IN THE SUPERIOR COURT OF THE STATE OF DELAWARE
IN AND FOR NEW CASTLE COUNTY

WENDOLYN TUMLINSON, JAKE TUMLINSON, JILLVEH ONTIVEROS and PARIS ONTIVEROS, by her natural mother and next friend JILLVEH ONTIVEROS,	)	Supreme Court No. 672, 2012D
Plaintiffs,	)	Superior Court New Castle County
v.	)	C.A. No.: 08C-07-106 FSS
ADVANCED MICRO DEVICES, INC.,	)	
Defendant.	)	

Submitted: August 16, 2013
Decided: October 15, 2013

On Remand to Decide Admissibility of Epidemiologist's Opinion under D.R.E. 702

SILVERMAN, J.

Plaintiffs allege that chemical exposure at Defendant's semiconductor factories caused birth defects in two of their children. Jake Tumlinson was born in 1987 and Paris Ontiveros was born in 1994, 21 and 14 years, respectively, before this lawsuit was filed. Jake was born with anal atresia and stenosis, neurogenic bladder, renal agenesis/hypoplasia, imperforate anus, and colo-vesicular fistula. These birth defects, in combination, are referred to as VATER association. Paris was born with pulmonic stenosis, congenital pulmonary valve atresia, ventricular septal defect, right pulmonary hypoplasia, lower limb reduction defects and *situs inversus* with dextrocardia, which, only for expedience, the court will henceforth refer to collectively as *situs inversus*. Paris's congenital heart problems are an important fact for this litigation's purposes. All these conditions are rare and, generally, their origins are unknown.

Previously, this court held that Texas substantive law applies here. Applying Texas's heightened epidemiology evidence threshold, this court granted Defendant's motion to exclude the opinions of Plaintiffs' expert, Dr. Linda Frazier. The Supreme Court affirmed the choice of law, but remanded for further inquiry as to the admissibility of Dr. Frazier's opinion under Delaware procedural law, specifically D.R.E. 702. This court was instructed to determine the "expert

testimony's reliability under Delaware law" to facilitate the "debate over what role sufficiency plays in admissibility."[1]

To prevail in a toxic tort case, plaintiff must show both general and specific causation. General causation concerns whether a particular substance causes anyone the specific harm alleged. Here, Plaintiffs must first prove that the chemicals to which Plaintiffs' parents were exposed at work can cause Plaintiffs' birth defects, including VATER association and *situs inversus*. Specific causation asks if the substance(s) actually caused Plaintiffs' injuries.[2] Dr. Frazier opines about general and specific causation and now the court is considering those opinions' reliability. Reliability is one factor for admissibility under D.R.E. 702. Later in litigation when the merits of the case are addressed, the sufficiency of the admissible evidence to meet Plaintiffs' burden comes into play.

Dr. Frazier layers assumptions and assertions without adequately explaining her sources or reasoning, but assuring the court that she has "faithfully followed the requirements of good science." Dr. Frazier's hypothesis, developed for this case, lacks the specificity of chemicals, exposure, or doses necessary to be testible. The opinion has never been peer reviewed. Dr. Frazier pieces together epidemiology, animal studies, *in vivo* studies, and *in vitro* studies that examine

[1] *Tumlinson v. Advanced Micro Devices, Inc.*, 2013 WL 4399144 (Del. Aug. 16, 2013).
[2] *King v. Burlington Northern Santa Fe Railway Company*, 277 Neb. 203 (2009).

tangential exposures and harms without any explanation as to the relative weight each study deserves. She applies established methods, like dose-response, in novel ways, again without necessary explanation. Finally, despite admitting these birth defects occur in unexposed people, Dr. Frazier broadly eliminates any cause other than the parents' exposure. As explained below, the analytical gaps between the data and the proferred opinions are simply too many and too wide.

I.

Expert opinion evidence under Delaware law is governed by Delaware Rule of Evidence 702, which provides:

> If scientific, technical or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training or education may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Delaware uses *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[3] to apply Rule 702.[4]

Daubert requires the trial judge to act as a "gatekeeper," determining whether the proffered evidence is both "relevant" and "reliable."[5] Under *Daubert*, "relevant" means the evidence relates to an issue and it will aid the fact finder. As

[3] *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993).
[4] *M.G. Bancorporation, Inc. v. Le Beau*, 737 A.2d 513, 521-522 (Del.1999).
[5] *Daubert*, 509 U.S. at 597.

mentioned above, the court already decided Dr. Frazier's opinions were irrelevant as the jury could not take them as proving under Texas law what they were meant to prove - causation.

"Reliable" means "testimony must be supported by appropriate validation—i.e., 'good grounds,' based on what is known."[6] In other words, an "inference or assertion must be derived by the scientific method."[7] *Daubert's* non-exclusive criteria for determining reliability include: (1) whether the expert's theory has or can be tested; (2) whether the theory has been subject to peer review; (3) the known or potential error rate associated with the theory; and (4) the extent to which the theory has been generally accepted in the scientific community.[8]

These criteria are applied to both the expert's ultimate opinion as well as foundational sources used in forming the opinion. While no individual criterion is dispositive, peer review and pre-litigation research are principal ways for demonstrating reliability.[9] Where neither can be shown, the expert "must explain precisely how they went about reaching their conclusions and point to some objective source—a learned treatise, the policy statement of a professional association, a published article in a reputable scientific journal or the like—to show that they have

[6] *Id.* at 590.
[7] *Id.*
[8] *Id.* at 593–594.
[9] *Daubert v. Merrell Dow Pharm., Inc.* (*Daubert II*), 43 F.3d 1311, 1319 (9th Cir. 1995).

followed the scientific method, as it is practiced by (at least) a recognized minority of scientists in their field."[10]

The reliability requirement, however, "must not be used as a tool by which the court excludes all questionably reliable evidence. The [...] touchstone [...] is helpfulness to the trier of fact."[11] Judge Quillen, while thoroughly explaining *Daubert*, observed:

> *Daubert* is a two-sided coin. On the one side, it is expansive, rejecting the exclusivity of the "general acceptance" requirement; on the other side, it is restrictive, with a focus on the Trial Judge's responsibility as a gatekeeper on reliability.[12]

The trial judge must guard against speculation, but plaintiffs "do not have to demonstrate to the judge by a preponderance of the evidence that the assessments of their experts are *correct,* they only have to demonstrate by a preponderance of evidence that their opinions are reliable."[13] As one court puts it: "In sum, while the trial court acts as the evidentiary gatekeeper, it is not a goalkeeper."[14]

The party offering the expert has the burden of demonstrating the expert is qualified and her opinion is relevant and reliable.[15] Accordingly, while Defendant's lack of an opposing expert is less common and unhelpful, it is by no

[10] *Id.*
[11] *United States v. Velasquez*, 64 F.3d 844, 850 (3d Cir. 1995) citing *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 744 (3d Cir. 1994).
[12] *Minner v. Am. Mortgage & Guar. Co.,* 791 A.2d 826, 841 (Del. Super. 2000).
[13] *In re Paoli*, 35 F.3d at 744.
[14] *King*, 277 Neb. at 227.
[15] *Bowen v. E.I. DuPont de Nemours & Co., Inc.*, 906 A.2d 787, 795 (Del. 2006).

means dispositive as Plaintiffs repeatedly imply. An opposing expert may help the court focus on weaknesses and otherwise inform the court. But, even if the court would have benefitted here from counter-opinion, its absence does not help Plaintiffs establish in the slightest that Dr. Frazier's opinions are scientifically reliable.

II.

Applying *Daubert* to different scientific fields has produced different analyses and results. Accordingly, non-epidemiological precedent and cases about different environmental toxins and exposure modalities are less helpful, and not dispositive. The admissibility of the epidemiologist's opinion here is a matter of first impression in Delaware. Nevertheless, this reliability analysis starts with briefly surveying Delaware cases applying *Daubert* in other contexts, then briefly surveying other jurisdictions that have specifically considered similar epidemiological opinions. Finally, within that analytical framework, the court will further consider Dr. Frazier's opinions, as the remand expects.

III.

Most Delaware cases applying *Daubert* involve substances with established toxicity.[16] *Long*, for example, holds that where clear scientific evidence demonstrates that ephedra caused cardiac events, proper differential diagnosis alone

[16] *E.g., General Motors Corp. v. Grenier*, 981 A.2d 531 (Del. 2009) (chrysotile, a form of asbestos, causes mesothelioma); *New Haverford Partnership v. Stroot*, 772 A.2d 792 (Del. 2001) (mold causes substantial health issues, including respiratory and cognitive problems); *Long v. Weider Nutritional Group, Inc.*, 2004 WL 1543226 (Del. Super. June 25, 2004) (clear scientific evidence links ephedra to cardiac events).

may prove specific causation and, therefore, epidemiology is unnecessary.[17] In *Grenier*, after an elaborate *Daubert* proceeding like the one in this case, this court properly admitted an expert's opinion that friction chrysotile was probably carcinogenic because it is so similar to unrefined chrysotile, a proven cause of mesothelioma. The expert based his opinion "on his own research, published in a peer-reviewed journal."[18] And, as to that, "his findings were consistent with the findings published in other peer-reviewed papers."[19] *Grenier* also admitted conflicting epidemiological testimony.[20] The established reliability of the, albeit conflicting, testimony in *Grenier* helps demonstrate how tenuous Dr. Frazier's opinions are. In summary as to *Grenier*, this case is far more like *Richardson,*[21] a contrary federal court decision, which was far easier to distinguish in *Grenier* than it is here.[22]

McMullen involved a "Pediatric Condition Falsification" diagnosis - a relatively new, but generally accepted condition. Where no published studies on general causation existed in the medical community, *McMullen* admitted a well structured, defined differential diagnosis where differential diagnosis is the only

[17] *Long*, *supra* note 16.
[18] *Grenier*, 981 A.2d at 536.
[19] *Id.*
[20] *But see Grenier, supra* note 16 (Steele, C.J., dissenting) (testimony rejected because the hypothesis was untested, not subject to peer review, and lacked reliable methodology).
[21] *Richardson by Richardson v. Richardson-Merrell, Inc.*, 857 F.2d 823, 824 (D.C. Cir. 1988)
[22] *Grenier*, 981 A.2d at 538-539.

means of medically diagnosing PCF.[23] Conversely, *Scaife* excluded a differential diagnosis opinion that the prescription medicine Seroquel caused plaintiff's diabetes because it was unsupported by defined methodology or an identified biological mechanism.[24]

Delaware also has cases where no specific toxin is implicated. For example, in *Minner*, a "toxic building" case, an expert attempting to "make a temporal connection between the Plaintiffs' illnesses and the building without a specific toxin identified [...] must demonstrate a deductive scientific process to support her conclusion."[25]

Minner reviewed 12 experts, detailing their opinions and methods. Judge Quillen excluded certain experts entirely and specific portions of the admitted experts' testimonies, separating wheat from chaff. For example, in admitting expert testimony that "volatile organic compounds, dusts and molds in the building" caused Toxic Encephalopathy, *Minner* states that plaintiffs made a "bare showing" that the experts methodology was reliable where a scholarly article "admits that it may be difficult to identify a specific causative agent in the workplace and states chronic solvent exposure can be associated with cognitive changes in an individual."[26] By linking the precise harm with a category of substances, the court was satisfied that the

[23] *State v. McMullen*, 900 A.2d 103 (2006).
[24] *Scaife v. Astrazeneca LP*, 2009 WL 1610575 (Del. Super. June 9, 2009).
[25] *Minner v. Am. Mortgage & Guar. Co.*, 791 A.2d 826, 855 (Del. Super. 2000).
[26] *Id.* at 858.

methodology was sufficient. Conversely, the court excluded opinion that exposure in the building caused Fibromyalgia because the expert "does not follow a logical, scientific, and deductive process to exclude other possible causative factors."[27] In short, as the established scientific proof for causation decreases, an expert's methodology for forming her opinion must be increasingly detailed. Under Delaware precedents alone, none admits an opinion including as many untested extensions of published studies as Dr. Frazier's here.

IV.

Epidemiology is the science of the relationship between human behaviors and patterns, causes, and effects of diseases across the population. "Epidemiology focuses on general causation."[28] Epidemiology observes exposure as related to disease risk and, accordingly, "frequently, plaintiffs find epidemiological studies indispensable in toxic tort cases when direct proof of causation is lacking."[29] Epidemiology can also be used to support specific causation when the association is particularly strong and the setting and subjects of the study are substantially similar to plaintiff.

As mentioned, while Delaware has not considered an epidemiological opinion under *Daubert* to support a causation hypothesis, other jurisdictions have.

[27] *Id.* at 855.
[28] *King*, 277 Neb. at 213.
[29] *Id.*

In its original decision here, the court relied on *Havner*[30] and *Garza*,[31] which meticulously set out what it takes for an epidemiologist to establish causation in Texas and how epidemiological opinion's admissibility must be analyzed under Texas law. Because this case will ultimately be decided under Texas law and Dr. Frazier does not offer what it takes to prove causation in Texas even if her opinion is admissible, the court did not consider whether the opinion is reliable under D.R.E. 702 and *Daubert*. Now that the court must consider reliability for D.R.E. 702 purposes, it must not only revisit *Havner* and *Garza*, which are non-binding authority on the issue here, but also non-binding authority from other jurisdictions.

Havner, in rejecting the epidemiological opinion supporting Plaintiff's jury verdict, held that the studies on which an epidemiologist's opinion is based must show: "the relative risk would need to exceed 2.0, and the confidence interval could not include 1.0, for the results to indicate more than a doubling of the risk and a statistically significant association."[32]

Plaintiff must also prove that he is similar to the study's subjects by showing that he "was exposed to the same substance, that the exposure or dose levels were comparable to or greater than those in the studies, that the exposure occurred before the onset of injury, and that the timing of the onset of injury was consistent

[30] *Merrell Dow Pharm., Inc. v. Havner*, 953 S.W.2d 706 (Tex. 1997).
[31] *Merck & Co., Inc. v. Garza,* 347 S.W.3d 256 (Tex. 2011).
[32] *Havner*, 953 S.W.2d at 725.

with that experienced by those in the study."[33] In 2011, *Garza* reaffirmed and emphasized this standard for admissible epidemiological opinion in Texas. *Garza* made plain that the *Havner* standards are *minimums*. Clearing *Havner* and *Garza*'s bar does not automatically justify admissibility.[34] Again, for present purposes, *Havner* and *Garza* are not controlling, but this court may adopt them.

As much as *Havner* clearly explains the statistical concepts and techniques it applied in establishing the 2.0 minimum, it is not flawless. Its analysis muddles general and specific causation.

Outside Texas, acceptance of *Havner's* 2.0 relative risk bright-line rule varies. Some jurisdictions follow it.[35] Others accept the statistical significance requirements as a measure of evidentiary sufficiency, but not as a threshold for admissibility.[36] And, others merely require a positive association, relying on the jury to determine the significance of the studies after proper instruction.[37]

General causation does not consider the likelihood that a certain exposure caused a certain harm. Rather, it only considers the possibility. Accordingly, as *King* holds, any epidemiological study showing a positive association

[33] *Id.* at 720.
[34] *Garza,* 347 S.W.3d at 265-266.
[35] *E.g. Siharath v. Sandoz Pharmaceuticals Corp.*, 131 F.Supp.2d 1347 (N.D. Ga. 2001) *aff'd sub nom. Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194 (11th Cir. 2002); *Estate of George v. Vermont League of Cities and Towns*, 993 A.2d 367 (Vt. 2010).
[36] *E.g. Lofton v. McNeil Consumer & Specialty Pharmaceuticals*, 682 F.Supp.2d 662 (N.D. Texas 2010) *aff'd*, 672 F.3d 372 (5th Cir. 2012).
[37] *E.g. King, supra*, note 2; *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d 1124 (2d Cir. 1995); *In re Prempro Products Liability Litigation*, 738 F.Supp.2d 887, 892 (E.D.Ark.2010).

can be part of a reliable opinion regarding general causation. Recognizing that the majority of courts equate a 2.0 minimum relative risk to plaintiff's burden of proof, *King* states that this requirement is too restrictive because no single epidemiological study will prove plaintiff's case.[38] This less rigorous approach is followed by some federal circuit courts.[39] The Second Circuit explains, "we believe that it would be far preferable [...] to *instruct* the jury on statistical significance and then let the jury decide whether many studies over the 1.0 mark have any significance in combination."[40]

As explained above, if epidemiology is offered to prove specific causation, then the standard of proof and logic dictate that the study must show plaintiff's injuries, more likely than not, were caused by the exposure. To that extent, a relative risk exceeding 2.0 makes sense because it means that, within that study's experimental group, there was more than a 50% chance that any individual defect was caused by exposure as opposed to something else. Of course, that statistic can not be extrapolated to plaintiff if he and his exposure are not fundamentally similar to the study subjects.

On the other hand, where epidemiology is offered to support general causation, whether the exposure could cause harm at all, a less stringent standard is,

[38] *King*, 277 Neb. at 231.
[39] *See e.g. In re Joint E. & S. Dist. Asbestos Litig.*, *supra* note 25; *In re Hanford Nuclear Reservation Litig.,* 292 F.3d 1124, 1137 (9th Cir. 2002).
[40] *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1134.

by definition, weaker but potentially probative. If, for example, someone wanted to determine if a coin was fair, it would not matter if heads came up at least twice as often as tails. Any "statistically significant" deviation from the expected 50/50 distribution would support the theory that the coin was not fair. "Statistically significant" essentially means that the unexpected thing happened often enough that there is a minimal likelihood it occurred by chance. To use the coin example, if a coin showed heads 600 times out of 1000 tosses, that result is unlikely to occur with a fair coin and suggests, without proving, that the coin is not fair. That is so even though the coin did not show heads twice as often as tails.

In epidemiology, certain standards govern statistical significance. "The generally accepted significance level or confidence level in epidemiological studies is 95%, meaning that if the study is repeated many times, the confidence interval indicates the range of relative risk values that would result 95% of the time."[41] Reliability under *Daubert* is fundamentally based on accepted methodology in the field. Accordingly, requiring results at the 95% confidence level is appropriate. It also makes sense to require that the entire confidence interval show a positive association—a relative risk over 1.0—to demonstrate that there is a positive association expected at least 95% of the time. Beyond that, however, there is no scientific reason to exclude a weaker positive association from a general causation

[41] *Havner*, 953 S.W.2d at 723.

analysis. At that point, it is in the expert's hands to demonstrate how a weak positive association supports her opinion through an articulate, defined methodology.[42]

V.

Dr. Frazier relies on several epidemiological studies, some of which satisfy *Havner's* statistical requirements, some do not. And there has been much back-and-forth about that. The reliability analysis here, however, turns less on statistics and more on methodology because Dr. Frazier fails to sufficiently explain her methods. That explanation is essential under all authorities.

Dr. Frazier is a well-qualified epidemiologist and occupational health professional. That finding is essential under *Daubert.* But, just as the absence of counter-opinion is not persuasive as to Dr. Frazier's reliability, neither is Plaintiffs' argument, *ad auctoritatem*, that Dr. Frazier's qualifications alone make her opinions reliable.

As discussed more thoroughly below, the methods used by an epidemiologist to form an opinion as to causation substantially rely on the expert's judgment in selecting and weighing her sources. Accordingly, courts require the expert to clearly define her methodology and application. Dr. Frazier fails to do that at several points. No quantum of evidence can overcome that.

[42] *See e.g. King*, 277 Neb. at 231-232.

VI.

Determining reliability under *Daubert* is a highly fact specific analysis based on the circumstances of the injury and exposure suffered by plaintiffs as well as the areas of science at issue. In their Supplemental Brief, Plaintiffs understate the necessity of establishing an association between the substances and harm in question before analyzing causation. Similarly, they understate the need to establish general causation before addressing specific causation through differential diagnosis. Conversely, Defendant overstates Plaintiffs' burden. Plaintiffs are not required to find a flawless, all-inclusive epidemiological study mirroring their precise circumstances.[43] Accordingly, neither side has been entirely helpful.

Critically analyzing Dr. Frazier's opinions takes several steps. The first is examining the testibility of her hypothesis, including specificity of substance, dose, and harm. That speaks directly to the first and third *Daubert* criteria. Next, under the second and fourth *Daubert* criteria, the court considers if the hypothesis has internal indicia of reliability to the scientific community through pre-litigation testing and peer review. An expert can also demonstrate reliability or bolster her opinion through a clearly defined weight-of-the-evidence analysis. Lastly, the court must determine if the hypothesis demonstrates specific causation as to Plaintiffs' injuries by ruling out other factors through differential diagnosis.

[43] *See, e.g., Grenier, supra* note 16.

A.

Again, the first criterion suggested under *Daubert* for determining reliability is whether Dr. Frazier's hypothesis can be or has been tested. Experimentation requires specificity, but neither the substance(s) nor dose element for a testable hypothesis is established by Dr. Frazier. Obviously, no one expects scientists to expose humans to harmful chemicals for a controlled, clinical experiment. Experimentation, however, can also be performed empirically through observation, as the epidemiological studies relied on in this case demonstrate. Regardless of the experimental method, a hypothesis must address a specific question, e.g. is exposure to X chemical(s) in Y dose for Z time likely to cause VATER association? Dr. Frazier acknowledges that "in designing a proper epidemiologic study it is important to properly define the characteristics of the group being studied."

As causative agents, Dr. Frazier names 10 chemicals, but she repeatedly asserts that other, unidentified toxins somehow contributed to the birth defects. Dr. Frazier never opines, however, which toxins specifically, alone or in combination, caused Plaintiffs' very different birth defects. Rather, she asserts that it is an "and/or" situation, where any or all of the chemicals, in undefined combinations caused the birth defects.

Similarly, Dr. Frazier refuses to specify dosages, relying instead on atmospheric concentration ranges as a surrogate. Yet, she also insists that the actual

dosages must be higher due to peak exposure episodes and dermal absorption. Further, despite the dissimilarity in their respective work experiences, Dr. Frazier claims that both adult Plaintiffs were exposed to the same quality and quantity of toxins. And, she opines that somehow this nondescript exposure caused two substantially different birth defects with little attempt to explain the differences. Those opinions gloss over the differences between the specific environments Plaintiffs' parents worked in, the different work they performed, the different chemicals they were exposed to, and the different exposure levels. Just because these may have been similar, they cannot be lumped together for each parent, much less for both.

Plaintiffs make much of cases where imprecision has been excused.[44] Those cases discuss whether general causation can be assumed where neither the specific dose required for human toxicity nor the specific dose plaintiffs received are known. In each case, however, the substance in question is known to be harmful at some exposure level and the plaintiff suffered the precise harm connected to that exposure.

Comparatively here, Dr. Frazier has to account for the fact that specific substances and doses are lacking where there is neither scientific consensus that these

[44] *See e.g. Hardyman v. Norfolk & W. Ry. Co.*, 243 F.3d 255 (6th Cir. 2001); *Clausen v. M/V NEW CARISSA*, 339 F.3d 1049 (9th Cir. 2003); *John's Heating Serv. v. Lamb*, 46 P.3d 1024 (Alaska 2002).

causation chemicals are toxic to humans nor a signature harm. Reliable scientific opinion cannot be formulated by one assumption on top of another. Dr. Frazier's untested hypothesis that adult Plaintiffs' exposure to chemicals at Defendant's facilities caused their children's birth defects is untestable for *Daubert* purposes.

B.

Assuming without deciding that the lack of specificity is not fatal to Dr. Frazier's opinion, as it is, *Daubert* next asks if the expert's hypothesis has been peer reviewed. Peer-review's importance speaks to the heart of *Daubert*. "[S]ubmission to the scrutiny of the scientific community is a component of 'good science,' in part because it increases the likelihood that substantive flaws in methodology will be detected."[45]

In summary as to Dr. Frazier's general causation opinion, she has found reliable foundational studies suggesting an association between working in the semiconductor industry and reproductive problems. Dr. Frazier, however, has not asked her peers to review what she has made of those studies, not through an article, case note, correspondence, or otherwise. Instead, Dr. Frazier contends, in effect, that because her personal opinion was formed by synthesizing peer reviewed foundational studies, that is as strong as if her opinion was peer reviewed. That notion is illogical and against the scientific method itself.

[45] *Daubert*, 509 U.S. at 593.

As mentioned above, as a corollary to considering whether an opinion has been peer reviewed, courts also frequently consider whether the theory was developed outside of litigation. *Daubert II* emphasizes the relative significance of research conducted independent of litigation:

> For one thing, experts whose findings flow from existing research are less likely to have been biased toward a particular conclusion by the promise of remuneration; when an expert prepares reports and findings before being hired as a witness, that record will limit the degree to which he can tailor his testimony to serve a party's interests. Then, too, independent research carries its own indicia of reliability, as it is conducted, so to speak, in the usual course of business and must normally satisfy a variety of standards to attract funding and institutional support. Finally, there is usually a limited number of scientists actively conducting research on the very subject that is germane to a particular case, which provides a natural constraint on parties' ability to shop for experts who will come to the desired conclusion.[46]

Here, Dr. Frazier's findings were made for this litigation. Even if it is tangentially related to research she has done, Dr. Frazier came to her opinion in response to Plaintiffs' request.

Peer review and research outside of litigation are the strongest indicia of reliability. Even so, "that the expert failed to subject his method to peer-review and to develop his opinion outside the litigation is not dispositive."[47] Where neither

[46] *Daubert II*, 43 F.3d at 1317.
[47] *Lust By & Through Lust v. Merrell Dow Pharm., Inc.*, 89 F.3d 594, 597 (9th Cir. 1996).

peer review nor prelitigation research can be shown, however, the expert's burden to prove reliability is higher. The expert "must explain precisely how they went about reaching their conclusions and point to some objective source—a learned treatise, the policy statement of a professional association, a published article in a reputable scientific journal or the like—to show that they have followed the scientific method, as it is practiced by (at least) a recognized minority of scientists in their field."[48] As mentioned above and discussed next, the personal way Dr. Frazier came to her opinions is not well-enough explained.

C.

Epidemiology alone does not prove causation; it only demonstrates an association. Accordingly, even the most widely accepted and strongest epidemiology is not a litmus test for toxic tort causation.[49] Nor is a lack of epidemiology fatal to plaintiff's case.[50] To bolster epidemiology, lacking or otherwise, the expert must explain her methodology in detail and point to an objective, reputable source to demonstrate that her methodology is accepted.[51]

The parties agree that epidemiologists generally rely on the "Bradford Hill" factors to show that a causal relationship can be inferred from an association. The factors are 1) temporal relationship, 2) strength of the association, 3) dose-

[48] *Daubert II*, 43 F.3d at 1319.
[49] *Havner*, 953 S.W.2d at 718.
[50] *Siharath v. Sandoz Pharm. Corp.*, 131 F. Supp. 2d at 1358.
[51] *Daubert II*, 43 F.3d at 1318-9.

response relationship, 4) replication of the findings, 5) biological plausibility, 6) consideration of alternative explanations, 7) cessation of exposure, 8) specificity of the association, and 9) consistency with other knowledge.[52] The enumerated factors are neither all-inclusive nor are they in hierarchical order; the factors merely provide a framework for establishing causation.

Experts can also evaluate data using a weight-of-the-evidence analysis, including available epidemiology, to assess causation. Other forms of evidence including toxicology, *in vivo* studies, *in vitro* studies, animal studies, and case studies can be used together to show causation. As explained above, the reliability analysis is performed on each bit of data used to formulate the ultimate opinion.

Bradford Hill and weight-of-the-evidence are discussed together because both rely on gathering, comparing, and weighing a wide range of data from various sources. And the same considerations go into the reliability of these foundational sources, including statistical significance and "fit," with either method. Both techniques are used to methodically extrapolate from association to causation. Bradford Hill contemplates beginning with epidemiology and using other sources as support. Weight-of-the-evidence, on the other hand, allows an expert to fit all the sources together like a puzzle. To some extent, relying on weight-of-the-evidence is an admission that the available epidemiology is weak. Put another way, non-peer

[52] *King*, 277 Neb. at 221 citing Reference Manual on Scientific Evidence 376 (Federal Judicial Center 2d ed. 2000).

reviewed weight-of-the-evidence opinion made for litigation is most suspect categorically.

When reliable studies from different scientific fields are weighed in a defined, reliable manner, Bradford Hill or weight-of-the-evidence methodology may be appropriate.[53] Due to the expansive potential sources of data for those analyses, establishing "fit" for each source is especially important when considering the source's reliability as part of a meta-analysis. That applies in spades here, where the data comes from Taiwanese Fab workers, Dutch house painters, electronics workers, the animal kingdom, and so on.[54]

"'Fit' is not always obvious, and scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes.[55]

> For example, in order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must constitute good grounds to reach conclusions about the animals themselves. Thus, the requirement of reliability, or "good grounds," extends to each step in an expert's analysis all the way through the step that connects the work of the expert to the particular case.[56]

[53] *E.g. In re Chantix (Varenicline) Products Liab. Litig.*, 889 F. Supp. 2d 1272 (N.D. Ala. 2012).
[54] *Tumlinson v. Advanced Micro Devices, Inc.,* 2012 WL 1415777 (Del. Super. Jan. 6, 2012).
[55] *Daubert*, 509 U.S. at 591.
[56] *Paoli*, 35 F.3d at 743.

Further, the Third Circuit explains, "not only must each stage of the expert's testimony be reliable, but each stage must be evaluated practically and flexibly without bright-line exclusionary (or inclusionary) rules."[57]

The first part of Dr. Frazier's opinion is epidemiological studies. For epidemiology, the first question is whether the foundational study shows a statistically significant association.[58] Dr. Frazier asserts that statistical significance is not part of the Bradford Hill or weight-of-the-evidence analysis. From a legal standpoint that is incorrect.[59] Regardless of whether the court adopts *Havner's* bright-line requirements or the more subjective ones in *King*, a study must demonstrate some positive association in order to have value as part of a larger meta-analysis. And, the weaker the association, the less it can contribute. Dr. Frazier seems to accept that.

As discussed in the original opinion, some of the epidemiology is unreliable.[60] Some fail to "fit" this case: the 2006 Hooiveld study involved different chemicals; the SIA study examined spontaneous abortion. The JHU/IBM study "observed no adverse effects on birth weight or gestational maturity, and no increased risk of birth defects or childhood neoplasms associated with either maternal or paternal work in the Clean Room Areas." Other studies possibly may barely show

[57] *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 155 (3d Cir. 1999).
[58] *Id.* at 220.
[59] *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1134.
[60] *Id.* at 6.

reliability, but suffer from significant infirmities. The 2008 Lin study and the 2009 Sung study involve foreign Fab workers, but fail to measure specific chemical exposures or doses. The Sung study also does not report a relative risk or odds ratio for its findings. The DEC study only found a slight positive association.

Dr. Frazier asserts that her using epidemiological and animal studies with spontaneous abortion as their endpoint "fit" this case. The joint affidavit conclusively states, "there is compelling evidence specifically linking spontaneous abortion with birth defect." She also bases her opinion on "dose-response relationship." Dose-response means increasing the intensity or duration of exposure increases the frequency or severity of an outcome. Dr. Frazier opines that if a large exposure causes spontaneous abortion, the dose response relationship establishes that a small exposure of any chemical causes birth defects. Therefore, in her opinion, scientific papers tending to show chemical exposure causes spontaneous abortions also prove that exposure in lower doses cause birth defects. That original reasoning helps Dr. Frazier opine that exposure to assorted solvents and other chemicals in unknown amounts probably caused one Plaintiff's VATER association and the other's *situs inversus*.

The court accepts that dose-response is a legitimate scientific and pharmacological concept. That does not mean, however, that Dr. Frazier is free to reach her own conclusions about how dose-response applies to chemicals, exposures,

and birth defects either generally or specifically in this case. Her application of dose-response here is untested, even in the animal studies. Further, it has not been subjected to peer review and it was created for this litigation.

The way Dr. Frazier uses dose-response has a direct bearing on the court's gatekeeping function under *Daubert*. Dr. Frazier's—if a big dose of a chemical is known to cause abortion, then a smaller dose probably causes birth defects—theory has a superficial ring to it. But how will a jury evaluate that? Even if Defendants produce a counter-expert, the jury room is not a substitute for an actual science laboratory. Accordingly, studies analyzing spontaneous abortion as an endpoint do not satisfy the "fit" requirement of reliability where specific birth defects are the endpoint in question. They also cannot be considered in Dr. Frazier's weight-of-the-evidence analysis.

Further, as to weight-of-the-evidence, there is no generally agreed upon method for weighing different data.[61] That is another reason why, to confirm the opinion's scientific reliability, an expert must detail her method of weighing the importance and validity of each data source to assemble a cohesive picture, particularly where the opinion is formed for litigation and not peer reviewed. Being presented with only the experts' qualifications, their conclusions and their assurances

[61] *King*, 277 Neb. at 221.

of reliability is not enough under *Daubert*.[62] In *Daubert II*, opinion was excluded where "plaintiffs' experts have relied on animal studies, chemical structure analyses and epidemiological data, [but] they neither explain the methodology the experts followed to reach their conclusions nor point to any external source to validate that methodology."[63]

Dr. Frazier consistently failed to explain her process. For example, in the Joint Affidavit, some epidemiological studies are discussed in detail. Dr. Frazier, however, never explains why these studies are worth discussion while others are not, nor how the other studies affected her conclusion, nor how each study was weighed against the others. The hearing testimony did not fill-in the gaps.

Dr. Frazier invokes both Bradford Hill and weight-of-the-evidence analysis to support her general causation hypothesis. As detailed above, both methods require the scientist to articulate her thought process, evaluation methods, and conclusions to establish reliability. As a matter of law, it is not enough if a scientist merely invokes her qualification in order to establish her judgments as reliable. Nor does baldly asserting in the joint affidavit "each of us has exercised our judgment in this manner in arriving at our opinion" satisfy the burden.

[62] *Id.*
[63] *Daubert II*, 43 F.3d at 1319.

For general causation, no study draws a conclusion between the causation chemicals and VATER assocation or *situs inversus*. Similarly no study other than the Lin study of male semiconductor workers in Taiwan draws a conclusion between the supposed causation chemicals and cardiac malformations. At best, this study suggests, but does not prove, a possible association, much less a causal relationship. Further, as recognized by the Lin study's authors, the study is wrought with infirmities. There were only nine cases of heart anomalies across the entire study population. The study only recorded birth defects that killed the children before age 5. It ignored an unknown population of children living with malformations. The study lacked adequate exposure measurements. The most the study concludes, in the author's words, is that "it is clear that many of [the semiconductor chemicals] are potential reproductive toxins." From this, Dr. Frazier wants the jury to find that an undefined mix of 10 named chemicals "and others," to which Plaintiffs' parents were exposed for unknown, different periods, could have caused Plaintiffs' birth defects.

D.

Once general causation is established, which Dr. Frazier does not do, Plaintiffs must still demonstrate specific causation. To return to the coin analogy, to prove that the 60% heads result was in fact due to an unfair coin, other possible causes must be eliminated, such as starting orientation. Differential diagnosis is an

accepted method for addressing specific causation, but it too relies on the expert's judgment and experience. Accordingly, to be legally reliable, the expert must describe how and why she ruled out other potential teratogens.

Assuming without deciding that Dr. Frazier's opinion on general causation were accepted by the scientific community, Dr. Frazier fails to apply differential diagnosis in an articulate, methodical way. Mostly, she conflates her differential diagnosis with her causation opinion. Dr. Frazier cannot differentiate between the possible causes of Plaintiffs' birth defects because no one knows what really causes them. So, because Dr. Frazier concluded that the parents' exposures can generally cause VATER association and *situs inversus*, and there are no other known causes to distinguish, Defendant must have caused Plaintiffs' birth defects. But, that only works if it has been proved that there is only one cause of those birth defects, such as the way asbestos causes mesothelioma. Even Dr. Frazier does not call VATER association or *situs inversus* signature diseases.

Viewed against that factual backdrop, it appears that Dr. Frazier's differential diagnosis for Jake Tumlinson sets up a strawman to knock down. For Jake Tumlinson, Dr. Frazier rules out the mother's obesity, a factor linked to birth defects generally, by finding unsupported differences between Mrs. Tumlinson and subjects in the studies linking maternal obesity and birth defects. Without explanation, Dr. Frazier rejects Mrs. Tumlinson's obesity as a cause because she was

not diabetic, yet Dr. Frazier acknowledges that studies have found "maternal obesity in the absence of diabetes was associated with birth defects."

For Paris Ontiveros, Dr. Frazier merely asserts that "[t]here are no alterative (sic) explanations for Paris Ontiveros' malformations." Yet, all the studies Dr. Frazier relies on, as well as Dr. Frazier herself in the same affidavit as the above assertion, acknowledge that, although rare, the birth defects occur in the population at large, often with no more evidence of causation than here. She offers no reason for ruling out these accepted, unexplained background causes.

For both children, she essential relies on circular logic to state that because the parents were likely exposed to these chemicals prior to conception and during gestation, the chemicals must have caused or predisposed the children to these very rare birth defects. Saying, in effect, "I can think of one way Plaintiffs' birth defects could have been caused and I can't think of another," does not amount to a differential diagnosis.

VII.

In conclusion, the court finds Dr. Frazier is well-qualified by training and experience to offer opinions concerning epidemiology and related environmental medicine. The court also acknowledges cause for her concern about the potential reproductive health effects for men and women working in computer chip

manufacturing facilities. Clearly, as experts in the field agree, there is need for further research.

Nevertheless, no scientific study has established a general link between female workers, such as Jake Tumlinson's mother, and his birth defects, including VATER association. And only one study generally links male workers with, potentially, one of Paris Ontiveros's several birth defects.

Because the general cause of Plaintiffs' birth defects is unknown, it cannot be said that the work Plaintiffs' parents did was the specific cause of their birth defects. But even if it has been proven that working in a computer chip manufacturing facility may cause birth defects like Plaintiffs', Dr. Frazier's opinion that those defects were caused by their parents' exposure to toxins at work, rather than other causes, is unreliable. Therefore, as a matter of Delaware law, Dr. Frazier's opinions are inadmissible under D.R.E. 702.

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