr. Freeman concedes this timing failure is an issue, he does not form any opinion of his own but instead claims to defer to other experts offering opinions which have not been revealed and therefore necessarily not subject to cross-examination.

[40] "Did the cart come before the horse"? Freeman, Hearing Transcript September 16. At Page 83: 24-25.

A. I know that there is a question as to timing, not temporality, but timing of when the drug was taken and when the condition may occur, which I would absolutely defer to other experts on because I'm not a teratologist or embryologist.[41]

Q You were asked, of course, to address specific causation in this case, right?
A I was.
Q You certainly wanted to make sure that she was on the medication of interest at the appropriate time in the development, didn't you?
A Well, I made the assumption that that is the case based on representations of other experts.
Q You relied on other experts for the developmental timing of her exposure; is that right.
A And when she was taking the drugs, that's correct.
Q Are you aware of Dr. Healy's opinion in this case that she began taking Zoloft about seven weeks or later into her pregnancy?
A Yes.
Q You saw that?
A Yes.
Q Do you have any reason to disagree with it?
A I do not.
Q Do you rely on it for that?
A I have not made a specific determination of that. I have not gone back and looked at any records. My assumptions and my analysis are all based on the representation that this lady was exposed to Zoloft.
THE COURT: Well, did you rely on another expert's opinion that she was exposed to Zoloft or taking Zoloft at seven weeks or did you not rely on it?
THE WITNESS: I did.[42]

Clinical differential diagnosis is a generally accepted methodology."[43] Dr. Freeman is not a clinician and does not profess to perform a clinical differential diagnosis of cause. Dr. Freeman has failed to rule out other potential causes. Dr. Freeman fails to properly rule out genetic causes. Dr. Freeman opines that 45-49% of omphalocele cases are due to genetic factors and that the remaining 50-55% of cases are due to non-genetic factors. Dr. Freeman relies on Bo Porter's genetic testing which did not identify a specific genetic cause for his injury. However,

[41] Freeman, Hearing Transcript September 16. At Page 70: 4-10.
[42] Freeman, Hearing Transcript September 16. At Page 205:10- 206:19.
[43] In *Kendal v. Wyeth, Inc.*,1154 EDA 2010, 2012 WL 112609 (Pa. Super. Ct. 2012). *Snizavich v. Rohm Haas,* 2013 Pa. Super 315, 83 A.2d 191 Pa Super 2013.

minor plaintiff has not been tested for all known genetic causes. Unknown genetic causes of course cannot yet be tested. Dr. Freeman has made no analysis at all, only unwarranted assumptions.

Q Let me ask you right there, what are the known genetic causes of omphalocele?

A I cannot tell you the entirety of those causes. That is outside of my normal scope of what I would do. There were just no genetic abnormalities that were identified when he was tested. That's all I can say.
Q Genetic causes of birth defects are discovered over time, correct?
A Sure.
Q At any point in time if the specific genetic problem that can be identified on a test has not yet been linked to the defect, then there is no test that will detect it, is there?
A I agree.
Q It is possible that there will be genetic causes of omphalocele discovered next year, five years from now or ten years from now, true?
A Certainly.
Q And if Bo Porter were tested genetically today, we would not be looking for any of those causes because they're not yet discovered, are they?
A Sure.
Q Would you agree that there are causes of omphalocele that are not yet known to medical science?
A I do agree with that.
Q What percentage of the genetically caused omphalocele can be detected by testingtoday?
A I don't think I can answer that as I sit here.
Q You don't know?
A I cannot answer that, so I don't know the specific answer to that.
THE COURT: What percentage of omphalocele is caused by a known genetic disorder?
THE WITNESS: In my report I refer to 45 to 49 percent.
THE COURT: So 45 percent of the children born with this birth defect, it's caused by a genetic disorder which can be identified. Is that your testimony?
THE WITNESS: No, my testimony would be that 45 to 49 percent of kids with omphalocele have a genetic – a chromosomal abnormality. Whether or not it was causal, that I cannot answer.
THE COURT: What percentage of babies with this birth defect do we know has been caused by a genetic defect?
THE WITNESS: I don't know that I can answer that more specifically than to say there's abnormality in 45 to 49 percent.
THE COURT: Do we know whether two percent of the children born with this birth defect it was caused by an abnormality?
THE WITNESS: Your Honor, I'd have to defer to somebody who was more familiar with that literature.[44]

[44] Freeman, Hearing Transcript September 16. At Page 192:25 – 196:15.

Dr. Freeman does not discuss and fails to rule out maternal risk factors such as age, obesity, cigarette smoking, alcohol, maternal stress, and family history. Dr. Freeman fails to exclude Paxil (Peroxetine) as a risk factor.

Q Do you have any discussion in your report of Mrs. Porter's age?
A I do not.
Q Do you have any discussion in your report of age as a risk factor for omphalocele?
A I don't recall if I addressed that. I don't think I did.
Q You have no discussion in your report of Mrs. Porter's weight, do you?
A No, that's correct.

Q Obesity is a risk factor for omphalocele, isn't it?
A It's a confounder.

Q You don't address any other medical conditions that Mrs. Porter may have had in this section of your report, do you?
A No.
Q You don't address whether or not Mrs. Porter took folic acid supplements, do you?
A I do not.
Q You don't address whether anything about the dosage of Zoloft she used, do you?
A I do not.
Q You don't address anything about the dosage of Paxil or Celexa that she may have taken, do you?
A I do not.[45]

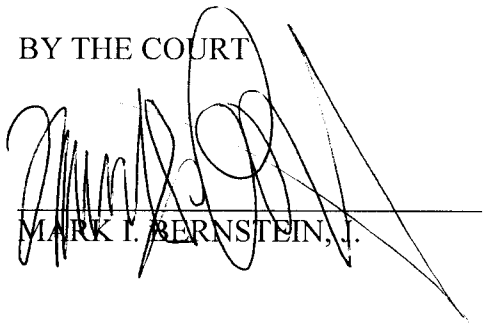
Dr. Freeman's failure to analyze, discuss, and exclude other possible causes departs from generally accepted methodology.

Defendants claim that plaintiff's expert Dr. Freeman utilizes an improper methodology which requires preclusion. For the foregoing reasons this Court concludes that the methodology

[45] Freeman, Hearing Transcript September 16. At Page 198:25 – 202:15.

is improper. The *Frye* motion as to general and specific causation is granted and Plaintiff's causation expert Dr. Freeman is not permitted to testify at trial.

BY THE COURT



12/9/15
DATE

MARK I. BERNSTEIN, J.