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STATE OF WASHINGTON

No. 82264-6

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IN THE SUPREME COURT
OF THE STATE OF WASHINGTON

BY RONALD R. CARPENTER

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JULIE ANDERSON, individually and on behalf of the Estate of
DALTON ANDERSON, and DARWIN ANDERSON individually,

Appellants

v.

AKZO NOBEL COATINGS, INC., and KEITH CROCKETT,

Respondents

BRIEF OF RESPONDENTS

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ORIGINAL

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INTRODUCTION

Respondents and Defendants below Akzo Nobel Coatings, Inc. (“Akzo Nobel”) and Keith Crockett (collectively, “Respondents”) respectfully submit this brief in response to the brief filed by Appellants Julie Anderson, individually and on behalf of the estate of Dalton Anderson (“Ms. Anderson”), and Darwin Anderson (collectively, “Appellants”). Appellants claim that Ms. Anderson was exposed to organic solvents while working at an auto paint distributorship owned by Akzo Nobel, located in Pacific, Washington, and that such exposure caused birth defects in her son, Dalton. This claim requires specialized, and novel, scientific evidence in the form of opinion testimony by experts. To put this evidence before the jury, however, Appellants must satisfy the test for admissibility set forth in *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923), as adopted and applied in Washington. They failed to do so.

The particular birth defects, or malformations, at issue are: a developmental malformation of the brain, which has been diagnosed by experts in this case as polymicrogyria or, more generally, as a neuronal migration defect; and, multicystic kidney disease. Appellants have come forward with only one piece of evidence supporting a link of any kind between prenatal exposure to organic solvents generally and brain malformation defects of any kind, and this one item consists of one child

out of 125 test subjects in one scientific article. The Superior Court correctly held that this degree of evidence was insufficient, as a matter of law, to demonstrate “general acceptance” of Appellants’ theory of causation in the relevant scientific community under *Frye*, and thus excluded Appellants’ medical causation experts from testifying, and subsequently granted summary judgment to Respondents. Appellants have failed to come forward with any additional evidence of “general acceptance” on appeal, and have failed to provide any reason why this Court should reach a different conclusion.

Appellants’ two additional assignments of error are also unavailing. First, they identify the Superior Court’s denial of Appellants’ motion to dismiss Respondents’ affirmative defense of contributory fault. Appellants claim that the trial court erroneously held that a woman may be held comparatively at fault as a result of her decision to work while pregnant. However, that issue was never addressed below. Respondents never made this argument to the Superior Court, and the Superior Court made no findings in this regard. In addition, the Superior Court’s ruling had absolutely no effect on the disposition of the case below; any error would thus be harmless.

Second, Appellants assign error to the Superior Court’s dismissal of Ms. Anderson’s claim for wrongful discharge in violation of public

policy. Appellants mischaracterize the trial court's ruling as holding that an exclusive statutory scheme is provided by the Washington Industrial Safety and Health Act (WISHA). In fact, the court held that Ms. Anderson's claim was barred because she chose to ignore an administrative remedy provided by the statutory scheme that adequately protects the public policy at issue. The Superior Court's ruling did not rely on a finding of exclusivity; thus, the issue identified by Appellants was not, in fact, addressed below. Moreover, the court's ruling was correct, and did not disregard binding precedent, as Appellants claim. To the contrary, the Superior Court expressly relied upon controlling precedent from this Court.

For the reasons stated below, this Court should affirm the Superior Court's decision to grant summary judgment dismissal of this case on grounds that Appellants' medical causation experts are excluded under *Frye*, and thus that Appellants have failed to establish a *prima facie* element of their case. The Court should also affirm the trial court's other rulings, including its decision to deny Appellants' motion to dismiss Respondents' affirmative defense of contributory fault, and its decision

granting Respondents' motion to dismiss Appellants' claim for wrongful discharge.¹

STATEMENT OF THE CASE

A. The Superior Court's Denial of Appellants' Motion to Dismiss Respondents' Affirmative Defense of Contributory Fault.

Appellants moved below for summary judgment dismissing affirmative defenses asserted by Respondents, including comparative fault on the part of Appellant Ms. Anderson. Respondents opposed Appellants' motion, arguing that there was evidence sufficient to raise a genuine issue of material fact regarding contributory fault because: (1) despite the fact that Ms. Anderson was the safety coordinator for the Akzo Nobel distributorship, she refused to wear a respirator while mixing paint; (2) Ms. Anderson continued to mix paint while pregnant after being advised not to do so by her supervisor and fellow employees; and (3) Ms. Anderson smoked while pregnant. CP 161-170. At no point did Respondents argue that Ms. Anderson was contributorily negligent *simply* because she continued working during her pregnancy. On the contrary, Respondents put forth evidence showing that "if Ms. Anderson mixed

¹ In their Statement of Grounds, Appellants also identified a ruling of the Superior Court denying Appellants' motion to exclude Respondents' experts on medical causation. Appellants appear to have now abandoned this assignment of error.

paint while she was pregnant, it was directly contradictory to the directions and admonitions she was receiving from her supervisor and co-workers.” CP 166.

The Superior Court entered an order denying Appellants’ motion to dismiss this affirmative defense on August 31, 2007. CP 194-196. The order contained no findings of fact, or explicit holding regarding the basis for the Court’s ruling. *Id.*

B. The Superior Court’s Grant of Respondents’ Motion *in Limine* to Exclude Appellants’ Medical Causation Experts under *Frye*

The background facts resulting in this appeal were ably set out by the trial court below as follows:

Dalton Anderson was born with birth defects: a malformation in his brain, and multi-cystic kidney. Dalton’s treating doctors have described his condition as a neuronal migration defect, meaning that during embryonic development, some of Dalton’s brain cells failed to develop in the specific anatomical area where they should have been located.

Plaintiffs claim that Dalton’s birth defects were caused by plaintiff Julie Anderson’s exposure to organic solvents at her workplace while she was pregnant with Dalton. Defendants argue that the theory that prenatal exposure to organic solvents can cause either neuronal migration defects or multicystic kidney disease is one that has not achieved general acceptance in the scientific community.

CP 784. Respondents moved *in limine* under Washington’s *Frye* standard to exclude the causation testimony of Appellants’ scientific experts. The

court granted Respondents' motion, and subsequently granted summary judgment in favor of Respondents. *See* CP 779-791; 806-807. It is these rulings that Appellants primarily are appealing.

Three of Appellants' experts were excluded by the trial court from testifying that Dalton Anderson's malformations were caused by *in utero* exposure to organic solvents, which resulted from his mother's alleged occupational exposure at Akzo Nobel: Sohail Khattak, M.D.; Thomas Schultz, Ph.D.; and Stephen Glass, M.D. Dr. Khattak is Appellants' primary expert on the issue of medical causation, and his testimony was the focus of the Superior Court's opinion below.²

1. **Dr. Khattak**

Dr. Khattak based his causation opinion on his training and experience, and upon the medical literature. With respect to experience, Dr. Khattak is the CEO, President and Chief Scientific Officer of Qualia Clinical Service, a pharmaceutical research and development company that provides outsource laboratory testing for pharmaceutical companies

² Dr. Schultz was excluded by the trial court on additional and independent grounds that he lacked sufficient professional expertise to offer an opinion regarding the cause of Dalton's birth defects, and Appellants do not appeal this ruling. CP 789. Dr. Glass based his opinion on that of Dr. Khattak, and his testimony added nothing to the grounds identified by Dr. Khattak as supporting Appellants' theory of causation. CP 790.

seeking regulatory approval. CP 614, 624. Qualia has no involvement in studies related to *in utero* occupational exposure to solvents. CP 625.

Concerning training, Dr. Khattak earned his first medical degree from the University of Peshawar in Pakistan. CP 616. After immigrating to Canada in 1989, he obtained a residency at the University of Toronto's Hospital for Sick Children. CP 615, 616. While at the Hospital for Sick Children, Dr. Khattak worked under Dr. Gideon Koren at the Motherisk Clinic, from 1994 to 1997. CP 617, 618. He continues to view Dr. Koren, who provided deposition testimony on behalf of Respondents in this matter, as his mentor. CP 617. Dr. Khattak testified that he has Canadian board certification in pediatrics and in clinical pharmacology toxicology, but holds no board certifications or credentials in the United States. CP 622. Asked whether he considers himself a teratologist,³ he answered, "I would say so, yes," stating that he received "formal training" in teratology while at the Motherisk Clinic. CP 622, 648. However, Dr. Koren (Dr. Khattak's mentor and head of the Motherisk Clinic), strongly

³ Teratology is the study of the causes and biological processes leading to abnormal development and birth defects.

disagreed, stating: “If he says that he is a teratologist I believe he is misstating his qualification [*sic*].” Sub No. 106.⁴

Dr. Khattak agreed with defense experts that Dalton Anderson may likely have polymicrogyria (“PMG”), and testified that he does not consider himself qualified to give an alternate diagnosis. CP 634, 646-47. PMG is a developmental malformation of the human brain characterized by an abnormal appearance of small convolutions on the surface of the brain. Sub No. 106. Although Dr. Khattak initially maintained that there evidence in the medical literature of an association between PMG and exposure to organic solvents, he only identified one source. CP 635. He ultimately acknowledged, however, that even this paper, published in 1995, did not, in fact, establish any such association:

Q: Okay, Dr. Khattak, this article does not establish on a more probable than not basis that --

A: Yeah, it doesn’t. I would agree, it doesn’t establish. But the fact is that there is, you know, some literature, some case reports, you know. This, don’t forget that these PMGs are very new diseases. They only started identifying them once the MRI was readily available . . . So our understanding is only evolving over the last 10, 15 years.

⁴ Documents identified only by “Sub No.” have been designated, but have not yet been assigned CP page numbers. Once page numbers have been assigned, Respondents will submit an Errata that provides citations to CP numbers. See RAP 9.6(a) (permitting a party to supplement the designation of clerk’s papers “prior to or with the filing of the party’s last brief”).

Id. Asked directly whether it is generally accepted in the scientific community that PMG is caused by exposure to organic solvents, Dr.

Khattak responded as follows:

I would say that, you know, the knowledge of this whole thing is just coming out. So whatever theory there may have been, you know, has not been fully tested. So there are probabilities . . . So, you know, I understand that I could take one particular instance and I can say there are possibilities, and we don't have enough research, you're absolutely right.

CP 659. Similarly, Dr. Khattak stated in a declaration filed in this matter that his opinion is based not on generally accepted scientific theories, but on "theoretical risks" which are "not a stretch to imagine." Sub No. 141; CP 830.

In reaching his opinions, Dr. Khattak purported to rule out other possible causes of Dalton's medical issues, including potential genetic abnormalities. However, he testified that he does not consider himself a geneticist and had not consulted with a geneticist in this matter. CP 623, 660.

As to his theory of causation, Dr. Khattak stated in a declaration filed prior to his deposition that "a single significant exposure to the chemicals at issue during the early phases of pregnancy, *i.e.*, first trimester, can cause the types of malformations suffered by Dalton." CP 224. In his deposition, however, Dr. Khattak retreated from this theory of

first trimester exposure, espousing a “multiple exposure” theory of causation.⁵ CP 636, 643. As for his methodology, Dr. Khattak based this conclusion on what Ms. Anderson told him during a single two-and-a-half-hour phone call that took place “a couple of days” prior to his deposition. CP 638-39. He testified that Ms. Anderson told him she was in the paint mixing room at the Akzo Nobel facility almost every day, that she was cleaning with paint thinner, and that she was made sick by the smell of paint fumes while working in her office. *Id.* He also testified that Ms. Anderson told him she did not receive any hazardous materials training on the job, and that he was unaware Ms. Anderson in fact had received specific training to be the Health, Safety and Environmental (HSE) Coordinator for the Seattle branch, prior to her pregnancy. CP 642. Dr. Khattak similarly relied on what Ms. Anderson told him to conclude that she showed symptoms of organic solvent exposure while she was working at the Akzo Nobel facility. CP 663. However, he admitted that he had not reviewed Ms. Anderson’s medical records to see if she was reporting these symptoms to her doctor during her pregnancy, and was unconcerned that her medical records from the time of her pregnancy

⁵ This change of position was undoubtedly a concession to the undisputed fact that PMG is a *post*-neuronal migration disorder occurring in the second trimester. Sub No. 106.

failed to show that she was symptomatic to any degree, let alone to a degree that would support his conclusions. *Id.*

Concerning the degree of exposure necessary to cause Dalton Anderson's malformations, Dr. Khattak agreed with his own testimony in a prior case that "significant" exposure, i.e., exposure sufficient to raise possible health concerns, requires "at least 20 hours working with the solvent or in the environment where you are handling solvents or exposed to solvents."⁶ CP 632. With respect to the concentration of solvent necessary to raise possible health concerns, however, Dr. Khattak testified that "quantification of concentration has been one of the missing piece [*sic*] of puzzle in this whole research," i.e., that there is insufficient information within the scientific community to quantify the concentration necessary to cause malformations. CP 632-33.

2. The 1999 JAMA Article

Dr. Khattak's experience as a litigation expert began following the publication of *Pregnancy Outcome Following Gestational Exposure to Organic Solvents*, JAMA, Mar. 24/31, 1999 (hereinafter, "1999 JAMA" article or study). Both Dr. Khattak and Dr. Koren were listed as authors of the article. Although Dr. Khattak's was the first name listed, he

⁶ There has been no evidence that Ms. Anderson worked with solvents for anything even close to this duration.

acknowledged that he had actually been in residency at the time, and that Dr. Koren was in fact the senior scientist on the paper. CP 619. Consistent with this, Dr. Koren explained in his deposition testimony that it is his practice to list trainees first on all of his papers, and that Dr. Khattak was a “trainee” at the time the 1999 JAMA article was published. Sub No. 106.

The 1999 JAMA article described the results of a “prospective” study that the Motherisk Clinic performed in the mid-1990’s.⁷ CP 231-34. In that study, 256 pregnant women were divided into two groups, those exposed to organic solvents (of a wide variety) during gestation and those who were not exposed. *Id.* Women in each group were then “matched” to each other, on the grounds of prior pregnancy history, smoking and drinking habits and other medical and environmental criteria. *Id.* The article reported results that 13 of the exposed women had children with various and diverse malformations. *Id.* One of the 13 observed malformations was described as a “neuronal migration defect and focal cortical dysplasia heterotopia.” CP 234. The article reported an “association” between occupational exposure to organic solvents during

⁷ Prospective studies take a population before exposure and study them as exposure occurs. “Retrospective” studies involve looking back on a population after exposure.

pregnancy and increased risk of fetal malformations, concluding that “more prospective studies will be needed to confirm the present results.”

Id. Several facts concerning that 1999 JAMA article are important for this case:

First, Dr. Koren, who was the senior scientist on the article, testified that the study does not establish a causal relationship between exposure to organic solvents and neuronal migration defects, or even between exposure and developmental defects generally. Sub No. 106. The article merely reported a general statistical correlation between organic solvent exposure during pregnancy and increased risk of various and diverse defects. The study failed to link any particular condition with any particular compound, which explains why it concluded that further study was warranted. Sub No. 106; CP 234.

Second, the study observed only one incidence of neuronal migration defect, or of any other type of developmental brain malformation. As the trial court found, all of the experts in this case agree that Dalton Anderson has a developmental brain malformation of some type. CP 828. Respondents’ expert William Dobyns, M.D., testified that Dalton’s defect is, in fact, PMG, Sub No. 106, and Dr. Khattak did not

dispute this diagnosis.⁸ CP 634. There is no support in the medical or scientific literature for a theory of causation linking PMG and exposure to organic solvents. The 1999 JAMA article was not to the contrary, as all it did was identify a *single* instance of one mother exposed to unspecified “organic solvents” (a broad category of chemicals) who had a child with a “neuronal migration defect” (itself, a broad category of brain conditions). The article did not establish a causal link between the chemicals and conditions at issue in this case, no matter how broadly defined by Appellants.

Third, the 1999 JAMA study did not involve any children with multicystic kidney disease, Dalton Anderson’s other major malformation. CP 637. In fact, Dr. Khattak agreed that multicystic kidney disease has *never* been associated with *in utero* exposure to organic solvents. *Id.* Dr. Koren likewise testified that no study has ever shown that neuronal migration defects and multicystic kidney disease have been caused by exposure to organic solvents.⁹ Sub No. 106.

⁸ Technically, PMG is not a “neuronal migration defect” because it occurs after the period of neuronal migration in the brain (roughly second trimester). As such, it is a “post” migrational defect. The distinction is academic here because Appellants failed to link the alleged exposure to any congenital brain malformation that could be associated with Dalton Anderson.

⁹ Defendant’s expert geneticist, Dr. Dobyms, testified that this type of kidney birth defect “is widely recognized as genetic.” Sub No. 106. There is no evidence to the contrary.

Fourth, the malformations observed in the 1999 JAMA study, in addition to being different in kind, were much milder than those of Dalton Anderson; as Dr. Koren explained:

In that study we measured functions of the brain of kids exposed to organic solvents to a function of kids not exposed to organic solvents through mom. We found very minor changes in one group exposed compared to non-exposed. None of these kids were perceived by their families to have a problem with the child, and none of the kids had neuronal migration defect.

Moreover . . . these are not randomized trials. It's a group of women who took it. It's not that I told half of them you work with organic solvents or not. So it could still be that the differences stem from other socioeconomic reasons typical of women who work or not work. For all these reasons one has to be extremely careful. The fact that it may affect brain development does not mean that it affect a particular neuronal migration effect . . .

Sub No. 106.

Fifth, the article did not identify where the women who were the subject of the study worked, what specific chemicals they were exposed to, the concentrations of those chemicals, or the durations of the exposures. This lack of detail is extremely problematic because all of the underlying data, which could have illuminated these issues, was lost or destroyed. CP 628.

Except for this one article, Appellants failed to identify any other evidence purportedly showing "general acceptance" of their theory that

Dalton Anderson's medical conditions were caused by his mother's occupational exposure to organic solvents.

C. The Superior Court's Grant of Respondents' Motion to Dismiss Ms. Anderson's Claim for Wrongful Discharge

Respondents moved below for summary judgment dismissing Ms. Anderson's individual claims, including a claim for wrongful discharge in violation of public policy. The Superior Court granted Respondents' motion. Relevant portions of the Superior Court's order are excerpted in section C of Respondents' Argument, *infra*. As those portions demonstrate, the Superior Court properly applied binding precedent from this Court, contrary to Appellants' assertions.

ARGUMENT

A. Appellants' First Assignment of Error: the Superior Court's Denial of Appellants' Motion to Dismiss Respondents' Affirmative Defense of Contributory Fault

Appellants' first assignment of error claims that the trial court "erred in holding that Ms. Anderson could be held comparatively at fault for causing Dalton's brain malformations simply for performing the essential functions of her job." App. Br., p. 3. This assignment of error is erroneous in two respects. First, the order at issue played no part in the disposition of this case below, and reversal would have no effect on the final judgment; thus, it does not raise an appealable issue. Second, the

trial court simply did not make the holding Appellant ascribes to it, i.e., this assignment of error is a fiction.

1. Even if Correct, Appellants Have Identified Only Harmless Error

The order at issue is the trial court's denial of Appellants' motion to dismiss certain affirmative defenses asserted by Respondents, including comparative fault. This ruling is completely irrelevant to the disposition of this case below. Judgment was entered because Respondents prevailed on summary judgment after the Superior Court excluded Appellants' medical causation experts. Even if the Superior Court had made the error described by Appellants, therefore, the court's ruling played no part in the disposition of the case. Any error would thus be harmless, as shown by the fact that if this Court were to reverse the trial court's decision, and were the trial court to then grant Appellants' motion to dismiss Respondents' affirmative defense of contributory fault, Respondents would still be entitled to entry of judgment in their favor. The trial court held that Appellants failed, as a matter of law, to establish an essential element of their claim, and granted summary judgment on that basis. Whether Respondents' affirmative defense was rightly dismissed is completely irrelevant to that holding.

2. Appellants Mischaracterize the Ruling Below

Even if reversal of the order complained of would in some manner alter the judgment below, the trial court in any event never made the ruling complained of by Appellants. Appellants assert that Respondents “argued, and the trial court agreed” that Appellant Julie Anderson “could be held comparatively at fault for Dalton’s injuries because she decided to work and perform the essential functions of her job during pregnancy.” App Br. at 10. No citation is provided by Appellants for the assertion that the trial court made this holding. That is because none exists. The order complained of contains no such findings, merely stating that Appellants’ “motion for summary judgment for the dismissal of [Respondent]’s comparative fault affirmative defense with respect to Julie Anderson is DENIED.” CP 195.

Nor is this a fair characterization of Respondents’ argument. Respondents argued in opposition to Appellants’ motion that there was evidence sufficient to raise a genuine issue of material fact concerning whether Ms. Anderson was contributorily at fault because: (1) despite the fact that she was the safety coordinator for the paint mixing facility, and trained to wear a respirator at all times in the mixing room, she refused to wear a respirator while mixing paint; (2) she continued to mix paint while pregnant after being advised not to by her supervisor and fellow

employees; and (3) she smoked while pregnant. CP 161-170. At no point did Respondents argue that Ms. Anderson was contributorily negligent simply “because she decided to work and perform the essential functions of her job during pregnancy.” To the contrary, Respondents put forth evidence showing that “if Ms. Anderson mixed paint while she was pregnant, it was directly contradictory to the directions and admonitions she was receiving from her supervisor and co-workers.”¹⁰ CP 166.

In short, Respondents never made the argument Appellants now ascribe to them, and the trial court did not make any such findings or holding. Appellants’ first assignment of error is a fiction. The Court need never get this far, however, because the ruling at issue played no part in determination of the matter, and its reversal would not alter the judgment below.

B. Appellants’ Second Assignment of Error: the Superior Court’s Exclusion of Appellants’ Expert Medical Causation Witnesses under *Frye*

Appellants challenge the trial court’s ruling excluding Appellants’ expert witnesses on medical causation on three basic grounds: (1) that the

¹⁰ Appellants avoid Respondents actual arguments below, because they were correct. Assuming for the sake of argument that the condition was not genetic, but had an environmental cause (something Appellant notably failed to support with evidence), there was ample evidence of Ms. Anderson’s contributory fault. It is unlikely that denial of Appellants’ summary judgment on this point was even a close call by the trial court, and Appellants have offered no reason for this Court to see it differently.

Court misinterpreted the *Frye* test; (2) that the testimony excluded should have been admitted under *Frye*; and (3) that this Court should abandon *Frye* altogether. Appellants are incorrect on the first two points – the Superior Court correctly interpreted and applied *Frye*. As to the third point, *Frye* is the law of Washington, and there is nothing unusual about this case that should encourage the Court to reconsider its many prior decisions adopting and applying the *Frye* test.

1. Standard for Admissibility Under *Frye*

The admissibility of expert testimony is governed by ER 702, which requires that the witness qualifies as an expert and that the testimony be helpful to the trier of fact, and by ER 703, which requires that an expert have a reasonable basis of information about the subject before offering his or her expert opinion. In addition, expert testimony concerning novel scientific evidence must satisfy the test for admissibility set forth in *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923).¹¹

Washington courts apply the *Frye* test in both criminal and civil cases. *Ruff v. Dep't of Labor and Industries*, 107 Wn. App. 289, 299, 28 P.3d 1 (2001). Under *Frye*, “evidence deriving from a scientific theory or principle is admissible only if that theory or principle has achieved general

¹¹ There is no dispute that Appellants’ causation evidence is novel, and thus that *Frye* applies.

acceptance in the relevant scientific community.” *Id.*; see also *State v. Copeland*, 130 Wn.2d 244, 255, 922 P.2d 1304 (1996). In examining a *Frye* question, a court must determine: “(1) whether the underlying theory is generally accepted in the scientific community and (2) whether there are techniques, experiments, or studies utilizing that theory which are capable of producing reliable results and are generally accepted in the scientific community.” *State v. Riker*, 123 Wn.2d 351, 359, 869 P.2d 43 (1994); *Grant v. Boccia*, 133 Wn. App. 176, 178, 137 P.3d 20 (2006). This inquiry turns on the level of recognition accorded to the scientific principle involved, i.e., *general acceptance* in the appropriate scientific community is required. Accordingly, “[i]f there is a significant dispute between qualified experts as to the validity of scientific evidence, it may not be admitted.” *State v. Cauthron*, 120 Wn.2d 879, 887, 846 P.2d 502 (1993), *overruled in part by State v. Buckner*, 133 Wn.2d 63, 941 P.2d 667 (1997).

The “core concern” of *Frye* is “whether the evidence being offered is based on established scientific methodology[,]” and “[t]his involves *both an accepted theory and a valid technique to implement that theory.*” *Cauthron*, 120 Wn.2d at 889 (emphasis added). It is insufficient to argue, therefore, that expert opinion testimony is admissible solely because it is based on accepted scientific techniques. Not only the techniques used to

accumulate scientific data or information, but also the theory of causation arrived at, must be “generally accepted” in the scientific community. The “use of a general methodology cannot vindicate a conclusion for which there is no underlying medical support.” *Grant*, 133 Wn. App. at 180.

Appellants nonetheless argue that the trial court erred by testing the causation theory of Appellants’ experts under *Frye*. This was error according to Appellants because, in *State v. Gregory*, 158 Wn.2d 759, 829, 147 P.3d 1201 (2006), this Court noted that “[t]he primary goal [under *Frye*] is to determine ‘whether the evidence offered is based on established scientific methodology.’” (Quoting *State v. Gore*, 143 Wn.2d 288, 302, 21 P.3d 262 (2001)). See App. Br., pp 12-13. In the very next sentence, however, the *Gregory* court stated as follows:

Both the scientific theory underlying the evidence and the technique or methodology used to implement it must be generally accepted in the scientific community for evidence to be admissible under *Frye*.

158 Wn.2d at 829. The Superior Court below quoted this language verbatim, highlighting the phrase “scientific theory underlying the evidence,” and concluding that, “for expert testimony to be admissible in Washington, the party offering such evidence must show that the *causation opinion itself* is accepted.” CP 782 (emphasis supplied by court).

The trial court was correct in so holding, and Appellants misconstrue Washington law to suggest otherwise. First, *Gregory* did not hold that the only consideration under *Frye* is general acceptance of an expert's technique or methodology; to the contrary, this Court explicitly held in *Gregory* that "the scientific theory underlying the evidence . . . must be generally accepted in the scientific community . . . to be admissible under *Frye*." 158 Wn.2d at 829. Second, this is far from the only such decision. This Court has held on multiple occasions that both the underlying scientific theory and the technique or methodology employed must be generally accepted in the relevant scientific community.¹² *E.g.*, *State v. Gentry*, 125 Wn.2d 570, 585, 888 P.2d 1105 (1995) ("In Washington, there are two prongs to the *Frye* test: (1) whether the scientific theory upon which the evidence is based is generally accepted in the relevant scientific community, and (2) whether the technique used to implement that theory is also generally accepted by that

¹² Appellants argue that Washington courts are "divided" because certain Division One cases "focused primarily and/or exclusively on the methodology underlying the expert testimony," while in a Division Three case, the court "focused . . . upon the specific causation theory underlying the testimony." App. Br., p. 16. It is irrelevant whether a particular case "focused" more on one element of the *Frye* test than the other because both are required. The emphasis of a particular case serves only to indicate what aspect of the particular experts' testimony was at issue in that case. It does not indicate a "divide" among the courts. The same is true of Appellants' assertion that courts from other jurisdictions "emphasize[] methodology." App. Br., p. 15.

scientific community.”); *Riker*, 123 Wn.2d at 359 (under *Frye*, court must determine: “(1) whether the underlying theory is generally accepted in the scientific community and (2) whether there are techniques, experiments, or studies utilizing that theory which are capable of producing reliable results and are generally accepted in the scientific community”).

Two recent decisions from the Court of Appeals illustrate the application of *Frye* under directly analogous circumstances. First, in *Ruff v. Dept. of Labor and Indus.*, 107 Wn. App. 289, 28 P.3d 1 (2001), the plaintiff claimed that workplace exposure to chemicals caused her to develop a rare, blood enzyme disorder called porphyria. *Id.* at 291. Her medical experts put forth a theory of causation that porphyria was caused by short-term exposure to chemicals in ambient air. *Id.* The trial court excluded both experts under *Frye*, and Division One affirmed. In so holding, the Court of Appeals found that the plaintiff’s experts “were a distinct minority with respect to their theory that exposure to ambient chemicals in the workplace during a building remodel causes porphyria,” and that “there are no journal articles substantiating [the] theory that exposure to unquantified amounts of chemicals in the ambient air causes porphyria.” *Id.* at 302. Dr. Khattak, likewise, is in a “distinct minority.” In fact, he appears to be a minority of one. As Dr. Koren stated, no teratologist would testify to a causal connection between neuronal

migration defects and organic solvent exposure, because no such connection has ever been shown. Sub No. 106. Appellants certainly failed to identify any other scientist in the field who shares Dr. Khattak's view. Also, as in *Ruff*, there is no support for the theory that exposure to organic solvents has ever caused PMG or multicystic kidney disease.

Grant is likewise on point. The plaintiff in *Grant* claimed that his fibromyalgia was caused by an automobile accident. The trial court excluded expert opinion testimony that physical trauma causes fibromyalgia, and the Court of Appeals affirmed. In so holding, the court assessed scientific evidence submitted by both parties, which revealed a "significant dispute" in the relevant scientific community. 133 Wn. App. at 181. The court found as follows: "None of the authorities presented . . . has the effect of persuasively establishing acceptance in the relevant community as to the cause of fibromyalgia or the causal role of trauma in the development of fibromyalgia. Under *Frye*, the evidence of such a consensus is necessary for admissibility of expert opinion testimony." *Id.* at 183. Accordingly, the court affirmed, holding as follows: "*Until medical science determines with sufficient reliability and acceptance that a causal relationship exists between trauma and fibromyalgia, such evidence is inadmissible under the Frye test as adhered to in this state.*" *Id.* at 185-86 (emphasis added). Dr. Khattak is attempting to take one

study and extrapolate from it a theory of causation that both the article itself and the head scientist on the article, Dr. Koren, explicitly disclaim. As in *Grant*, medical science has not determined “with sufficient reliability and acceptance” that such a causal relationship exists. And, like in *Grant*, Dr. Khattak’s opinion should thus be excluded under *Frye*.

Finally, it should be noted that Washington is not alone in requiring that a scientific theory must be generally accepted in the relevant medical or scientific community to be admissible under *Frye*, rather than requiring that just the methodology or technique employed be generally accepted. In fact, “[m]ost courts have interpreted *Frye* as requiring general acceptance of both (1) the underlying theory supporting the scientific conclusion and, (2) the techniques and experiments employing that theory.” *People v. Shreck*, 22 P.3d 68, 73 (Colo. 2001); *see also, e.g., People v. Dalcollo*, 669 N.E.2d 378, 386 (Ill. App. Ct. 2d Dist. 1996) (“[T]he *Frye* test requires that both the theory and the techniques or procedures implementing the theory must be generally accepted in the relevant scientific community.”). Accordingly, the trial court’s suggestion that Washington is unusual in its application of *Frye*, *see* CP 780-82, is not accurate. Washington’s interpretation, and the ruling of the Superior Court, are both in keeping with other jurisdictions’ reading of *Frye*.

2. **Appellants' Theory of Medical Causation is Not Generally Accepted in the Relevant Scientific Community**

a. ***The Medical Literature Does Not Establish General Acceptance***

The trial court exhaustively reviewed the evidence put forward by Appellants, concluding that Appellants “cited only one item of medical literature that found an association between prenatal exposure to organic solvents and a child born with a neuronal migration defect,” i.e., the 1999 JAMA article. CP 785. As discussed in section B.2 of Respondents’ Statement of the Case, *supra*, the article reported the results of a prospective study, in which 13 diverse malformations, or birth defects, were observed in a group of approximately 125 women who were exposed to unspecified organic solvents, as compared to one malformation observed in a control group of unexposed women. One of the 13 observed malformations was described as a “neuronal migration defect and focal cortical dysplasia heterotopia.”¹³

The Superior Court below assessed the significance of the 1999 JAMA article in terms of establishing “general acceptance” of the causation theory put forward by Appellants’ experts, as follows:

¹³ The other 12 malformations observed in the study were not related to the brain, further highlighting the fact that the article does not link any particular condition with exposure to any particular chemical.

Because the study stated that 13 of the children born to mothers who had been exposed to organic solvents had “major malformations” and listed 13 different “major malformations,” the implication is that *only one* of the children both to mothers in the exposed group showed a neuronal migration defect. [Appellants’ causation expert] Dr. Khattak acknowledged at his deposition that PMG is found in at least 1 out of every 2,500 births, even in populations with no known organic solvent exposures. In light of the possibility that this single neuronal migration defect was the result of chance, this court would need additional information to determine whether that one event was significant.

In any event, while the 1999 JAMA study certainly suggests that exposure to organic solvents is associated with an increased risk of major malformations, it alone does not demonstrate any general consensus in the scientific community that prenatal exposure to organic solvents specifically causes PMG or any other type of neuronal migration defect. Indeed, no medical expert in this case has opined that one study that contained one finding of a particular type of birth defect would be generally relied upon by scientists to establish a cause-and-effect relationship.

CP 786-87 (emphasis supplied by court).

The trial court thus correctly held that one case of an observed association in one study does not equate to general acceptance of a theory of causation. In so finding, the trial court drew a contrast with *Berry v. CSX Transp.*, 709 So. 2d 552 (Fla. Dist. Ct. App. 1998), a case relied upon by Appellants below, and in their briefing on appeal. The court noted that, in contrast to the single study (and single association within that study) in this case, in *Berry*,

the experts relied on ‘numerous’ epidemiological studies to support their opinion that exposure to organic solvents caused a particular type of brain damage *in adults*: “The record reflects that *appellants’ proposed expert testimony was grounded upon numerous peer-reviewed and published epidemiological studies demonstrating an association between exposure to organic solvents and toxic encephalopathy.*” The court in *Berry* noted: “The validity of scientific conclusions is often based upon the replication of research findings, and consistency in these findings is an important factor in making a judgment about causation.” There was no evidence presented by [Appellants] of any such replication of the results from the 1999 JAMA article.

CP 787 (emphasis supplied by court). Finding no evidence of acceptance of Appellants’ causation theory other than the 1999 JAMA article, the trial court correctly concluded as follows: “Given the current state of medical knowledge, [Appellants] are unable to show that there is a general consensus in the medical community that birth defects of the type exhibited by Dalton Anderson are caused by prenatal exposure to organic solvents.” CP 790.

Nor is there any other support in the scientific literature for Appellants’ causation theory. Appellants point to a 2004 article that appeared in *Archives of Pediatrics and Adolescent Medicine*, entitled *Child Neurodevelopmental Outcome and Maternal Exposure to Solvents*. See App. Br. 25-26. This article, like the 1999 JAMA article, was authored by Respondents’ expert Dr. Koren. When deposed, Dr. Koren testified that this article was not evidence that organic solvents caused

neuronal migration defects, but rather identified an association with mild cognitive or language problems, which were not associated with Dalton Anderson. The trial court specifically noted Dr. Koren's testimony on this point, quoting him as follows:

“[V]ery minimal changes in some cognitive functions were shown by one group, our own group, yet not confirmed by other groups, and even for that, although we conducted the study, even that need [*sic*] more corroboration from other groups before we can prove it.”

CP 788. The article thus did not purport to establish a causal link between prenatal exposure to organic solvents and developmental malformations of the brain. Appellants also put several other medical articles before the trial court below, however, as the court found, “none of these studies showed even an association – let alone a causal relationship – between . . . exposure [to organic solvents] and neuronal migration defects, PMG, or multicystic kidney disease.”¹⁴ CP 785.

The 1999 JAMA article is thus the only medical article that reports any association between prenatal organic solvent exposure and the type of defect suffered by Dalton Anderson. The trial court held that where the only evidence supporting Appellants' theory of causation is one study, and

¹⁴ Appellants conceded in argument on the *Frye* motion below that Dalton's multicystic kidney disease was not caused by the alleged exposure of Ms. Anderson to organic compounds while working at the Akzo Nobel distributorship. Sub No. 147.

where that one study observes only one instance of a developmental malformation, that there has not been a showing of “general acceptance” in the relevant scientific medical community. Appellants have not come forward with any additional evidence of “general acceptance” on appeal. The Superior Court’s ruling excluding Appellants’ medical causation experts should be affirmed.

***b. Appellants’ Own Expert, Dr. Khattak,
Acknowledged Lack of General Acceptance for
His Theory***

As discussed in section B.1 of Respondents’ Statement of the Case, *supra*, Dr. Khattak did not dispute Respondents’ expert Dr. Dobyns’ diagnosis that the particular type of developmental brain malformation suffered by Dalton Anderson is PMG. When he was asked in his deposition whether he believed there was general acceptance in the scientific community that PMG is caused by organic solvent exposure, Dr. Khattak responded that scientific knowledge regarding PMG is “evolving” and stated: “we don’t have enough research, you’re absolutely right.” CP 635, 659. Dr. Khattak’s characterization of the state of scientific knowledge as “evolving” amounts to a tacit admission, under *Frye*, that general acceptance of his theory of causation has not taken place. Dr. Khattak may consider himself ‘ahead of the curve’ in identifying this connection, but that is precisely the type of scientific testimony that *Frye*,

with its emphasis on “general acceptance,” is designed to keep out. *See State v. Greene*, 139 Wn.2d 64, 70, 984 P.2d 1024 (1999) (inquiry under *Frye* “turns on the level of recognition accorded to the scientific principle involved”).

Similarly, Dr. Khattak submitted a new declaration late in the case, notably after the trial court’s ruling excluding him from testifying, in which he stated that his opinion is based on “theoretical risks” which are “not a stretch to imagine.” CP 830; Sub No. 141. Again, the test under *Frye* is not whether a particular scientist can “imagine” a causal link; rather, it is whether the scientific community, as a whole, *has recognized* such a link. Plaintiffs are attempting to establish in this case, through Dr. Khattak, what science has not, i.e., that organic solvents cause PMG (or neuronal migration defects, for that matter). Such links should not be made in courtrooms when they have not been made in laboratories. *See Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996) (“[T]he courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it.”). This is why *Frye* and ER 702 render such evidence inadmissible.

c. Neither the Florida Berry Decision nor Any Other Case Establishes General Acceptance

Appellants suggest that *Berry*, discussed *supra* at pp 28-29, “has already established that workplace exposure to organic solvents causes brain damage.” App. Br. at 20. First of all, findings of fact in unrelated cases are hearsay, and not directly admissible as evidence. As the Superior Court correctly noted, for the evidence adduced in *Berry* to be relevant in this case, “it would have been incumbent on [Appellants] to produce the actual scientific evidence itself, rather than relying on another court’s finding in a different case, in a different jurisdiction, that the scientific evidence in that case was sufficient to meet the *Frye* standard.” CP 829. Appellants in fact failed to come forward with any of the epidemiological studies relied upon by the court in *Berry*, or any of the other cases cited by Appellants in briefing below. *Id.*

More fundamentally, as the Superior Court correctly recognized, *Berry* “did not involve claims that brain damage which occurred during fetal development was caused by maternal exposure to organic solvents.” *Id.* What the experts in *Berry* actually testified to was that “long-term exposure to excessive levels of organic solvents can and does cause toxic encephalopathy.” 709 So. 2d at 560. Not PMG (or any other form of developmental brain malformation) and not multicystic kidney defect, i.e.,

the malformations that Dalton *actually* has. Appellants' reliance on *Berry* is misplaced.¹⁵

Finally, the *Berry* opinion ultimately supports the Superior Court's ruling by providing a useful contrast as to what must be shown to establish "general acceptance" in the relevant scientific community. In *Berry*, the plaintiffs' expert "reviewed approximately 150 journal articles," and found that "the studies correlating long-term exposure to organic solvents and toxic encephalopathy outweigh the negative studies by eight or nine to one." *Id.* at 560. Others of the plaintiff's experts provided similar opinions. Under those circumstances, the court held that it was proper for the expert to rely on epidemiological studies in reaching their opinions. In contrast, as discussed at pp 11-15 *supra*, Appellants have provided only one article showing one association of any kind, and that one article includes only one such case.

¹⁵ Appellants' reliance on *Intalco v. Dept. of Labor & Indus.*, 66 Wn. App. 644, 833 P.2d (1992), is similarly misplaced. *See* App. Br. at 26-27. Appellant make essentially the same claim regarding this case as they do regarding *Berry*, i.e., they characterize *Intalco* as "embrac[ing] the scientific principle that workplace exposure to neurotoxins (which includes organic solvents) causes brain damage." App. Br. at 26. In fact, the *Intalco* plaintiffs claimed central nervous system dysfunctions resulting from their own exposure to compounds at an aluminum plant. *Id.* at 9. There was no issue of brain damage suffered during fetal development.

d. The Law Review Article Cited by Appellants Does Not Establish General Acceptance

Appellants draw the Court's attention to a 1994 law review article: Steven S. Paskal, *Liability for Prenatal Harm in the Workplace: The Need for Reform*, 17 Puget Sound L. Rev. 283 (1994). See App. Br. at 27-28. Appellants appear to rely on this article primarily for the proposition that "medical causation in this case should have been left for the jury to determine." App. Br. at 28. In support of this conclusion, Appellants quote the article as stating that "[o]ther jurisdictions have also been very reluctant to take prenatal injury cases away from a jury on the basis of tenuous causation evidence, preferring to leave the issue to a battle of the experts." App. Br. at 27.

As with Appellants' reliance on *Berry*, this article has no bearing on whether there is general acceptance of Appellants' theory of causation under *Frye*. Appellants have made no effort to bring forward the evidence adduced in the other cases referred to by the article, nor have they made any showing that those other cases involved developmental malformations of the brain allegedly caused by prenatal exposure to organic solvents.

The article is simply irrelevant to the inquiry under *Frye*. Appellants' reference to it has a transparent motive, however. Having failed to come up with evidence under *Frye* to support their case,

Appellants are hoping the Court will simply excuse the scientific evidentiary standards normally required of Washington litigants because the case involves a congenital condition. This ploy touches on one of the primary reasons *Frye* exists: to prevent plaintiffs from creating scientific ‘links’ based on sympathy, rather than on science.

e. The MSDS Sheet Does Not Establish General Acceptance

Appellants also purport to rely on a Material Safety Data Sheet (MSDS) for a paint thinner that Appellants claim was “often used by Ms. Anderson for cleaning spills and damages [*sic*] shipments.” App. Br. at 28. As an initial matter, Appellants’ claim that Ms. Anderson “often” cleaned up paint spills and damaged shipments while pregnant is not remotely supported by the evidence in the record (with the exception of Ms. Anderson’s self-serving declaration, which was filed late in the case).

More fundamentally, however, the warning contained in the MSDS sheet is, again, irrelevant to the *Frye* inquiry. It states: “Absorption thru skin may be harmful. Studies with laboratory animals indicate this product can cause damage to fetus.” CP 483. Again, as with *Berry*, and the law review article, if Appellants purport to rely on these animal studies they must: (1) bring the actual studies before the Court; and (2) show that the studies involve the same type of malformations with which Dalton has

been diagnosed, and demonstrate a generally accepted theory that links the alleged exposure to the condition. Even taken at face value, the MSDS sheet is completely irrelevant to whether or not there is general acceptance of Appellants' causation theory in the relevant scientific community. Appellants' citation to it serves only to further highlight the absence of any real evidence supporting the causation element of their case.

f. Appellants Must Prove a Causal Link between Prenatal Organic Solvent Exposure and the Type of Malformations Suffered by Dalton Anderson, Not Some Other Condition

Finally, Appellants assert that they do not need to establish general acceptance of the theory that *in utero* exposure to organic solvents may cause PMG (or neuronal migration disorder) and multicystic kidney disease, but only need to show that such exposure may cause birth defects generally, or “encephalopathy.” App. Br. at 38-40. This is an argument that Appellants raised below *for the first time* on reconsideration of the trial court's ruling excluding Appellants' experts, as the trial court noted:

Plaintiffs' briefing and argument at the original *Frye* hearing was that Dalton's injury is a “neuronal migration defect” – a malformation of the brain that occurs during pre-birth development. Plaintiffs now disavow that argument, and instead urge the court to accept that Dalton suffers from “encephalopathy” caused by his mother's exposure to organic solvents, and to hold that the issue of whether prenatal exposure to organic solvents causes “encephalopathy” should be determined by a jury in this case.

CP 827. Appellants, having based their entire case on one theory of causation (a theory to which all of Respondents' discovery, including depositions of all of Appellants' experts, was directed) should not be permitted, after receiving an adverse ruling, to suddenly switch course.

Be that as it may, the trial court, in any event, correctly held that Appellants new argument was meritless. As the court noted, the term "encephalopathy" is "extremely broad." *Id.* It is defined by Dorland's Medical Dictionary as "any degenerative brain disease," and includes at least fourteen separate subtypes. CP 827-28. Particularly relevant in this case, these subtypes are not limited to developmental malformations of the brain. As the Superior Court found: "The one thing that all of the treating physicians and experts agree on in Dalton's case is that his cognitive defects were caused by a *developmental malformation* of his brain." CP 828 (emphasis added by court). Thus, the issue put before the court was "whether there is general acceptance in the relevant scientific community that prenatal exposure to organic solvents can cause such developmental malformations." *Id.* Merely showing an association between such exposure and "encephalopathy," held the court, is not sufficient:

There is a fundamental difference between "encephalopathy, *i.e.*, generalized organic brain damage that occurs after birth, and developmental malformations of the brain that occur during fetal development . . . While it may be entirely possible that the same chemical agent

could cause both pre-birth developmental brain malformations and generalized organic brain damage or “encephalopathy” in adults, it is clear under current Washington law that, for a case involving a developmental malformation of the brain to go to the jury, the plaintiff must produce evidence that there is general acceptance in the relevant scientific community that the chemical agent in question can cause developmental malformations, such as those with which Dalton Anderson has been diagnosed.

CP 829. The court also offered the following helpful example:

[T]he fact that there is general acceptance in the scientific community that cigarette smoking causes lung cancer diseases . . . would not translate into “general acceptance” that a mal-formed lung in a child born to a mother who smoked during pregnancy was caused by prenatal exposure to cigarette smoke. To create an issue for the jury, such a child would need to produce evidence of general acceptance in the relevant scientific community that prenatal exposure to cigarette smoke can cause malformations in a baby’s lungs.^[16]

CP 829-30.

The Superior Court was absolutely correct, and Washington case law backs up the court’s conclusions. For example, in *Ruff*, the plaintiffs

¹⁶ As another example, in *Allen v. Pennsylvania Engineering Corp.*, 102 F.3d 194 (5th Cir. 1996), the plaintiff sought to prove that the decedent’s brain cancer was caused by occupational exposures to ethylene oxide (“EtO”). The trial court barred the plaintiff’s expert’s opinion on medical causation, and the Fifth Circuit affirmed, noting that “[e]vidence has been found that suggests a connection between EtO exposure and human lymphatic and hematopoietic cancers, but this is not probative on the causation of brain cancer.” *Id.* at 197; *See also Siharath v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347, 1352 (N.D. Ga. 2001) (“There is no ‘fit’ where there is ‘simply too great [an] analytical gap between the data and the opinion offered,’ as when an expert offers animal studies showing one type of cancer in laboratory mice to support causation of another type of cancer in humans.”) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997))).

were required to show general acceptance of a theory of causation involving porphyria, a “rare, mostly hereditary disorder of blood enzymes.” 107 Wn. App. At 291. It would not have been sufficient for the plaintiffs in *Ruff* to show a causal link to blood disorders of a sort different than porphyria, i.e., the plaintiff’s actual diagnosis. Likewise, showing a link to encephalopathy does not establish general acceptance of a causal connection to developmental malformations of the brain such as neuronal migration disorder. *Grant* is also on point. In terms of specificity, the disorder at issue in that case – fibromyalgia – is more akin to a diagnosis of neuronal migration disorder or other type of developmental brain malformation than it is to encephalopathy. The equivalent category for encephalopathy in *Grant* would be something like ‘immune system disorder.’

In short, evidence supporting a high level association between organic solvent exposure and “encephalopathy,” or brain damage generally, or birth defects generally (all of which Appellants put forward at various points in their brief) is not sufficient, under *Frye*, to show “general acceptance” of the theory that prenatal exposure to organic solvents may cause developmental malformations of the brain. As discussed above, only one child in only one study has been observed with a neuronal migration defect after prenatal exposure to some unspecified

level of some unspecified organic solvent or solvents. Not surprisingly, given the paucity of data in that study, even that one article concluded that more study was necessary to determine whether there was an association between prenatal organic solvent exposure¹⁷ and malformations generally, let alone between such exposure and the particular type of malformations suffered by Dalton Anderson.

g. The Methodology Employed by Dr. Khattak was Insufficient

Appellants argue that the methodology applied by Dr. Khattak to reach his causation opinion is sufficient, focusing especially on his assessment of Ms. Anderson's symptomology. As discussed at length above, the validity of an experts' methodology alone is insufficient to establish general acceptance. As was stated in *Grant*, the "use of a general methodology cannot vindicate a conclusion for which there is no underlying medical support." 133 Wn. App. at 180.

It should also be noted, however, that the methodology applied by Dr. Khattak was, in any event, deficient. First, as discussed above, the types of malformations observed in the 1999 JAMA article study were

¹⁷ "Organic solvents" is a broad category of diverse chemical compounds, as broad as "encephalopathy" or any of the other general categories Appellants use to try to link the 1999 JAMA study to this case. It simply cannot be stretched that far.

different in type and degree than those of Dalton Anderson. As Dr. Koren noted, none of the children in the study were perceived by their families to have any sort of malformation. Sub No. 106. Nor did any of them have PMG, or multicystic kidney. Dr. Khattak's reliance on this study is thus not justified.¹⁸

Second, Dr. Khattak's assessment of Ms. Andersons' symptomology is based on a single conversation that took place only days before his deposition, i.e., well after the onset of litigation. CP 638-39. He admitted that Ms. Anderson was likely biased in her recounting of the facts, but nevertheless chose to rely on what she told him. CP 663-64. In addition, he chose to ignore the fact that her account is contradicted by her medical records.¹⁹ In particular, he based his opinion on Ms. Anderson's representation that she suffered from symptoms of organic solvent exposure while she was pregnant with Dalton, despite the fact that she reported no such symptoms to her treating physicians during her pregnancy. CP 663. *Torno v. Hayek*, 133 Wn. App. 244, 135 P.3d 536

¹⁸ Dr. Khattak's reliance on the 1999 JAMA article is also flawed because all of the supporting data for the study was lost, making comparison with Dalton's condition impossible. CP 628. It would be fundamentally unfair to allow him to testify on the basis of the study when the defense has been denied access to the underlying data.

¹⁹ This is in marked contrast to the methodology employed in the 1999 JAMA study, which entailed reviewing medical records and obtaining written medical surveys from the study subjects. CP 231.

(2006), is on point. The plaintiff's expert in that case offered testimony that the plaintiff's temporomandibular jaw condition was caused by two car accidents "because it was based exclusively on [the plaintiff]'s recollection that the condition was fixed and stable before the accidents," and the expert had not reviewed her medical records. *Id.* at 250. That expert was not allowed to testify. The parallel to Dr. Khattak's reliance on Ms. Anderson's recollection to the exclusion of her medical records is exact.

Third, Dr. Khattak admitted that quantification of the concentration of organic solvent necessary to raise exposure to toxic levels is a "missing piece of [the] puzzle," i.e., there is no scientific information available to quantify the concentration necessary to cause malformations generally, even if one ignores the specific conditions at issue here. CP 632. That admission alone should render his opinion inadmissible under *Frye*.

Fourth, Dr. Khattak ruled out genetics as a possible cause of Dalton's medical issues, even though he testified that he does not consider himself qualified in this area, and has not consulted with a geneticist. CP 623, 660. Dr. Khattak's cavalier dismissal of genetics as a cause is flatly contradicted by the testimony of Respondents' genetics expert Dr. Dobyms, who expressed the opinion that Dalton's birth defects were most likely genetic. Unlike Dr. Khattak's suspect methodology, Dr. Dobyms

relied on his observation of Dalton's MRI, which showed distinctive features of PMG, and on the presence of Dalton's multicystic dysplastic kidney, which, like PMG, is a known genetic condition. Sub No. 106; CP 788-89.

In short, there is ample reason to find Dr. Khattak's methodology insufficient and unreliable under *Frye*, independent of the Superior Court's finding that his theory of causation lacks "general acceptance" in the relevant scientific community. However, it bears emphasis that *Frye* requires general acceptance of both the technique or methodology applied, and the underlying theory. In the absence of general acceptance of either, an expert is properly barred under Washington law from giving an opinion regarding novel scientific evidence.

3. **This Case Demonstrates the Wisdom of *Frye* and Why it Should Remain the Law of Washington**

Appellants ask this Court to abandon the *Frye* test, arguing that it is "antiquated and virtually impossible to apply with any degree to reasonableness or predictability." App. Br. at 42-43. As this Court held in *State v. Copeland*, 130 Wn.2d 244, 258, 922 P.2d 1304 (1996), however, any difficulty in applying the *Frye* test arises not from the test itself, but from the science at issue in a particular case, which would be the same for any test:

The State maintains that this court should abandon *Frye* and adopt *Daubert*. The State argues that *Frye* is difficult to apply. While *Frye* may be difficult to apply in some contexts, this is a result of the complexity of the particular science at issue, the extent to which the scientific community has made its views known, and the extent of any dispute in the scientific community. The same, or similar problems, arise under *Daubert* . . . Nevertheless, the *Frye* standard has endured for over 70 years, indicating that it has not been so difficult to apply as to call for its abandonment.

Nothing about this case sheds a new or different light on the enduring validity of *Frye*. Indeed, this case is a testament to the wisdom of Washington courts in adopting *Frye*.

C. Appellants' Third Assignment of Error: the Superior Court's Dismissal of Appellants' Claim for Retaliatory Discharge

Appellants assert as their third, and final, assignment of error that the Superior Court “erred in dismissing Ms. Anderson’s retaliatory discharge claim when ruling that Ms. Anderson was required to follow RCW 4.16.160 prior to bringing a private cause of action for a retaliatory discharge.” App. Br. at 4. The ruling complained of is the Superior Court’s dismissal of Appellants’ common law claim of wrongful discharge in violation of public policy. Sub No. 48.

Appellants claim that the Superior Court failed to follow binding precedent from Division One of the Court of Appeals, *Wilson v. City of Monroe*, 88 Wn. App. 113, 943 P.2d 1137 (1997). See App. Br. at 43-44.

This is simply a misrepresentation of the Superior Court's order, which expressly relies on a decision of the Washington Supreme Court decision that post-dates *Wilson: Korslund v. Dyncorp Tri-Cities Servs., Inc.*, 156 Wn. 2d 168, 125 P.3d 119 (2005). The court's order provided, in relevant part, as follows:

In *Korslund*, the Supreme Court held that the common law tort of wrongful retaliation in violation of public policy was not available because there were adequate statutory remedies in the administrative procedures established by the Energy Reorganization Act of 1974 ("ERA") 42 U.S.C. § 5851 . . .

The Supreme Court observed that to establish the common law tort of wrongful discharge in violation of public policy, a claimant must prove that discouraging the disclosure of unlawful employment practices would jeopardize that public policy. Further, a plaintiff must show that other means of promoting the public policy are inadequate . . .

[Appellants] here argue that *Korslund* is not dispositive of this wrongful discharge claim because the administrative remedies available through [WISHA] do not adequately address the public policy element at issue . . .

However, a comparison of the ERA and WISHA procedures show that each statute provides for an administrative process for those claimants who believe that they had been wrongfully discharged . . . [B]oth statutory schemes provide a legislatively determined means to promote and protect the public policy against wrongful discharge. It appears that the legislature, in enacting [WISHA], established a process that provided an adequate means to preserve and protect the public policy against unlawful employment terminations.

Sub No. 48. The Superior Court thus recounted the holding in *Korslund*, expressly considered and rejected Appellants' argument that *Korslund* was not dispositive, and then held as follows:

Because the administrative procedures of RCW 49.17.160 adequately provided an alternate means to promote and safeguard the public and because Anderson chose to ignore this statutory remedy, she cannot now argue that public policy against wrongful discharge is threatened if her common law tort claim is not recognized.

Sub No. 48. Simply because the trial court did not agree with Appellants' argument concerning whether *Korslund* was controlling does not mean that the court disregarded controlling precedent.

Nor are Appellants correct in asserting that the Superior Court held that RCW 49.17.060 provides an exclusive remedy for a claim of wrongful discharge allegedly in retaliation for reporting a WISHA violation. The trial court found that the statutory scheme "provided an adequate means to preserve and protect the public policy against unlawful employment terminations," and held, following *Korslund*, that, because Ms. Anderson had chosen to ignore the statutory policy, she could not argue that public policy against wrongful discharge would be threatened if her common law tort claim was not recognized. Sub No. 48. The issue was not one of the exclusivity of the statutory scheme, but rather one of adequacy.

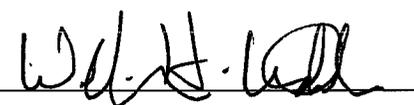
Because the exclusivity of the statutory scheme was not at issue in this case, but only its adequacy in light of Ms. Anderson's choice to ignore her statutory remedy, the issue identified by Appellants is not before this Court on appeal. In any event, the Superior Court's ruling, and reliance on *Korshund*, was correct, and should be affirmed.

CONCLUSION

For all the foregoing reasons, Respondents respectfully request that this Court affirm the decisions of the King County Superior Court.

RESPECTFULLY SUBMITTED this 17th day of February, 2009.

CORR CRONIN MICHELSON
BAUMGARDNER & PREECE LLP

By 

Kelly P. Corr

WSBA No. 00555

Steven W. Fogg

WSBA No. 23528

William H. Walsh

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CORR CRONIN MICHELSON
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RECEIVED
SUPREME COURT
STATE OF WASHINGTON

CERTIFICATE OF SERVICE

2009 FEB 17 P 2:55

The undersigned declares as follows:

BY RONALD R. CARPENTER

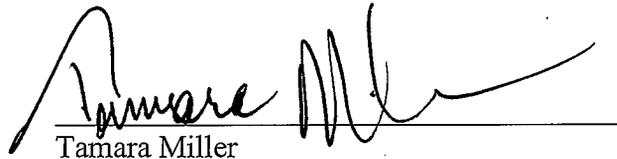
1. I am employed at ~~Corr Cronin Michelson Baumgardner & Preece LLP~~, attorneys of record for defendant Akzo Nobel Coatings Inc.

2. On this date I caused true and correct copies of the foregoing document to be served on counsel below via hand delivery:

Lincoln Beauregard
John R. Connelly, Jr.
Law Offices of John R. Connelly, Jr.
2301 N. 30th Street
Tacoma, WA 98403

I declare under penalty of perjury under the laws of the State of Washington that the foregoing is true and correct.

DATED this 17th day of February, 2009, at Seattle, Washington.



Tamara Miller

RECEIVED
SUPREME COURT
STATE OF WASHINGTON

No. 82264-6 2009 FEB 17 P 2:55

BY RONALD R. CARPENTER
IN THE SUPREME COURT
OF THE STATE OF WASHINGTON
CLERK

JULIE ANDERSON, individually and on behalf of the Estate of
DALTON ANDERSON, and DARWIN ANDERSON individually,

Appellants

v.

AKZO NOBEL COATINGS, INC., and KEITH CROCKETT,

Respondents

**APPENDIX OF NON-WASHINGTON AUTHORITIES
SUPPORTING BRIEF OF RESPONDENTS**

Kelly P. Corr
WSBA No. 00555
Steven W. Fogg
WSBA No. 23528
William H. Walsh
WSBA No. 21911
CORR CRONIN MICHELSON
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ORIGINAL

Respondents and Defendants below Akzo Nobel Coatings, Inc. and Keith Crockett respectfully submit the following non-Washington authorities in support of Respondents' Brief:

CASES

Allen v. Pennsylvania Engineering Corp., 102 F.3d 194 (5th Cir. 1996)

Berry v. CSX Transp., 709 So. 2d 552 (Fla. Dist. Ct. App. 1998)

Frye v. United States, 293 F. 1013 (D.C. Cir. 1923)

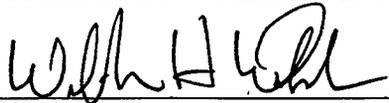
People v. Dalcollo, 669 N.E.2d 378 (Ill. App. Ct. 2d Dist. 1996)

People v. Shreck, 22 P.3d 68 (Colo. 2001)

Siharath v. Sandoz Pharms. Corp., 131 F. Supp. 2d 1347 (N.D. Ga. 2001)

RESPECTFULLY SUBMITTED this 17th day of February, 2009.

CORR CRONIN MICHELSON
BAUMGARDNER & PREECE LLP

By 

Kelly P. Corr
WSBA No. 00555

Steven W. Fogg
WSBA No. 23528

William H. Walsh
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CERTIFICATE OF SERVICE

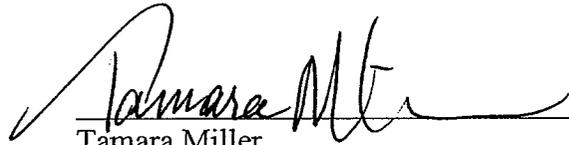
The undersigned declares as follows:

1. I am employed at Corr Cronin Michelson Baumgardner & Preece LLP, attorneys of record for defendant Akzo Nobel Coatings Inc.
2. On this date I caused true and correct copies of the foregoing document to be served on counsel below via hand delivery:

Lincoln Beauregard
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Tacoma, WA 98403

I declare under penalty of perjury under the laws of the State of Washington that the foregoing is true and correct.

DATED this 17th day of February, 2009, at Seattle, Washington.



Tamara Miller



LEXSEE 102 F3D 194

Walter Mixon ALLEN, Jr., et al., Plaintiffs, Mattie Gayle Allen, Barry Lane Allen, Plaintiffs-Appellants, v. PENNSYLVANIA ENGINEERING CORP., et al., Defendants, American Sterilizers Company, Defendant-Appellee.

No. 96-30209.

UNITED STATES COURT OF APPEALS FOR THE FIFTH CIRCUIT

102 F.3d 194; 1996 U.S. App. LEXIS 33975; 46 Fed. R. Evid. Serv. (Callaghan) 215; CCH Prod. Liab. Rep. P14,832

December 31, 1996, Decided

SUBSEQUENT HISTORY: [**1] The Name of this Case has been Corrected by the Court December 31, 1995. The Name of this Case has been Corrected by the Court January 23, 1997.

PRIOR HISTORY: Appeal from the United States District Court for the Middle District of Louisiana. 91-CV-562-B. Frank J Polozola, US District Judge.

DISPOSITION: AFFIRMED.

COUNSEL: For MATTIE GAYLE ALLEN, BARRY LANE ALLEN, Plaintiff - Appellant: Edward J Walters, Jr, Moore, Walters, Shoenfelt & Thompson, Baton Rouge, LA. Keith Patrick Richards, Moore, Walters, Shoenfelt & Thompson, Baton Rouge, LA.

For AMERICAN STERILIZERS COMPANY, Defendant - Appellee: Bert L Wolff, Skadden, Arps, Slate, Meagher & Flom, New York, NY. Judith R Atkinson, Thomas E Balhoff, Roedel, Parsons, Hill & Koch, Baton Rouge, LA.

JUDGES: Before WISDOM, JONES and WIENER, Circuit Judges.

OPINION BY: EDITH H. JONES

OPINION

[*195] EDITH H. JONES, Circuit Judge:

Walter Allen died of a brain cancer known as glioblastoma multiforme after having been a maintenance worker at Baton Rouge General Hospital for over

20 years. During that time, he occasionally replaced cylinders containing ethylene oxide ("EtO"), a chemical that has been widely used in this country to sterilize heat and moisture sensitive medical and surgical devices. Allen's widow and son (the "Allens") filed suit against numerous defendants, including American Sterilizer Company, the manufacturer of EtO sterilizers. On motions for judgment as a matter of law, the district court held both that two of the Allens' three expert witnesses were not qualified to render opinions that exposure to EtO caused Allen's fatal cancer and that the opinions of all three experts were inadmissible in federal court for lack of sufficient scientific grounding.

We affirm. Where, as here, no epidemiological study has found a statistically significant link between EtO exposure and human brain cancer; the results [**2] of animal studies are inconclusive at best; and there was no evidence of the level of Allen's occupational exposure to EtO, the expert testimony does not exhibit the level of reliability necessary to comport with *Federal Rules of Evidence 702* and *703*, the Supreme Court's *Daubert* decision,¹ and this court's authorities. Moreover, under the circumstances of this case, [*196] the fact that EtO has been classified as a carcinogen by agencies responsible for public health regulations is not probative of the question whether Allen's brain cancer was caused by EtO exposure.

¹ *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993).

This court reviews the judgment as a matter of law on two levels. First we must evaluate the trial court's evidentiary ruling under the manifest error standard, and

then, with the record defined, we review *de novo* the order granting judgment as a matter of law. *Christophersen v. Allied-Signal Corp.*, 939 F.2d 1106, 1109 (5th Cir.1991) (en [*3] banc), cert. denied, 503 U.S. 912, 112 S. Ct. 1280, 117 L. Ed. 2d 506 (1992). If the trial court has excluded evidence essential to maintain a cause of action, the propriety of summary judgment depends, as here, entirely on the evidentiary ruling. *Id.*

In *Daubert*, the Supreme Court meticulously explained the criteria for admitting expert scientific testimony pursuant to *Federal Rule of Evidence 702*:

Proposed testimony must be supported by appropriate validation--i.e., "good grounds," based on what is known ... The requirement that an expert's testimony pertained to "scientific knowledge" establishes a standard of evidentiary reliability. (footnote omitted) *Daubert*, 509 U.S. at 590, 113 S. Ct. at 2795.

Further, the Court held that a trial court has a duty to screen expert testimony for both its relevance and reliability. *Id.* An expert's opinion must have a "reliable basis in the knowledge and experience of his discipline." 509 U.S. at 592, 113 S. Ct. at 2796. Specifically, the court must determine that the reasoning and methodology underlying the testimony is scientifically valid and that the reasoning and methodology can properly be applied to [*4] the facts in issue. 509 U.S. at 592-93, 113 S. Ct. at 2796.

The Court added that under *Rule 703*, an expert must base his opinion on facts and data of a type reasonably relied on by experts in the field. *Id.* at 595, 113 S. Ct. at 2797-98.

Although the trial court wrote a cursory opinion on the admissibility of Allen's expert evidence, the parties developed a considerable record, and the court heard oral argument before rendering a decision that the experts' evidence, testimony and opinions did not satisfy the standards set forth in *Daubert* or relevant authorities of this Court. Those standards may readily be applied to the evidence before us.

Appellants produced three expert witnesses, Dr. Page, Dr. Kelsey and now--Dr. LaMontagne,² whose opinions may be summarized as follows. First, human epidemiological evidence "suggests" an association between EtO exposure and an increased risk of brain cancer. Second, scientific studies conducted on rats have shown EtO capable of causing tumors in certain of those animals. Third, EtO is known as a mutagen and genotoxin. Consequently, these witnesses theorize, EtO

reaches brain tissue, alkylates DNA and "clearly" causes animal brain tumors. [*5] The experts employ a "weight of the evidence" analysis used by organizations such as the World Health Organization's International Agency for Research on Cancer (IARC), OSHA, and the EPA to rate the carcinogenicity of various substances in humans. We will examine each of the types of evidence on which appellants' experts rely: epidemiological studies, animal studies, cell biology, and health organization conclusions. We must also consider the "weight of the evidence" methodology.

2 Dr. Anthony LaMontagne and Dr. Norbert Page each hold master's degrees in toxicology. At the time of his deposition for trial, Dr. LaMontagne, who had not yet received his doctorate degree, had written a doctoral dissertation concerning the medical surveillance of hospital employees exposed to EtO in Massachusetts. Dr. LaMontagne now has an Sc.D. in Occupational and Environmental Health, and is a research fellow at the Harvard School of Public Health, with a research emphasis on the implementation of OSHA requirements for exposure monitoring and worker training as preventive measures for EtO exposure in Massachusetts hospitals. Dr. Page is a doctor of veterinary medicine, who provides expert consultation on chemical and radiation toxicology. Dr. Karl Timothy Kelsey is a medical doctor and Assistant Professor of Occupational Medicine at the Harvard School of Public Health. He has received several grants to study the effect of EtO on humans and primates.

[*6] [*197] First, although occupational exposure to EtO has been studied for many years, not a single scientific study has revealed a link between human brain cancer and EtO exposure. In fact, numerous reputable epidemiological studies covering in total thousands of workers indicate there is not a correlation between EtO exposure and cancer of the human brain. See, e.g., L. Stayner, et al., *Exposure-Response Analysis of Cancer Mortality in a Cohort of Workers Exposed to Ethylene Oxide*, 138 Am.J.Epid. 787, 797 (1993) (concluding that the study's "findings do not provide evidence for a positive association between exposure to [EtO] and cancers of the ... brain..."). The National Institute for Occupational Safety and Health ("NIOSH") conducted this study. This analysis follows the prior published epidemiological study by the same NIOSH researchers. See K. Steenland, et al., *Mortality Among Workers Exposed to Ethylene Oxide*, 324 N.E.J.Med. 1402 (1991). Evidence has been found that suggests a connection between EtO exposure and human lymphatic and hematopoietic cancers, but this is not probative on the causation of brain cancer.³ This court has said that:

Undoubtedly, [**7] the most useful and conclusive type of evidence in a case such as this is epidemiological studies. *Brock v. Merrill-Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 311 (5th Cir.1989), modified by 884 F.2d 166 (5th Cir.1989), cert. denied, 494 U.S. 1046 [110 S. Ct. 1511, 108 L. Ed. 2d 646] (1990).

While appellants' experts acknowledge the lack of statistically significant epidemiological evidence, they rely on certain studies as "suggestive" of a link between EtO exposure and brain cancer. "Suggestiveness" is not by the experts' own admission statistical significance, nor did the appellants' experts show why and how mere "suggestiveness" scientifically supports a causal connection; this basis for their scientific opinion must be rejected.⁴

3 See, e.g., *Lust v. Merrell Dow Pharmaceuticals*, 89 F.3d 594, 597-98 (9th Cir.1996) (holding that an expert's reasoning, which concluded from the fact that the drug in question caused some types of birth defects that it also caused hemifacial microsomia, was not scientific). The *Lust* court noted that the expert's testimony "was influenced by litigation-driven by financial incentive" and that the expert's premise was not recognized by even a "relevant minority." *Id.*

[**8]

4 Courts should particularly pay close attention when expert witnesses depart from generally accepted scientific methodologies. As the Seventh Circuit noted in *Braun v. Lorillard Inc.*, 84 F.3d 230 (7th Cir.1996), cert. denied, No. 96-377, 1996 WL 526463 (U.S. Nov. 18, 1996), "A judge or jury is not equipped to evaluate scientific innovations. If, therefore, an expert proposes to depart from the generally accepted methodology of his field and embark upon a sea of scientific uncertainty, the court may appropriately insist that he ground his departure in demonstrable and scrupulous adherence to the scientist's creed of meticulous and objective inquiry." *Id.* at 235.

Second, the experts rely on two studies that found brain tumors in F-344 rats exposed to inhaled EtO, and on other animal studies that have found EtO-associated increases in the rodents' various solid and hematopoietic cancers. In *Brock*, this court noted "the very limited usefulness of animal studies when confronted with questions of toxicity." *Brock*, 874 F.2d at 313. *Brock* goes on to outline a number of reasons [**9] why studies of the effects of chemicals on animals must be carefully quali-

fied in order to have explanatory potential for human beings. So it is here. Although in these particular studies, F-344 rats contracted brain cancer after being exposed to EtO, Allen's experts concede that the same effect did not occur in mice studies. As an expert for appellee concludes:

Thus, the lack of capacity for the F-344 rat to predict how even the mouse model responds necessarily undercuts confidence that the rat will predict accurately how other species including humans will respond [to EtO exposure].

Reliance on these animal studies furnishes at best speculative support for appellants' causation theory.⁵

5 In support of the use of animal studies to establish medical causation, the Allens have cited *In re Paoli R.R. Yard PCB Litigation*, 35 F.3d 717 (3d Cir.1994), cert. denied sub nom. *General Elec. Co. v. Ingram*, U.S. , 115 S. Ct. 1253, 131 L. Ed. 2d 134 (1995), in which the Third Circuit held that the animal studies relied on by the plaintiffs in that case passed *Daubert* muster. 35 F.3d 717 at 781. However, the *Paoli* court recognized that other cases have held animal studies inadmissible, and distinguished *Paoli* as a case in which the EPA had ruled that the substance in question was a probable human carcinogen, there was "reason to think that [these] animal studies are particularly valuable because animals react similarly to humans with respect to the chemical in question," and the epidemiological data was inconclusive, with some of it supporting a finding of causation. *Id.* at 780-81. In the instant case, in contrast, we note that the animal studies relied on by the plaintiffs are unreliable, and the epidemiological evidence clearly does not support a finding of causation. In any case, *Paoli* is not binding on this court and we do not adopt its reasoning.

[**10] [*198] Third, the cell biology data show only that EtO has mutagenic and genotoxic capabilities in living organisms, not that it necessarily causes brain cancer in humans or in Allen's particular case. That EtO may have these effects on living cells or genes is the beginning, not the end of the scientific inquiry and proves nothing about causation without other scientific evidence.

On examination, none of the scientific data on which appellants' experts rely furnishes a scientifically valid basis for the conclusion they would draw. The paucity of

epidemiological evidence, the unreliability of animal studies, and the inconclusiveness of cell biology combine to undercut the expert testimony.

We are also unpersuaded that the "weight of the evidence" methodology these experts use is scientifically acceptable for demonstrating a medical link between Allen's EtO exposure and brain cancer. Regulatory and advisory bodies such as IARC, OSHA and EPA utilize a "weight of the evidence" method to assess the carcinogenicity of various substances in human beings and suggest or make prophylactic rules governing human exposure. This methodology results from the preventive perspective that the agencies [**11] adopt in order to reduce public exposure to harmful substances. The agencies' threshold of proof is reasonably lower than that appropriate in tort law, which "traditionally makes more particularized inquiries into cause and effect" and requires a plaintiff to prove "that it is more likely than not that another individual has caused him or her harm." *Wright v. Willamette Industries, Inc.*, 91 F.3d 1105, 1107 (8th Cir.1996). In addition, in this case, the public health agencies acted at least partly on the basis of epidemiological studies that showed a relationship between EtO exposure and other kinds of human cancer, so their use of a "weight of the evidence" methodology was grounded in stronger probative evidence than appellants' experts have adduced to show a link between EtO annclusion at best weakly supported, if not contradicted, by the evidence on which they rely, but they all declined to say that they would subject their findings to the test of peer review for publication. *Daubert* notes that this is "a component of 'good science' in part because it increases the likelihood that substantive flaws in methodology will be detected." *Daubert*, 509 U.S. at 593, 113 S. [**12] Ct. at 2797 (1993). Dr. LaMontagne, in fact, inadvertently described exactly the problem this court faced in evaluating his and appellants' other expert testimony:

This is not a scientific study. This is a legal opinion. [Dr. LaMontagne Deposition at 187, lines 14-15.] *Pace* Dr. LaMontagne.

The goal of *Daubert* and this court's previous cases has been to bring more rigorous scientific study into the expression of legal opinions offered in court by scientific and medical professionals. In the absence of scientifically valid reasoning, methodology and evidence supporting these experts' opinions, the district court properly excluded them.

An additional ground for excluding the opinions lies in *Federal Rule of Evidence* 703, which requires that the facts on which the expert relies must be reasonably relied

on by other experts in the field. In this case, there is no direct evidence of the level of Allen's exposure to EtO. The Kelsey/LaMontagne opinion relies principally on the affidavit of a coworker and on extrapolations concerning EtO handling at the hospital where Allen worked based on conditions in other hospitals in the 1970's. The experts actually knew more [**13] about Allen's exposure to EtO through his smoking a pack of cigarettes a day than they did about his occupational exposure to the chemical. Nevertheless, Dr. Kelsey and Dr. LaMontagne discounted the effect of tobacco, while speculating that the [*199] workplace exposure was the cause of his brain cancer. ⁶ Scientific knowledge of the harmful level of exposure to a chemical, plus knowledge that the plaintiff was exposed to such quantities, are minimal facts necessary to sustain the plaintiffs' burden in a toxic tort case. *See Wright*, 91 F.3d at 1107. Not only was the scientific knowledge absent, but the experts' background information concerning Allen's exposure to EtO is so sadly lacking as to be mere guesswork. The experts did not rely on data concerning Allen's exposure that suffices to sustain their opinions under R. 703. *See Christophersen v. Allied-Signal Corp.*, 939 F.2d 1106, 1114-1115 (5th Cir.1991) (en banc), cert. denied, 503 U.S. 912, 112 S. Ct. 1280, 117 L. Ed. 2d 506 (1992) (holding that the district court did not abuse its discretion in excluding an expert's opinion that was based on insufficient data regarding the dosage of a harmful substance and the duration of [**14] exposure to that substance); *Viterbo v. Dow Chemical Co.*, 826 F.2d 420, 423 (5th Cir.1987) (concluding that evidence from animal studies is insufficient based in part on the lack of evidence that the plaintiff was exposed to comparable amounts). *See also Wright*, 91 F.3d at 1107-08 (holding expert opinions inadmissible in the absence of evidence of exposure to toxic substance).

6 The Eighth Circuit was faced with a similar issue. In *Sorensen v. Shaklee Corp.*, 31 F.3d 638 (8th Cir.1994), the district court in a suit alleging that EtO exposure had caused mental retardation in the plaintiff had criticized an expert witness for, among other things, failing to establish that "no other agent containing ETO, such as ... cigarette smoking, could be a cause." *Id.* at 649. The district court went on to find that the expert's method was therefore "subject to great potential for error." *Id.* The Eighth Circuit expressly approved the district court's observations and concluded that it had properly held the expert testimony inadmissible. *Id.* at 650.

[**15] The other issue on appeal was whether the district court erred in finding that Dr. LaMontagne (who at the time of his expert deposition had not yet obtained his Sc.D.) and Dr. Norbert Page (D.V.M.) were not

102 F.3d 194, *; 1996 U.S. App. LEXIS 33975, **;
46 Fed. R. Evid. Serv. (Callaghan) 215; CCH Prod. Liab. Rep. P14,832

qualified to testify as experts on the issue of medical causation in this case. We need not decide this issue, as the testimony of all three experts is in any event inadmissible.

CONCLUSION

For the foregoing reasons, the judgment of the district court is AFFIRMED.



LEXSEE 709 SO 2D 552

CAROL BERRY, as personal representative of the Estate of Roy Lee Berry, Jr., deceased, Appellant, v. CSX TRANSPORTATION, INC., Appellee. JAMES CHRISCO, Appellant, v. CSX TRANSPORTATION, INC., Appellee.

CASE NO.: 95-3131, CASE NO.: 95-3618

COURT OF APPEAL OF FLORIDA, FIRST DISTRICT

709 So. 2d 552; 1998 Fla. App. LEXIS 2243; 23 Fla. L. Weekly D 686

March 3, 1998, Opinion Filed

SUBSEQUENT HISTORY: [**1] As Corrected. Released for Publication March 19, 1998. Petition for Review Denied July 2, 1998, reported at: 1998 Fla. LEXIS 1339.

PRIOR HISTORY: An appeal from the Circuit Court for Duval County. Michael Weatherby, Judge.

DISPOSITION: REVERSED and REMANDED for further proceedings consistent with this opinion.

COUNSEL: Joel D. Eaton of Podhurst, Orseck, Josefsberg, Eaton, Meadow, Olin & Perwin, P.A., Miami; Korn, Zehmer & Gellatly, P.A., Jacksonville (Berry); Lane & Gossett, P.C., Brunswick, Georgia (Berry); The Beckham Firm, Jacksonville (Chrisco); Gary F. Easom of Easom & Pierce, Jacksonville (Chrisco), for Appellants.

Joseph P. Milton and Eric L. Leach of Milton, Leach & D'Andrea, P.A., Jacksonville; Robert P. Smith and James C. Goodlett of Hopping Green Sams & Smith, Tallahassee, for Appellee.

JUDGES: VAN NORTWICK, J., JOANOS AND PADOVANO, JJ., CONCUR.

OPINION BY: VAN NORTWICK

OPINION

[*554] VAN NORTWICK, J.

In these consolidated appeals, James Chrisco and Carol Berry, as personal representatives of the Estate of Roy Lee Berry, Jr., deceased, appeal from a final judgment

and a partial final summary judgment,¹ respectively, which were entered after the trial court excluded the testimony of appellants' expert witnesses. In their actions brought pursuant [**2] to the Federal Employers' Liability Act, 45 U.S.C. § 51, et. seq. (FELA), appellants allege that appellee, CSX Transportation, Inc., exposed Berry and Chrisco, railroad employees of CSX, to excessive levels of organic solvents causing them to suffer from toxic encephalopathy.² In both cases, asserting that the expert opinions were not generally accepted in the scientific community and relying upon *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013 (D.C. Cir. 1923), and its Florida progeny, CSX objected to the proposed expert testimony that long-term exposure to excessive levels of organic solvents can and did cause appellants' toxic encephalopathy. The record reflects that appellants' proposed expert testimony was grounded upon numerous peer-reviewed and published epidemiological studies demonstrating an association between exposure to organic solvents and toxic encephalopathy.³ The trial court nevertheless found that the proposed expert opinions were not based on a "scientific principle or discovery" that has been sufficiently established to have gained general acceptance in the particular field to which it belongs. Accordingly, by separate orders, the trial court disqualified [**3] all of the appellants' experts.

1 There remains pending below a suit on behalf of Roy Lee Berry, Jr., for injuries due to alleged exposure to excessive levels of asbestos.

2 Toxic encephalopathy occurs when there has been an alteration to the brain and central nervous system function due to exposure to various toxins. See generally Neil L. Rosenberg, M.D., Occupational and Environmental Neurology, 116-17 (1995)(herein Occupational and Environmental

Neurology). As explained in William N. Rom, M.D. (ed.) *Environmental and Occupational Medicine* at 849 (1992):

The nonspecific effects of long-term exposure to solvents range from a general negative affective state to a subtle reduction in functional reserve capacity to perform well when fatigued or in a distracting environment, to mild slowing of psycho-motor performance, to memory disturbance, and finally to severe intellectual deficits. The most severe condition, which has been called psycho-organic syndrome, presenile dementia, and severe chronic toxic encephalopathy, is also the most controversial. Although the existence of chronic solvent encephalopathy has been questioned, experts now generally agree that it occurs but not on its prevalence.

(Footnotes deleted).

[**4]

3 Some, but by no means all, of the studies relied upon by appellants' experts are set forth in "Appendix A."

This is the first time a Florida appellate court has been asked to decide the issue of what evidence must be Frye tested in the context of toxic tort litigation. We commend the trial court for its thorough and exhaustive review of the proposed expert testimony. We believe, however, that the trial court went beyond addressing the threshold question of admissibility of expert testimony under Frye, which was the issue before it, and in effect engaged in an analysis of the weight to be assigned to the expert testimony or the sufficiency of the evidence. As a result, even though appellants adequately demonstrated the reliability of their experts' proposed testimony, the trial court erroneously ruled that testimony inadmissible. Thus, we reverse the final judgment and partial final judgment [*555] and remand these actions for proceedings consistent with this opinion.

Procedural Background

Roy Lee Berry, Jr., deceased, worked as an electrician for CSX for over 20 years. James Chrisco [**5] worked as a machinist for CSX for over 10 years. Their suits alleged exposure to unreasonably hazardous levels of organic solvents in their workplace at CSX. The four organic solvents at issue in this case are trichloroethane (TCA), trichloroethylene (TCE), perchloroethylene (PCE), and mineral spirits. The trial court conducted a lengthy evidentiary hearing in Berry's suit in connection with CSX's motion to disqualify the opinion testimony of Berry's treating physician, Michael Kelly, M.D. In support of Dr. Kelly's proposed testimony, Berry proffered the supporting testimony of several other expert wit-

nesses. CSX also filed a similar motion in the Chrisco suit. Although the trial court entered separate orders disqualifying the expert testimony in each case, the court considered essentially the same evidence in both cases. Thus, for purposes of this appeal, the evidence and cases will be considered together.

The Frye Reliability Standard

The issue of the admissibility of expert testimony is governed by the Florida Evidence Code, *section 90.702, Florida Statutes* (1995). That section provides:

Testimony by experts. - If scientific, technical, or other specialized [**6] knowledge will assist the trier of fact in understanding the evidence or in determining a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education may testify about it in the form of an opinion; however, the opinion is admissible only if it can be applied to evidence at trial.

Like its federal counterpart, *Federal Rule of Evidence 702, section 90.702* is "silent as to any requirement that there be general acceptance of a newly developed scientific technique or principle in the particular field in which it belongs." *Hawthorne v. State*, 470 So. 2d 770, 783 (Fla. 1st DCA 1985) (Ervin, J., concurring and dissenting). This "general acceptance" test applied to scientific evidence had been espoused decades earlier in the case of *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013 (D.C. Cir. 1923). The Frye court succinctly stated the test as follows:

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 force of the principle must be recognized, and while courts will go a long way in admitting expert [**7] 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.

293 F. at 1014.

After the adoption of the Florida Evidence Code, of which *section 90.702* is part, disagreement arose among the district courts of appeal as to whether (i) the relevancy test under *section 90.702* combined with the so-called balancing test of *section 90.403* or (ii) the Frye test was to be applied to determine the admissibility of novel scientific evidence. See *Hawthorne*, 470 So. 2d at 783-787 (Ervin, J., concurring and dissenting; see also Ehrhardt, *Florida Evidence*, § 702.3 at 526 & 528 n.18 (1997). This debate ended when the Florida Supreme Court decided *Stokes v. State*, 548 So. 2d 188 (Fla. 1989).

In *Stokes*, the Florida Supreme Court held that post-hypnotic testimony may not be admitted unless it meets the Frye test. *Stokes*, 548 So. 2d at 194-95. "This test requires that the scientific principles undergirding this evidence be found by the trial court to be generally accepted by the relevant members [**8] of its particular field." *Hadden v. State*, 690 So. 2d 573, 576 (Fla. 1997). In reaching its conclusion in *Stokes*, the Court explained its rationale for continuing the application of the Frye test:

The underlying theory for this rule [Frye] is that a courtroom is not a laboratory, and as such it is not the place to conduct scientific experiments. If the scientific community considers a procedure or process unreliable for its own purposes, then [*556] the procedure must be considered less reliable for courtroom use.

Stokes, 548 So. 2d at 193-94.

Later, in *Hadden*, the court further amplified the reasons supporting its allegiance to the Frye reliability test:

We firmly hold to the principle that it is the function of the court to not permit cases to be resolved on the basis of evidence for which a predicate of reliability has not been established. Reliability is fundamental to issues involved in the admissibility of evidence. It is this fundamental concept which similarly forms the rules dealing with the admissibility of hearsay evidence. . . . Novel scientific evidence must also be shown to be reliable on some basis other than simply that it is [**9] the opinion of the witness who seeks to offer the opinion.

Hadden, 690 So. 2d at 578.

At the same time, a similar debate was ongoing in the federal courts concerning whether Frye or *Federal Rule of Evidence 702* should govern the admissibility of scientific evidence. The United States Supreme Court answered this question in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993). In what has become known as the "scientific validity" test, the *Daubert* court set forth four non-exclusive factors that courts should consider in determining the admissibility of such evidence: "(1) testability (or falsifiability), (2) error rate, (3) peer review and publication and (4) general acceptance." David L. Faigman, David H. Kaye, Michael J. Saks & Joseph Sanders, *Modern Scientific Evidence: The Law and Science of Expert Testimony* § 1-3.3 (1997)(herein *Modern Scientific Evidence*).⁴

4 In their recent treatise, Professors Faigman, Kaye, Saks and Sanders have explained the differences between Frye and *Daubert* thusly:

In fact, if *Daubert* is a significant break from the past, the departure lies in the changed focus

of the admissibility determination. Frye asks judges to decide the admissibility of scientific expert testimony by deferring to the opinions of scientists in the "pertinent field." Thus, under Frye, judges need not have any facility with scientific methods to make the admissibility decision. They must merely have some basis for knowing what scientists believe. Under *Daubert*, the trial court itself is initially responsible for determining the admissibility of scientific expert testimony by determining that the science supporting that opinion is valid.

Modern Scientific Evidence at § 1-3.0. These authors have further characterized Frye as "easy to apply and requiring little scientific sophistication on the part of judges." *Id.* at § 1-2.3. "Whereas Frye requires judges to survey the pertinent field to assess the validity of the proffered scientific evidence, *Daubert* calls upon judges to assess the merit of the scientific research supporting an expert's opinion." *Id.* at Preface p. viii.

[**10] As might be expected, the Florida Supreme Court was faced with the decision whether to continue following Frye or to adopt *Daubert*. In *Flanagan v. State*, 625 So. 2d 827 (Fla. 1993), the court noted the United States Supreme Court's decision in *Daubert*, but "reaffirmed the applicability of Frye." Ehrhardt, *Florida Evidence* § 702.4 (1997 Edition).

Flanagan was followed by the court's decision in *Ramirez v. State*, 651 So. 2d 1164 (Fla. 1995), wherein the court emphasized that the burden is on the proponent of the evidence to prove the general acceptance of both the underlying scientific principle and the testing procedures used to apply that principle to the facts of the case at hand. . . . The general acceptance under the Frye test must be established by a preponderance of the evidence.

Id. at 1168. In *Ramirez*, the court delineated a four-step process for applying Frye in passing on the admissibility of expert opinion testimony concerning a new or novel scientific principle:

First, the trial judge must determine whether such expert testimony will assist the jury in understanding the evidence or in determining a fact in issue. . . . [**11] Second, the trial judge must decide whether the expert's testimony is based on a scientific principle or discovery that is "sufficiently established to have gained general acceptance in the particular field in which it belongs."

Frye v. United States, 54 App. D.C. 46, 293 F. 1013, 1014 (D.C. Cir. 1923) . . . The third step in the process is for the trial judge to [*557] determine whether a particular witness is qualified as an expert to present opinion testimony on the subject in issue. . . . Fourth, the judge

may then allow the expert to render an opinion on the subject of his or her expertise, and it is then up to the jury to determine the credibility of the expert's opinion, which it may either accept or reject. . . .

Ramirez, 651 So. 2d at 1167.

Finally, we note that the appropriate standard for our review of a Frye issue is *de novo*. *Brim v. State, 695 So. 2d 268, 274 (Fla. 1997)*; *Hadden, 690 So. 2d at 579.*⁵ Thus, we review the trial court's ruling on the admissibility of expert opinion testimony, which is purportedly based on an underlying novel scientific principle or technique, as a matter of law, rather than under an abuse of discretion standard. [**12] *Id.*; see also *Vargas v. State, 640 So. 2d 1139, 1144 (Fla. 1st DCA 1994)*, quashed on other grounds, *667 So. 2d 175 (Fla. 1995)*. Our *de novo* review of the Frye issue in these cases includes an examination of three methods of proof: (1) expert testimony, (2) scientific and legal writings, and (3) judicial opinions. *Flanagan v. State, 586 So. 2d 1085, 1112 (Fla. 1st DCA 1991)*(Ervin, J., concurring and dissenting).

⁵ Recently in *Joiner v. General Elec. Co., U.S. , 139 L. Ed. 2d 508, 118 S. Ct. 512, 66 U.S.L.W. 4036 (December 15, 1997)*, the United States Supreme Court has held that an abuse of discretion standard of review applies to the review of a trial court's determination of admissibility under Daubert.

Scientific Background

The evidence and testimony in these cases span several fields, most notably epidemiology and toxicology. As recognized by the trial court, the epidemiological research upon which the numerous experts relied related to studies [**13] of subjects ranging from "Danish painters to Venezuelan gluemakers and from Silicon Valley chipmakers to Michigan autoworkers." Because of the highly technical nature of this epidemiological evidence, to facilitate understanding of these cases and the arguments of the parties, it is necessary for us to provide a brief, but by no means exhaustive, discussion of certain scientific terms and concepts employed by the parties.

"Epidemiology" is a branch of science and medicine which uses studies to "observe the effect of exposure to a single factor upon the incidence of disease in two otherwise identical populations." *DeLuca v. Merrell Dow Pharm., Inc., 911 F.2d 941, 945 (3d Cir. 1980)*, quoting Bert Black & David E. Lilienfeld, *Epidemiological Proof in Toxic Tort Litig., 52 Fordham L. Rev. 732, 755 (1984)*. Epidemiology focuses on the question of general causation, that is, whether a substance is capable of causing a particular disease, rather than specific causation,

that is, whether the substance did cause the disease in a specific individual. Federal Judicial Center, *Reference Manual on Scientific Evidence, 126 (1994)*(herein the Reference Manual [**14]).

To establish that a given substance was a necessary causal link to the development of an individual's disease, in theory a scientist might obtain reliable information by engaging in experimental studies with human beings. For example, to determine whether exposure to a certain level of a suspected toxin is associated with a particular disease, the scientist might compare two randomly selected groups of people. One of the groups would be exposed to certain doses of the toxin over a prescribed length of time and the other group would not. For obvious ethical reasons, however, experimental studies with human beings are proscribed where the subject chemical agent is known or thought to be toxic. See *Ethyl Corp. v. United States Envtl. Protection Agency, 176 U.S. App. D.C. 373, 541 F.2d 1, 26 (D.C. Cir.)*, cert. denied, *426 U.S. 941, 96 S. Ct. 2663, 49 L. Ed. 2d 394, 96 S. Ct. 2662 (1976)*; Reference Manual at 129.

Because of these ethical proscriptions, rather than experimental methods, epidemiologists use observational methods to study persons exposed to a suspected toxic substance to determine whether an association exists between exposure to the chemical and the development of a disease. These [**15] epidemiological studies use "statistical methods to detect abnormally high incidences of disease in a study population and to associate these incidences with unusual exposures to suspect environmental factors." (emphasis supplied). In re "Agent Orange" *Prod. Liab. Litig., 611 F. Supp. 1223, 1231 (E.D.N.Y. 1985)* [**558] quoting Michael Dore, A Commentary on the Use of Epidemiological Evidence in Demonstrating Cause-in-Fact, 7 *Harv. Envtl. L. Rev.* 429, 431 (1983); *In re Swine Flu Immunization Prods. Liab. Litig., 508 F. Supp. 897, 907 (D. Colo. 1981)*, aff'd sub nom., *Lima v. U.S., 708 F.2d 502 (10th Cir. 1983)*("Where . . . the exact organic cause of a disease cannot be scientifically isolated, epidemiologic data becomes highly persuasive.").

Through epidemiological studies, scientists can assess the existence (and strength) or absence of an association between an agent and the disease. But "association is not *causation*." Reference Manual at 126. Association is a term used to describe the relationship between exposure to a chemical agent and disease that occurs more frequently together than one would expect by chance. *Id.* at n.7. Establishing an association [**16] does not necessarily mean that there is a causal effect between the exposure and the disease. *Id.* Causation, by comparison, constitutes an association between two events in which one event is a necessary link in a chain of events that results in the effect. *Id.* Nevertheless, while

"epidemiological methods cannot prove causation . . .," epidemiological studies can provide a basis on which an epidemiologist can infer and opine that a certain agent causes a disease. *Id.*

In the event an epidemiological study finds an association between exposure to a substance and a disease, scientists can analyze the study to consider whether the reported association reflects a cause-and-effect relationship or, alternatively, is a spurious finding. *Id.* at 157. "Researchers first look for alternative explanations for the association, such as bias or confounding factors. . . ." *Id.* The primary types of biases are selection bias and information bias. "Selection bias occurs when the exposed group is selected in a way that makes it more or less susceptible to disease for reasons independent of exposure." Michael D. Green, *Expert Witnesses and Sufficiency of Evidence in Toxic Substance [**17] Litigation: The Legacy of Agent Orange and Bendectin Litigation*, 86 *Nw. U. L. Rev.* 643, 649 (1992). Similarly, information bias exists where the participants incorrectly give information about either exposure or health effects. This may exist where an interviewer whose "awareness of the identity of cases and controls . . . may influence the structure of the questions and the interviewer's manner, which in turn may influence the response." David E. Lilienfeld & Paul D. Stolley, *Foundations of Epidemiology* 237 (1994).

Although epidemiologists cannot totally control such variables as the genetic background or lifestyle choices of their human subjects or the amount and duration of their exposure to the studied substance, Reference Manual at 129, the researchers have systematic methods for assessing the characteristics of the people in the study and their risk of disease to rule out known sources of bias and errors. *Id.* at 127. For example, to eliminate information bias, whenever possible an interviewer should conduct "blind" interviews without prior knowledge of the cases and controls. *Foundations of Epidemiology* at 237.

Further, even when a statistical association [**18] exists and no bias is present, the association may be the result of some other confounding factor, or a so-called "confounder." A confounding factor may be itself a risk factor for the disease or associated with the exposure of interest. Reference Manual at 158. As an example, assume a study finds that individuals with grey hair have a higher rate of death than those with another hair color. Instead of hair color impacting on death, however, the test results might be explained by the confounding factor of advanced age. Thus, when a researcher finds an association between an agent and disease, he or she must determine whether the association is causal or the result of confounding. *Id.*

After the researcher has analyzed the epidemiological study for alternative explanations for an association, researchers then consider generally accepted guidelines for determining whether the association between exposure to a substance and a disease is causal. See *Smith v. Ortho Pharm. Corp.*, 770 *F. Supp.* 1561, 1575-76 (*N.D. Ga.* 1991). Although the guidelines are composed of various [*559] criteria,⁶ in the instant cases the factors of strength of association, consistency with other research, [**19] and biological plausibility are raised in the arguments of the appellee.

6 One generally accepted set of standards for evaluating epidemiological studies is known as the Koch Postulates. Those standards are composed of the following seven factors:

1. strength of association;
2. temporal relationship;
3. consistency of the association in other research;
4. biological plausibility;
5. consideration of alternative explanations;
6. specificity of the association; and
7. dose-response relationship.

Federal Judicial Center, Reference Manual on Scientific Evidence 161 (1994)(herein the Reference Manual); see also Bert Black & David E. Lilienfeld, *Epidemiological Proof in Toxic Tort Litigation*, 52 *Fordham L. Rev.* 732, at 762-63 (1984).

Strength of Association. Epidemiologists commonly use "relative risk" to measure the strength of the association between exposure and disease. Reference Manual at 126. Relative risk is the ratio of the risk of disease among [**20] the group exposed to the chemical agent compared to the risk of disease among the unexposed group. *Id.* at 176. For example, a relative risk of 2.0 indicates that the risk of developing a disease in the exposed group is two times higher than the risk of developing that disease in the unexposed group. A relative risk of 1.0 indicates no association. The higher the relative risk, the stronger or more powerful is the association between exposure to the substance and development of the disease.⁷

7 The "relative risk" concept is sometimes referred to as the "odds ratio" depending upon the type of study involved. However, for ease of reference, we will refer to relative risk only. Reference Manual at 149.

Scientists use the concept of a "confidence interval" as the means by which an epidemiologist can express confidence in a specific finding of relevant risk. For instance, if relative risk in a study is found to be 2.0, the epidemiologist can estimate the range of numeric values above and below 2.0 in which [**21] the relationship of a study sample would be likely to fall if the same study were repeated numerous times. *Id.* at 173. "The width of the confidence interval provides an indication of the precision of the point estimate or relative risk found in the study . . ." *Id.* In this appeal, citing *Black & Lilienfeld*, *supra*, 52 *Fordham L. Rev.* at 757, the railroad urges that the confidence interval should be expressed with estimated 95% accuracy, that is, as a range in which relative risk will predictably fall 95 times out of 100 replications of the study.

Consistency with Other Research. The validity of scientific conclusions is often based upon the replication of research findings, and consistency in these findings is an important factor in making a judgment about causation. See *Kehm v. Procter & Gamble Co.*, 580 *F. Supp.* 890, 901 (*N.D. Iowa* 1982), *aff'd*, 724 *F.2d* 613 (8th *Cir.* 1983) (noting the persuasive power of multiple independent studies, each of which reached the same finding of an association between the toxic shock syndrome and tampon use); *Cadarian v. Merrell Dow Pharm., Inc.*, 745 *F. Supp.* 409, 412 (*E.D. Mich.* 1989) (holding a single Benedictin study [**22] insufficient to support an expert's opinion, because "the study's authors themselves concluded that the results could not be interpreted without independent confirmatory evidence").

Biological Plausibility. Biological plausibility involves the application of the "existing knowledge about human biology and disease pathology to provide a judgment about the plausibility that an agent caused a disease." Reference Manual at 172. Thus, for example, a conclusion that high cholesterol is a cause of coronary heart disease is biologically plausible because cholesterol is found in atherosclerotic plaques. *Id.* at 163.

Briefly, we turn to another scientific discipline, toxicology. Toxicology is defined as "the study of the adverse effects of chemical agents on biological systems." *Id.* at 185. One of the central tenets of toxicology is that "the dose makes the poison" implying that all chemical agents are harmful - it is only a question of dose. *Id.* Thus, even water if consumed in large enough quantities can be toxic. *Id.* A toxicologist attempts to determine at what doses foreign agents produce their effects, and animal studies are used by toxicologists to predict toxic [**23] responses in humans. [*560] *Id.* In toxicology, a dose-response relationship is a relationship in which a change in amount, intensity, or duration of exposure is associated with a change - either an increase or decrease - in risk of disease. *Id.* at 173.

The Scientific Evidence Below

The appellants proffered the testimony or affidavits of expert witnesses Dr. W. Lynn Augenstein, Dr. Richard L. Lipsey, Dr. Edward L. Baker, Jr., Dr. Douglas H. Linz, and Dr. Michael Kelly in the Berry case.

Dr. Augenstein. Dr. W. Lynn Augenstein, a medical doctor with a board certification in medical toxicology who teaches at the University of Florida Health Science Center, reviewed approximately 150 journal articles, textbooks, and notes of international conferences. He opined that, of the epidemiological studies which had been performed, the studies correlating long-term exposure to organic solvents and toxic encephalopathy outweigh the negative studies by eight or nine to one. He acknowledged that there were negative studies, but he opined that these studies dealt with short term or low level exposures.

Regarding toxic encephalopathy, he explained that it is usually divided into three [**24] categories: minimum, moderate and severe. In the lowest category of toxic encephalopathy, a patient suffers from tiredness, mood problems, irritability, sleep disturbances, possibly some poor memory function, depression, headaches and dizziness. A patient suffering moderate toxic encephalopathy shows more specific neurologic signs that would be detectable on neuropsychological testing: memory problems; slower reaction times; and problems with spatial orientation. The patient has more persistent mood and behavioral problems. In the severe category, there is significant global brain dysfunction. The individual is almost in a vegetative state where he cannot function, has very poor memory, and there are significant findings on x-ray tests showing brain atrophy. Dr. Augenstein opined that it is not necessary for a worker to become unconscious in order to suffer toxic encephalopathy.

He further explained that the dose-response relationship, which is a cornerstone of toxicology, is very difficult to assess in an epidemiological study because epidemiological studies are performed on a retrospective basis.

Dr. Lipsey. Richard Lipsey, Ph.D., who stated his profession as a pesticide environmental [**25] toxicologist, concurred that in his review of the literature, there was a general consensus in the scientific community that long-term exposure to excessive levels of organic solvents can and does cause toxic encephalopathy.

Dr. Baker. Edward L. Baker, Jr., M.D., is board-certified in occupational medicine and internal medicine. In addition to his doctor of medicine degree, he has two masters degrees from Harvard University, a Master of Public Health with emphasis on epidemiology and a

Master of Science with emphasis on epidemiology and occupational health. He has practiced medicine in the Occupational/Environmental Health Clinic at Emory University; has been employed as a professor at Harvard, where he directed research into the health effects of organic solvents; has served as Deputy Director of the National Institute for Occupational Safety and Health, the federal agency responsible for research in occupational health; and, at the time of the evidentiary hearing, was the Director of the Public Health Practice Program Office at the federal government's Center for Disease Control and Prevention.

Dr. Baker has authored chapters for at least four medical textbooks which address [**26] the subject at issue; he has published 98 journal articles of which approximately 20 are directly related to the subject at issue; and he has served on the editorial boards, as peer reviewer for submitted articles, of several journals and publications, including the American Journal of Industrial Medicine. He was the only United States scientist to participate in an international conference of scientists, convened in Copenhagen in 1985 by the World Health Organization to reach a consensus on the chronic effects of organic solvents on the central nervous system. The report generated from the Copenhagen conference concludes that "epidemiological and experimental data indicate that long-term occupational [*561] exposure to organic solvents may cause adverse effects in the central and peripheral nervous systems." Dr. Baker participated in a second international conference which produced the same consensus opinion. As a result of a conference held in 1990, it was agreed that "chronic toxic encephalopathy does occur in workers with excessive exposure to solvents."

Significantly, as can be seen from his credentials, Dr. Baker began studying the effects of solvents well before this litigation arose [**27] and arrived at his conclusions independent of his involvement in this lawsuit.⁸ As a result of his very considerable study on the subject, he has concluded that long-term excessive exposure to organic solvents can cause toxic encephalopathy.

⁸ As stated by the court in *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995):

One very significant fact to be considered is whether the experts are proposing to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for purposes of testifying. . . . In determining whether proposed expert testimony amounts to good science, we may not ignore the fact that a scientist's normal workplace is

the lab or the field, not the courtroom or the lawyer's office.

That an expert testifies based on research he has conducted independent of the litigation provides important, objective proof that the research comports with the dictates of good science.

[**28] Specifically, he opined that if an individual is exposed more than ten years to a concentration that is sufficient to cause acute symptomology (intoxication, light-headedness, dizziness, inebriation) on a regular basis, that person is at risk for developing toxic encephalopathy. He said it was a general consensus in the scientific community that there is a risk of toxic encephalopathy in people excessively exposed to solvents. The only real debate at present, according to Dr. Baker, was over the safe levels of exposure and the degree of reversibility of the damage. He disagreed with appellee's experts that, for there to be a causal relationship, a patient must have been rendered unconscious by the exposure.

Dr. Baker testified that the Occupational Safety and Health Administration (OSHA) has published recommended maximum safe exposure levels for the various solvents at issue in this case. OSHA has arrived at a number 350 parts per million as an eight-hour time-waited exposure for the workplace for TCA that is deemed to be a safe level. Nonetheless, as Dr. Baker recognized, this level does not take into consideration solvent exposure through the skin. He opined that solvents penetrate [**29] the skin and can get into the body through percutaneous exposure as well as through inhalation exposure. Thus, even a workplace allegedly below the safe level of 350 parts per million might nonetheless subject a worker to excessive exposure.

Although he was uncertain of the exact biological "mechanism" by which these solvents cause damage, Dr. Baker offered a biologically plausible explanation. He explained that solvents typically accumulate in fat-rich tissues and that the adipose tissues of the brain are tissues that have a high fat content. He postulated that since many organic solvents are highly lipid soluble, they can accumulate in the brain or in the adipose tissue.

Dr. Linz. Douglas H. Linz, M.D., who is board-certified in internal medicine and occupational medicine, submitted an affidavit. His speciality included diagnosing and treating injuries and conditions caused by acute and chronic overexposure to chemicals and solvents. Initially, Dr. Linz had been asked by CSX to examine several of the railroad's employees who, like appellants, worked in the diesel shop. He opined that the employees had suffered neurological and neuropsychological conditions caused by their [**30] recurrent exposures to solvents while working for the railroad and that there was a medically significant pattern among the examined diesel

shop employees of the railroad who were suffering from solvent-induced brain injury. The employees had described heavy exposures: large amounts of solvents were used at full strength; the solvent was sprayed under pressure which atomized it; respirators were not worn; and employees washed their hands and clothes in solvent. They had the following complaints: headaches; dizziness; nausea; feelings of drunkenness [*562] and/or confusion; and acute mucosal complaints. He opined that it was well recognized that repeated exposures such as the kind noted above over a period of years can result in neurological and neuropsychological conditions including organic brain damage.

Dr. Linz came to the conclusion that the diesel employees had suffered solvent induced brain damage only after interviewing the patients and discussing with them their general health, their medical histories, and their occupational histories; reviewing the manufacturer safety data sheets on the solvents which were provided to him by the railroad (which included the solvents that are at [**31] issue in this case); reviewing the medical records of the employees; performing physical examinations on the men; reviewing diagnostic studies such as neuropsychological evaluations and balance testing performed on the men; reviewing the scientific literature which has been published with regard to solvents; and after eliminating other causes to a reasonable degree of medical certainty. He opined that the overwhelming epidemiological evidence confirms the relationship between long-term exposure to solvents and brain damage.

Dr. Kelly. Michael Kelly, M.D., is board-certified in internal medicine and occupational medicine. Currently he is the Medical Director of Occupational Health Services and Chief of Medicine at St. Lawrence Hospital in Lansing, Michigan. He has extensive experience in diagnosing and treating solvent-exposed workers from all over the country, including approximately 200 railroad workers. He opined that it was a general consensus in the medical and scientific community that long-term exposure to organic solvents can cause toxic encephalopathy.

In arriving at his conclusion that Mr. Berry suffered from solvent-induced toxic encephalopathy, Dr. Kelly employed [**32] a differential diagnosis procedure which he opined was the standard methodology utilized in the field of occupational health. He took a history from both Mr. Berry and his wife concerning his current medical problems. After reviewing Mr. Berry's work history and symptoms, Dr. Kelly opined that Berry had been exposed to very high levels of organic solvents in excess of OSHA standards, which excessive exposure had been confirmed by other railroad employees. Dr. Kelly also conducted a thorough physical examination. He caused various laboratory tests to be performed on Berry, and obtained an MRI and an EEG of Berry. He

referred Berry to a neuropsychiatrist for evaluation, which revealed that Berry had severe cognitive defects. A psychiatrist to which Berry was also referred reported back that Berry's cognitive defects were more likely consistent with toxic encephalopathy than with mere depression. Dr. Kelly had a SPECT scan of Berry performed, and the physician who performed the scan reported that it showed that Berry suffered diminished activity and function in several areas of the brain, consistent with neurotoxic insults. Dr. Kelly asked Berry questions about cigarettes, alcohol [**33] and other possible confounders.

9 "Differential diagnosis" is a term used "to describe a process whereby medical doctors experienced in diagnostic techniques provide testimony countering other possible causes . . . of the injuries at issue." *Hines v. Consolidated Rail Corp.*, 926 F.2d 262, 270 n.6 (3d Cir. 1991).

Regarding his occupational history, Mr. Berry told Dr. Kelly that he used materials out of a 55 gallon drum hooked up to house air, as he called it, to spray off the locomotives. He worked in the pit area under the locomotive. He would dip his hands in the material, and wash his clothes with it. He described being wet with the solvent material. He developed headaches, and was tired and lethargic. He had to take naps when he came home from work. Dr. Kelly opined that these symptoms indicated Berry had been exposed to "pretty high exposure levels occurring over a fairly long period of time." Berry could not remember names, could not remember directions, and could not remember his assignment at work. [**34] He was frequently angry, irritable, and was having some sleep disturbances. His gait was abnormal. When he walked, his feet were wide apart indicating a balance disturbance. Regarding Berry's cognitive difficulties, Dr. Kelly concluded that Berry's ability to interpret visual spacial configurations was at best low average, whereas one would expect an [*563] electrician to be able to visualize diagrams and remember them.

Regarding a biologically plausible explanation for the toxic encephalopathy, Dr. Kelly concurred with Dr. Baker that solvents have the ability to dissolve fatty materials. He felt that this characteristic allowed them to damage the body. He added that the fact these solvents are chlorinated probably adds to their toxicity, because the chlorine atom is more difficult for the body to metabolize and prolongs the exposure. He said there was no support for the notion that it is necessary to have an acute exposure causing unconsciousness before a person can suffer toxic encephalopathy.

CSX presented the expert testimony of Dr. Raymond Harbison and Dr. Robert James.

Dr. Harbison. Raymond Harbison, Ph.D., a toxicologist on the faculty of the University of Florida, opined [**35] that there was no biologically plausible explanation for a solvent exposure to cause toxic encephalopathy. As an example, he said that TCA is rapidly eliminated from the body and does not damage the nervous system because it cannot be converted to a chemical that interacts with the nervous system to cause damage. His testimony regarding TCE and PCE was similar. According to him, nothing in the molecular structure of the chlorinated hydrocarbon is able to produce any pathology in the nervous system. Contrary to plaintiffs' experts, he opined that TCA cannot "bioaccumulate in the brain." He maintained that it was generally accepted among toxicologists that TCA is not able to cause toxic encephalopathy unless there has been a dose sufficient to impair respiration resulting in lowering of the oxygen level in the body or unconsciousness. However, he admitted no study supports his contention that unconsciousness was required.

He was generally of the opinion that the literature contained insufficient evidence of a real causal connection between long-term exposure to organic solvents and toxic encephalopathy because real exposures could not be determined without making accurate air quality [**36] measurements, and because only precisely controlled double blind studies could be expected to establish causation. According to him, one should not use patient history to make the diagnosis but should use analytical data and be able to conduct measurements of the actual exposure received. Contrary to Dr. Kelly, he opined that a patient's symptoms could not be used to measure exposure. Instead, to make the diagnosis of toxic encephalopathy one would have to evaluate such factors as the level of chemicals in the workplace, the available ventilation, the temperature, and the air exchange rates in the work area.

Dr. Harbison opined that, before the toxicological scientific community would acknowledge the validity of an epidemiological study relating exposure to disease, there would have to be a known verified exposure, valid testing that is objective, and this testing methodology must have been subjected to a double blind evaluation where neither the investigator nor the individual who was being evaluated knew what the exposure was or what the potential outcome should be.

Dr. James. Robert James, Ph.D., also a toxicologist on the faculty at the University of Florida, presented an [**37] analysis of the studies demonstrating an association between exposure to organic solvents and toxic encephalopathy. Dr. James opined that most of the studies were negative and that of the ones which were positive, when flawed methodology was considered as well as other factors, only a few studies could be considered

truly positive. Based upon his reanalysis, he said the studies did not demonstrate that long-term exposure to excessive amounts of organic solvents can cause toxic encephalopathy or that this hypothesis was generally accepted by the scientific community at this time. He advocated his reanalysis of the studies as more credible because it eliminated from the classification of positive studies those studies which failed to provide clear and convincing evidence of strong associations and big differences. The studies he eliminated he characterized as false positive studies which had not controlled for confounders. He conceded that he and Dr. Baker had obviously interpreted the literature differently.

[*564] While it was his opinion that epidemiology and toxicology use essentially the same type of analysis, nonetheless, Dr. James testified that toxicologists use a more rigorous standard [**38] to evaluate the data before determining whether or not a substance causes a particular disease in any population. He rejected studies that do not show a strong dose-response relationship, commenting that if the response does not change as a result of the dose or there is not a dose-response curve, the chemical agent is not the cause of the disease.

To the extent other scientific evidence is deemed relevant, it is discussed in other parts of this opinion.

Trial Court's Order

In the proceedings below, CSX challenged the admissibility of the appellants' expert testimony, contending that the plaintiffs' theory of general causation was based on "junk science" which did not meet the Frye/Ramirez test of reliability and that Dr. Kelly's specific causation testimony was not credible. The trial court found that the central issue in these cases was the general acceptance of the scientific principles underlying the testimony of appellants' expert witnesses. The appellants argued that Frye does not require that the experts' opinions themselves must be generally accepted; but, rather, that only the scientific techniques or methodology upon which the expert relies must [**39] be generally accepted in the scientific community. The trial court rejected this argument, ruling that Frye not only applies to scientific methodology, but that the scientific conclusion of the expert witness itself must be generally accepted in the scientific community to which it pertains.

The trial court concluded that there remains a substantial disagreement within the scientific community as to whether or not organic solvents can cause brain damage. In reaching this conclusion, the court recited the findings of numerous of the epidemiological studies upon which the appellants relied. In these studies, the researchers found an association between exposure and injury, but used the seemingly equivocal term of "asso-

ciation" rather than causation. Moreover, these studies admitted the controversial nature of this subject, and several called for further investigation. The trial court was plainly troubled by the "qualifying phrases and disclaimers" used in the articles. This led the trial court to the conclusion that there remains a substantial disagreement within the scientific community as to whether or not organic solvents, particularly the ones at issue in the instant case, [**40] can cause brain damage, particularly chronic toxic encephalopathy, of the nature allegedly experienced by the plaintiffs in [these] cases. Said another way, the Court concludes that it is not generally accepted that exposure to organic solvents causes the condition of which the plaintiffs complain.

Arguments of the Parties

Appellants argue that the effect of the trial court's admissibility ruling was to decide the causation issue itself - that is, whether exposure to the four solvents causes toxic encephalopathy - which is a jury issue. They contend that the trial court erred as a matter of law in concluding that it was the experts' ultimate opinions, rather than the underlying methodology from which they derived their opinions, that had to be Frye tested. See, e.g., *Ferebee v. Chevron Chem. Co.*, 237 U.S. App. D.C. 164, 736 F.2d 1529, 1535 (D.C. Cir.), cert. denied, 469 U.S. 1062, 105 S. Ct. 545, 83 L. Ed. 2d 432 (1984); accord *Osburn v. Anchor Lab., Inc.*, 825 F.2d 908, 915-16 (5th Cir. 1987), cert. denied, 485 U.S. 1009, 108 S. Ct. 1476, 99 L. Ed. 2d 705 (1988); and *Cella v. United States*, 998 F.2d 418, 425 (7th Cir. 1993). Appellants [**41] argue that the "principle or discovery" language in Frye upon which the trial court seized to arrive at its conclusion that an expert's opinion must be generally accepted in the medical community was merely language used by the Frye court to label the novel "systolic blood pressure deception test" at issue in that case. They submit that an expert opinion derived from the generally accepted methodology of the science of epidemiology - where numerous published, peer-reviewed epidemiological studies and medical textbooks provide support for the opinion - is reliable, and therefore admissible.

[*565] Regarding the trial court's exclusion of Dr. Kelly's specific opinion on causation, appellants argue that Dr. Kelly followed a "differential diagnosis" methodology which is the standard methodology utilized in the field of occupational health. *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 758 (3d Cir. 1994), cert. denied sub nom., *General Elec. Co. v. Ingram*, 513 U.S. 1190, 115 S. Ct. 1253, 131 L. Ed. 2d 134 (1995); *Hines v. Consolidated Rail Corp.*, 926 F.2d 262, 274 (3d Cir. 1991). Further, although the trial court was troubled by the fact that Dr. Kelly had merely estimated [**42] the levels of exposure to the organic solvents, appellants

argue that this was necessary as the railroad had not monitored the work rooms, and therefore verifiable knowledge of the levels of solvents does not exist. Thus, Dr. Kelly could only rely upon an informed estimate derived from the statements of Berry and the other people who worked in the shops everyday to arrive at a diagnosis. If this estimate is erroneous, submit the appellants, CSX will have the opportunity to dispute the claimed levels of exposure at trial.

CSX argues that the causal proposition - that long term exposure to TCA, TCE, PCE and mineral spirits at workplace level sufficient to produce transient irritation, dizziness or disorientation, but not hypoxia or anoxia,¹⁰ can cause irreversible central nervous system damage - must pass the Frye test. Appellee contends that upon a *de novo* review of this issue, this court will be compelled to conclude that this causal proposition does not pass the Frye test. CSX directs our attention to several publications which show some epidemiologic disagreement about causality between long-term exposure to organic solvents and toxic encephalopathy. Further, CSX [**43] criticizes the studies upon which appellants' experts rely, contending these studies did not sufficiently take into account the presence of confounders or information bias, or involved exposure to much more damaging chemicals than those at issue in the instant cases. Finally, CSX argues that these studies are deficient because they fail to offer a biologically plausible explanation for the stated effects and do not adequately address the dose response relationship.

10 Hypoxia is a "decrease below normal levels of oxygen in inspired gases, arterial blood, or tissue, short of anoxia;" anoxia is an "absence or almost complete absence of oxygen." *Stedman's Medical Dictionary*, at 90 and 756 (25th ed. 1989).

CSX suggests that for an epidemiological study to show a statistically significant association between a certain risk factor and disease in the exposed group such that causation may be inferred by the scientists, there must be a relative risk greater than 2.0 within a 95% confidence interval greater than [**44] 1.0, and that the calculations must adequately guard against selection and information biases and other confounders. After reviewing the studies, CSX argues there are only three positive studies, or at most five positive studies, and of those, four were subject to obvious selection and information bias.

The appellants reply that the microscopic level of critical analysis to which the railroad has resorted belongs only to the experts. They suggest that neither the trial court nor this court can assume the role of an amateur scientist, examine the materials upon which the ex-

pert scientists rely, draw its own scientific conclusion as to whether the material support the opinions of the plaintiffs' experts or not and then declare one set of opinions the victor by excluding the other set of opinions from evidence. See *Joiner v. General Elec. Co.*, 78 F.3d 524, 530-33 (11th Cir. 1996), rev'd on other grounds, U.S. , 139 L. Ed. 2d 508, 118 S. Ct. 512, 66 U.S.L.W. 4036 (December 15, 1997); *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d 1124, 1137 (2d Cir. 1995).

Frye Analysis

At the outset of our Frye analysis, we must resolve the issue [**45] over what must be Frye tested in this case -- the opinion testimony of the witnesses or the underlying scientific principle or methodology utilized by the experts in arriving at their opinions. Frye expressly addressed whether it is the expert opinion or the underlying principle and methodology from which the opinion is deduced which must be generally accepted in the scientific community. The Frye court explained: "the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular [*566] field in which it belongs." *Frye*, 293 F. at 1014.

Further, the federal cases following Frye have applied the Frye test to the underlying scientific principle or methodology on which the opinion is based. See, e.g., *Cella v. United States*, 998 F.2d 418, 425 (7th Cir. 1993)("the Frye standard requires that the methodology and reasoning used by an expert in reaching a conclusion be generally accepted within the relative scientific community"); *Christophersen v. Allied-Signal Corp.*, 939 F.2d 1106, 1111 (5th Cir. 1991)(in applying Frye test ask whether the expert, in reaching his conclusion, used a well [**46] founded methodology or mode of reasoning), cert. denied, 503 U.S. 912, 112 S. Ct. 1280, 117 L. Ed. 2d 506 (1992); *Peteet v. Dow Chem. Co.*, 868 F.2d 1428, 1433 (5th Cir. 1989)(as long as expert's methodology is well-founded, the nature of his conclusion is generally irrelevant, even if it is controversial or unique), cert. denied sub nom., *Dow Chem. Co. v. Greenhill*, 493 U.S. 935, 110 S. Ct. 328, 107 L. Ed. 2d 318 (1989); *Osburn v. Anchor Lab., Inc.*, 825 F.2d 908, 915 (5th Cir. 1987)("an expert's opinion need not be generally accepted in the scientific community before it can be sufficiently reliable and probative in support of a jury finding"), cert. denied, 485 U.S. 1009, 108 S. Ct. 1476, 99 L. Ed. 2d 705 (1988); *Ferebee v. Chevron Chem. Co.*, 237 U.S. App. D.C. 164, 736 F.2d 1529, 1535-36 (DC Cir.)(rejecting defendant's argument that expert opinion testimony must be generally accepted in the scientific community before it can be introduced as evidence), cert. denied, 469 U.S. 1062, 105 S. Ct. 545, 83 L. Ed. 2d 432 (1984):

The Florida Supreme Court has, until recently, consistently described the Frye test as a standard which "requires a determination, [**47] by the judge, that the basic underlying principles of scientific evidence have been sufficiently tested and accepted by the relevant scientific community." *Brim*, 695 So. 2d at 272 (emphasis added). In *Hadden*, however, the court stated that it would "not permit factual issues to be resolved on the basis of opinions which have yet to achieve general acceptance in the relevant scientific community." *Hadden*, 690 So. 2d at 578 (emphasis added). Specifically, the court held in *Hadden* that "a psychologist's opinion that a child exhibits symptoms consistent with . . . 'child sexual abuse accommodation syndrome' . . . has not been proven by a preponderance of scientific evidence to be generally accepted by a majority of experts in psychology" and that such opinion could not be used in a prosecution for child abuse where a proper objection is raised to its introduction. *Id.* at 575. The court distinguished such testimony from pure opinion testimony (testimony which is personally developed through clinical experience) on the grounds that profile and syndrome evidence rely on conclusions based upon studies and tests. "Consequently, the expert's opinion was based upon [**48] diagnostic standards which must pass the Frye test." *Id.* at 581.

However, we decline to interpret this language in *Hadden* as meaning that in all cases expert opinion testimony, not otherwise developed through clinical experience, must be Frye tested. Instead, we believe that this language in *Hadden* must be confined to the facts in that case and the psychological syndrome testimony which was being proposed. It is clear that the syndrome testimony in *Hadden* was not based upon scientifically accepted methodology. As Judge Ervin opined in his dissenting opinion in *Hadden v. State*, 670 So. 2d 77, 89 (Fla. 1st DCA 1996)(en banc), approved by the supreme court, the diagnosis of sexual abuse through a syndrome analysis is not a generally accepted method of diagnosing sexual abuse nor is there a consensus among experts that it is useful as substantive evidence of guilt. 690 So. 2d at 579.

In *Hadden*, the expert's opinion testimony was inextricably intertwined with an unacceptable diagnostic methodology. This circumstance is factually and legally distinguishable from the proposed expert opinion causation testimony in the instant toxic tort case. The proposed expert [**49] opinions here are based upon peer reviewed published epidemiological studies undertaken independently of the instant action and clearly recognized in the case law as important sources of evidence of toxic causation. As the Third Circuit observed in *DeLuca*, 911 F.2d at 954:

[*567] The reliability of expert testimony founded on reasoning from epidemiological data is generally a fit subject for judicial notice; epidemiology is a well-established branch of science and medicine, and epidemiological evidence has been accepted in numerous cases.

Commentators have further explained:

Epidemiological studies have been well received by courts trying mass tort suits. Well conducted studies are universally admitted. The widespread acceptance of epidemiology is based in large part on the belief that the general techniques are valid.

Modern Scientific Evidence at § 28-1.1; see also Green, 86 *Nw. U. L. Rev.* at 659, 663-64 (1992).

Thus, we hold that, under Frye and its Florida progeny, when the expert's opinion is well-founded and based upon generally accepted scientific principles and methodology, it is not necessary that the expert's opinion be generally [*50] accepted as well. We find persuasive the rationale of the court in Christophersen:

In *Osburn* [*Osburn v. Anchor Lab., Inc.*, 825 F.2d 908 (5th Cir. 1987)] the plaintiff's and the defendant's experts relied on essentially the same diagnostic methodologies but drew opposite conclusions from the available information. We did not attempt to determine which expert's conclusion was more in line with the consensus in the scientific community. Instead we stated, "a jury must be allowed to make credibility determinations and weigh conflicting evidence in order to decide the likely truth of a matter not itself initially resolvable by common knowledge or lay reasoning." *Id.* at 916. "An expert's opinion need not be generally accepted in the scientific community before it can be sufficiently reliable and probative in support of a jury finding." *Osburn*, 825 F.2d at 915.

939 F.2d at 1111 (emphasis added).

Our conclusion is supported by the opinion of the Florida Supreme Court in *Brim*. There, the court recognized that Frye allows opposite opinion testimony from experts relying upon the same generally accepted scientific principles and methodologies. In [*51] *Brim*, the court was faced with a Frye challenge to DNA test results. The *Brim* court held that, for DNA test results to be admissible, both the first step of the testing process (which relies upon principles of molecular biology and chemistry) and the second step (which involves a calculation of population frequency statistics) must satisfy Frye. *Brim*, 695 So. 2d at 269. With regard to the second step, the court found that multiple statistical calculations might simultaneously satisfy Frye. ¹¹ *Id.* at 272. "It is clear that scientific unanimity is not a precondition to a finding of general acceptance in the scientific community." *Id.* The court explained that although two conflict-

ing scientific principles cannot simultaneously satisfy Frye, it would allow multiple reasonable statistical calculations when based upon generally accepted principles of population, genetics and statistics. *Id.*

11 While the court had already ruled in *Ramirez*, 651 So. 2d at 1168, that general acceptance under Frye must be established by a preponderance of the evidence, in *Brim* the court added to the analysis by defining "general acceptance" as meaning acceptance by a clear majority of the members of the relevant scientific community, with consideration by the trial court of both the quality and quantity of those opinions. *Brim*, 695 So. 2d at 272.

[**52] For all these reasons, we must respectfully disagree with the trial court's conclusion that it was the appellants' expert opinion testimony that was required to be Frye tested in these cases.

Turning to the trial court's further reasoning for denying admissibility - that the underlying epidemiological studies were equivocal as to causation - we find that the trial court ultimately misunderstood the nature of epidemiological studies and was unnecessarily concerned that the studies did not prove causation. As discussed above, epidemiological studies are designed to assess the existence and strength or absence of an association between an agent and a disease. *Supra*, page 12. As Dr. Baker explained in his testimony, epidemiological studies do not fix the cause - they merely demonstrate the probabilities of cause. See also Green, 86 *Nw. U. L. Rev.* at 647 ("At best, epidemiology assesses the likelihood [*568] that the agent caused a specific individual disease."). From epidemiological studies demonstrating an association, an epidemiologist may or may not infer that a causal relationship exists. However, the epidemiological studies themselves are not designed to demonstrate whether [*53] a particular agent did cause the disease, and the trial court erred in concluding that the studies were unreliable because they failed to establish causal relationship. ¹²

12 Further, the fact that a epidemiological study calls for further research does not indicate uncertainty on the part of the researchers. As explained below by expert witness David Hartman, Ph.D., who submitted an affidavit in the *Chrisco* case:

Any research design assessing clinical data in the real world will always be considered incomplete by critical reviewers. By its very nature, the medical researcher cannot control all possible factors in the human population under study. Therefore, one must distinguish between a truly erroneous study, and the study which is simply an

expression of a particular population . . . [and] is correctly constructed and analyzed. . . .

Almost all genres of research articles in the medical and behavioral sciences conclude their discussion with qualifying statements such as "there is still much to be learned." This is not, as might be assumed, an expression of ignorance, but rather an expression that all scientific fields are open-ended and can progress from their present state. . . .

Medical and behavioral statistics is a methodology that seeks to measure degrees of probability, not causality. Uncertainty is never completely abolished in any form of behavioral or medical science statistical manipulation. Therefore, conclusions must be defined in terms of "suggestions" or "associations" rather than causes. This is not due to some inaccuracy or vagueness of the technique or conclusion, but rather is intrinsic to the properties of statistics.

Mr. Hartman's opinion is consistent with other authorities on the subject. See, e.g., Reference Manual at 157 ("Most researchers are conservative when it comes to assessing causal relationships, often calling for stronger evidence and more research before a conclusion of causation is drawn.").

[**54] Nonetheless, CSX argues that the epidemiological studies upon which appellants' experts rely are infirm because they contain methodological flaws. It is the railroad's position that even if the experts' opinions themselves do not have to be Frye tested, here the underlying methodology upon which the opinions rely, the epidemiological studies, fail the Frye test.

Before turning to a discussion of the critical analysis employed by CSX, we must emphasize at this juncture that the issue in Frye and in the instant cases involves the admissibility of expert testimony, not the sufficiency of that testimony. An inquiry regarding the "sufficiency" of the evidence concerns whether the party has produced sufficient evidence to convince a reasonable juror that the opinion of the party's expert is correct. *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d at 744. "Admissibility," in contrast, "entails a threshold inquiry over whether a certain piece of evidence ought to be admitted at trial." *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1132 (emphasis in original).

At this admissibility stage of the proceedings, under Frye the court is asked to decide [**55] whether the basis of the evidence upon which plaintiffs' experts rely has a sufficient indicia of reliability. "Reliability is fundamental to issues involved in the admission of evi-

dence." *Hadden*, 690 So. 2d at 578. We agree with the appellants that under Frye they have demonstrated the reliability of the scientific evidence upon which their experts rely. While, as Dr. Baker acknowledged in his proffered testimony, there continues to be scientific debate about the safe levels of exposure with respect to certain toxins and the degree of reversibility of the effect of exposure to the toxins, we find the epidemiological science and methodology underlying his testimony to be established, reliable, and well-founded.

CSX asserts that, in deciding the question of admissibility here, as a part of our *de novo* review we must engage in a highly detailed level of critical analysis of each epidemiological study. While an analysis of each study for relative risk, confidence interval, biases, confounders, criteria of causality and other numerous factors may be appropriate in considering the sufficiency of the evidence, that is not appropriate or necessary under the circumstances here [**56] or at this stage of the litigation. Further, such a detailed analysis would require this court not [*569] only to have an appreciation for the methodological errors and inadequacies in the studies, an ability to assess the validity of a reanalysis of those studies, and an understanding of the biological underpinnings associated with the disease in question, but also to possess a firm grounding in the concepts of relative risk, statistical significance and confidence intervals, and their relationship to the preponderance of the evidence standard. *Green*, 86 Nw. U. L. Rev. at 681. While certainly courts must become educated on these subjects when necessary to adjudicate issues regarding the sufficiency of the evidence in the toxic torts arena, the record in these cases is lacking the necessary evidence upon which to make these judgments at this stage of the proceeding. See, e.g., *DeLuca*, 911 F.2d at 955 (declining to rule as a matter of law that any expert opinion rooted in a statistical analysis where the results of the underlying studies are not significant at a .05 level would not be allowed where the record contained virtually no relevant help from the parties or from qualified [**57] experts); *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1134 (an argument that an epidemiological study must show a relative risk greater than 2.0 is a sufficiency argument not an admissibility argument).¹³

13 Though there are certainly a number of cases that suggest a relative risk greater than 2.0 can permit an inference that an individual's disease was more likely than not caused by exposure to the toxic agent, there are also cases which have recognized that a plaintiff may satisfy his or her burden of production even if a relative risk less than 2.0 emerges from the epidemiological evidence. Reference Manual at 170. See, e.g., *Grassis v. Johns-Manville Corp.*, 248 N.J. Super. 446,

591 A.2d 671, 675 (N.J. Super. Ct. App. Div. 1991):

The physician or other qualified expert may view the epidemiological studies and factor out other known risk factors such as family history, diet, alcohol consumption, smoking . . . or other factors which might enhance the remaining risks, even though the risk in the study fell short of the 2.0 correlation.

[**58] Our conclusion is strongly influenced by the fact that the epidemiological studies here were conducted independently of this litigation and were peer-reviewed and accepted by journals that are widely acknowledged in the scientific and medical communities. See generally *Modern Scientific Evidence* at § 1- 3.3.3 (noting the importance of peer review and publication in highly regarded journals for the purpose of establishing scientific validity under Daubert). Although there is a debate as to whether publication in peer-reviewed journals or other professional literature is necessary to give a study an indicia of reliability, when there exists a mature epidemiological record with numerous peer-reviewed, published studies supporting the expert's analysis, an aura of reliability and validity is accorded those studies. See *Green*, 86 Nw. U. L. Rev. at 694; *Richardson v. Richardson-Merrell, Inc.*, 649 F. Supp. 799, 802-03 (D.D.C. 1986), *aff'd*, 273 U.S. App. D.C. 32, 857 F.2d 823 (D.C. Cir. 1988), *cert. denied*, 493 U.S. 882, 110 S. Ct. 218, 107 L. Ed. 2d 171 (1989). While the existence of numerous peer-reviewed, published, epidemiological studies does not guarantee that the studies are without [**59] flaws, such publication here alleviates the necessity of thorough judicial scrutiny of each study at the admissibility stage "to sort out the disputes over methodologic errors in studies." *Green*, 86 Nw. U. L. Rev. at 694. ¹⁴ At least [**570] until a more refined screening mechanism can be devised, we are satisfied that under *Frye* peer review and publication lends sufficient reliability and validity to these studies to allow an expert's testimony based upon these studies to be admissible. ¹⁵

14 In an action against CSX factually similar to the instant cases, the Tennessee Supreme Court recently upheld the admission into evidence of expert testimony based upon epidemiological studies showing an association between exposure to certain organic solvents and toxic encephalopathy. *McDaniel v. CSX Transp., Inc.*, 955 S.W.2d 257, 1997 WL 594750 (Tenn., September 29, 1997). We believe that the *McDaniel* court correctly explained the role of the trial court in cases such as this:

Although the trial court must analyze the science and not merely the qualifications, demeanor

or conclusions of experts, the court need not weigh or choose between two legitimate but conflicting scientific views. The court instead must assure itself that the opinions are based on relevant scientific methods, processes, and data, and not upon an expert's mere speculation. The trial court should keep in mind that the preliminary question . . . is one of admissibility of the evidence. Once the evidence is admitted, it will thereafter be tested with the crucible of vigorous cross-examination and countervailing proof. After that occurs, a defendant may, of course, challenge the sufficiency of the evidence by moving for a directed verdict at the appropriate times. Yet it is important to emphasize that the weight to be given to stated scientific theories, and the resolution of legitimate but competing scientific views, are matters appropriately entrusted to the trier of fact.

Id. at 265 (citations omitted).

[**60]

15 A review of case law in the toxic torts area demonstrates that the intensity of the "admissibility" inquiry evolved as a result of Agent Orange and benedictin cases. See *Green*, 86 Nw. U. L. Rev. 643. But unlike the present situation, the initial published studies involving both of those allegedly toxic agents were negative and the plaintiffs were trying to introduce expert testimony contrary to the published epidemiological studies.

In our ruling here we are not advocating the abdication of the judicial "gate-keeping" role, contemplated by *Frye*, to the editors of scientific and medical journals. In part, our ruling is a recognition that at this stage of these proceedings a sufficient record is not in place which would allow judicial scrutiny of these studies, spanning several scientific and medical disciplines, to determine the existence and seriousness of any methodological errors. While the experts in these cases testified at length, they testified only in a very general way about the qualities of the studies upon which they relied. Although the studies themselves are in the [**61] record, there is insufficient expert testimony on the quality of those studies to guide the court in making any legal conclusion about the probity of the studies. Researchers have methods for assessing the characteristics of persons included in the study and the risk of disease which can be used to rule out known sources of biases and error. On the basis of this record, this court cannot say that the researchers involved in these studies failed to employ such methods.

In addition, any such errors in these studies would principally affect the weight to be accorded the opinions based thereon. Our focus at this stage, however, is a more narrow one - whether to exclude expert testimony

based on mere speculation or unreliable science. *Joiner v. General Elec. Co.*, 78 F.3d at 532.¹⁶

16 Though certain of the federal decisions cited or discussed in this section of the opinion employ a Daubert analysis, rather than a Frye analysis, these opinions are nonetheless focusing on the reliability of the expert's methodology. Florida's Frye test is ultimately concerned with the reliability of the scientific principles or methodology upon which the expert bases his opinion. See generally, C. Ehrhardt, Florida Evidence §§ 702.3, 702.4 (1997). It is yet a matter of debate whether the Daubert test, in requiring that the reasoning or methodology underlying the testimony be scientifically valid, will be more liberal and allow more expert testimony than the Frye requirement that there be general acceptance of the underlying methodology. Modern Scientific Evidence at § 1-3.3.4. But we are satisfied that for the purposes of the analysis here, under the Frye test of general acceptance, that peer-reviewed epidemiological studies conducted independently of the instant litigation are the scientifically accepted means of analyzing human response to exposures to certain substances.

[**62] Finally, we decline to adopt the railroad's suggestion that we reject "statistically insignificant" studies. The use of "statistical significance" to reject an epidemiological study has been roundly criticized by the experts in the field. See, e.g., Green, 86 Nw. U. L. Rev. at 681-93. Professor Green, for example, concludes that rejecting studies that are not statistically significant would be cursory and foolish. We find his explanation instructive:

The Brock [*Brock v. Merrell Dow Pharm., Inc.*, 874 F.2d 307 (5th Cir. 1989), cert. denied, 494 U.S. 1046, 110 S. Ct. 1511, 108 L. Ed. 2d 646 (1990)] decision, in ascribing wondrous powers to the concept of statistical significance, contributes to doubts that these matters are ones that reasonably can be mastered by generalist judges. Statistical significance addresses only random error due to the sampling inherent in any epidemiologic study. It cannot and does not speak to systematic error, which requires an informed review of the methodology employed in conducting the study. Moreover, statistical significance is merely an instrument for assisting in evaluating a study, not a truth serum that can be simplistically [**63] prescribed.

86 Nw. U. L. Rev. at 681-82.

In sum, for the above reasons we decline to accept the railroad's invitation to examine these studies in detail ourselves and conclude without the basis of record evi-

dence that they are deficient for the variety of reasons advanced by the railroad. CSX's claims of [*571] bias, lack of biological plausibility, and alleged other defects in these studies go to the weight, rather than the admissibility, of the studies. See *Ellis v. International Playtex, Inc.*, 745 F.2d 292, 303 (4th Cir. 1984). If there are weaknesses or technical deficiencies in the published epidemiological studies supporting the plaintiffs' experts' opinions as the railroad claims, those perceived deficiencies are appropriate matters upon which to examine and cross examine the experts at trial and, then, for consideration by the fact finder. *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1132. In the instant cases, however, the claimed deficiencies are not a valid reason for excluding the experts' opinions.

As argued by the appellants, the trial in the instant cases will be primarily a so-called "battle of the experts." The fact that the experts have all derived [**64] their opinions from the same generally-accepted methodology, the epidemiological studies contained in the record, but simply disagree upon how to interpret the scientifically (and legally) reliable data, is not a valid reason for excluding the plaintiffs' experts' opinions altogether. As the court said in *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d at 1135:

For the district court to seize on the putative flaws of studies favorable to plaintiff, and then to privilege certain studies favorable to the defendant, was impermissibly to place a thumb on defendant's side of the scale and to encroach on the jury's prerogative to weigh the relative merits and credibilities of competing studies . . . Thus, to the extent that none of the studies is flawless or dispositive, their relative merits seems to us to be a classic question for the jury. Trial courts should not arrogate the jury's role in "evaluating the evidence and the credibility of expert witnesses" by "simply choos[ing] sides in [the] battle of the experts." *Christophersen v. Allied-Signal Corp.*, 902 F.2d 362, 366 (5th Cir. 1990).

Finally, we must respectfully disagree with the trial court's rejection of Dr. [**65] Kelly's testimony on specific causation. Dr. Kelly employed the differential diagnosis method which is scientifically acceptable. *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d at 758; *Hines v. Consolidated Rail Corp.*, 926 F.2d at 274. Using this differential diagnosis, Dr. Kelly attempted to eliminate the other possible causes of Berry's symptoms. Unlike the situation in *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, and other cases, Dr. Kelly had physical contact with Berry and personally examined him as well as supervised his treatment by other professionals. Dr. Kelly's opinion was not only based upon Berry's statements of his symptoms, but was based upon Berry's personal history, medical records, physical examinations and medical tests. In short, Dr. Kelly's opinion was based

upon sufficient epidemiological data, facts and personal observation, and was therefore reliable.

REVERSED and REMANDED for further proceedings consistent with this opinion.

JOANOS AND PADOVANO, JJ., CONCUR.

APPENDIX

Edward L. Baker, M.D., et al., Neurobehavioral Effects of Solvents in Construction Painters, 30 J. Occup. Med. 116 (1988)

Barbara Bazylewicz-Walczak, [**66] et al., The Psychological Effects of

Chronic Exposure to White Spirit in Rubber Industry Workers, 3 Polish J. Occup. Med. 117 (1990)

Stig-Arne Elofsson, Ph.D., et al., Exposure to Organic Solvents,

6 Scand. J. Work Envtl. Health 239 (1980)

Evelin Escalona, M.D., et al., Neurobehavioral Evaluation of

Venezuelan Workers Exposed to Organic Solvent Mixtures, 27

Am. J. Indus. Med. 15 (1995)

Anne T. Fidler, et al., Neurobehavioral Effects of Occupational

Exposure to Organic Solvents Among Construction Painters,

44 Brit. J. Indus. Med. 292 (1987)

Helena Hanninen, et al., Exposure to Organic Solvents and

Neuropsychological Dysfunction: A Study on Monozygotic

Twins, 48 Brit. J. Indus. Med. 18 (1991)

Lisa A. Morrow, Ph.D., et al., Alterations in Cognitive and

Psychological Functioning [*572] After Organic Solvent Exposure,

32 J. Occup. Med. 444 (1990)

Lisa A. Morrow, Ph.D., et al., A Distinct Pattern of Personality

Disturbance Following Exposure to Mixtures of Organic

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Andreas Seeber, Neurobehavioral Toxicity of Long-Term Exposure to Tetrachloroethylene, [**67] 2 Neurotoxicology and Teratology 579 (1989)

A. Spurgeon, Ph.D., et al., Neurobehavioral Effects of Long-Term

Occupational Exposure to Organic Solvents: Two Comparable

Studies, 22 Am. J. Indus. Med. 325 (1992)

Kurt Rasmussen, M.D., et al., Solvent-Induced Chronic Toxic

Encephalopathy, 23 Am. J. Indus. Med. 779 (1993)



LEXSEE 293 F. 1013

FRYE v. UNITED STATES

No. 3968

Court of Appeals of District of Columbia

54 App. D.C. 46; 293 F. 1013; 1923 U.S. App. LEXIS 1712; 34 A.L.R. 145

November 7, 1923, Submitted

December 3, 1923, Decided

PRIOR HISTORY: [**1] Appeal from the Supreme Court of the District of Columbia.

OPINION BY: VAN ORSDEL

OPINION

[*1013] Before SMYTH, Chief Justice, VAN ORSDEL, Associate Justice, and MARTIN, Presiding Judge of the United States Court of Customs Appeals.

VAN ORSDEL, Associate Justice. Appellant, defendant below, was convicted of the crime of murder in the second degree, and from the judgment prosecutes this appeal.

A single assignment of error is presented for our consideration. In the course of the trial counsel for defendant offered an expert witness to testify to the result of a deception test made upon defendant. The test is described as the systolic blood pressure deception test. It is asserted that blood pressure is influenced by change in the emotions of the witness, and that the systolic blood pressure rises are brought about by nervous impulses sent to the sympathetic branch of the autonomic nervous system. Scientific experiments, it is claimed, have demonstrated that fear, rage, and pain always produce a rise of systolic blood pressure, and that conscious deception or falsehood, concealment of facts, or guilt of crime, accompanied by fear of detection when the person is under examination, [**2] raises the systolic blood pressure in a curve, which corresponds exactly to the struggle going on in the subject's mind, between fear and attempted control of that fear, as the examination [*1014] touches the vital points in respect of which he is attempting to deceive the examiner.

In other words, the theory seems to be that truth is spontaneous, and comes without conscious effort, while

the utterance of a falsehood requires a conscious effort, which is reflected in the blood pressure. The rise thus produced is easily detected and distinguished from the rise produced by mere fear of the examination itself. In the former instance, the pressure rises higher than in the latter, and is more pronounced as the examination proceeds, while in the latter case, if the subject is telling the truth, the pressure registers highest at the beginning of the examination, and gradually diminishes as the examination proceeds.

Prior to the trial defendant was subjected to this deception test, and counsel offered the scientist who conducted the test as an expert to testify to the results obtained. The offer was objected to by counsel for the government, and the court sustained the objection. [**3] Counsel for defendant then offered to have the proffered witness conduct a test in the presence of the jury. This also was denied.

Counsel for defendant, in their able presentation of the novel question involved, correctly state in their brief that no cases directly in point have been found. The broad ground, however, upon which they plant their case, is succinctly stated in their brief as follows:

"The rule is that the opinions of experts or skilled witnesses are admissible in evidence in those cases in which the matter of inquiry is such that inexperienced persons are unlikely to prove capable of forming a correct judgment upon it, for the reason that the subject-matter so far partakes of a science, art, or trade as to require a previous habit or experience or study in it, in order to acquire a knowledge of it. When the question involved does not lie within the range of common experience or common knowledge, but requires special experience or special knowledge, then the opinions of witnesses skilled in that particular science, art, or trade to which the question relates are admissible in evidence."

54 App. D.C. 46; 293 F. 1013, *;
1923 U.S. App. LEXIS 1712, **; 34 A.L.R. 145

Numerous cases are cited in support of this rule. Just when a scientific [**4] principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential 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.

We think the systolic blood pressure deception test has not yet gained such standing and scientific recognition among physiological and psychological authorities as would justify the courts in admitting expert testimony deduced from the discovery, development, and experiments thus far made.

The judgment is affirmed.



LEXSEE 669 N.E.2D 378

THE PEOPLE OF THE STATE OF ILLINOIS, Plaintiff-Appellee, v. ANGELO
DALCOLLO, Defendant-Appellant.

No. 2-93-1291

APPELLATE COURT OF ILLINOIS, SECOND DISTRICT

282 Ill. App. 3d 944; 669 N.E.2d 378; 1996 Ill. App. LEXIS 629; 218 Ill. Dec. 435

January 3, 1996, SUBMITTED

August 19, 1996, FILED

NOTICE: [***1] UNPUBLISHED IN PART
PURSUANT TO SUPREME COURT RULE 23
ORDER.

SUBSEQUENT HISTORY: Rehearing Denied Sep-
tember 12, 1996. Released for Publication September 12,
1996.

PRIOR HISTORY: Appeal from the Circuit Court of
Winnebago County. No. 90--CF--1260. Honorable Fre-
derick J. Kapala and John W. Nielsen, Judges, Presiding.

DISPOSITION: Affirmed.

COUNSEL: For Angelo Dalcollo, Defendant-Appellant:
G. Joseph Weller Deputy Defender, Office of the State
Appellate Defender, Elgin, IL. COURT APPOINTED.
APPEARANCE ENTER DATE: 11/09/93. Patrick M.
Carmody, Office of the State Appellate Defender, Elgin,
IL. COURT APPOINTED. Sherry R. Silvern, Office of
the State Appellate Defender, Elgin, IL. NOTE: GJW,
SRS., On brief. COURT APPOINTED. APPEARANCE
ENTER DATE: 03/31/95. TRIAL COUNSEL: Sahl-
strom, R. Craig.

For People, Plaintiff-Appellee: Honorable Paul A. Logli,
Winnebago County State's Attorney, Rockford, IL. Wil-
liam L. Browers Deputy Director, State's Attorney Ap-
pellate Prosecutor, Elgin, IL. APPEARANCE ENTER
DATE: 10/10/95. Diane L. Campbell, State's Attorneys
Appellate Prosecutor, Elgin, IL. NOTE: PAL, WLB,
DLC., [***2] On brief. APPEARANCE ENTER
DATE: 10/06/95.

JUDGES: JUSTICE BOWMAN delivered the opinion
of the court. COLWELL and RATHJE, JJ., concur.

OPINION BY: BOWMAN

OPINION

[*946] [**379] JUSTICE BOWMAN delivered
the opinion of the court:

A jury convicted defendant, Angelo Dalcollo, of
criminal sexual assault (Ill. Rev. Stat. 1989, ch. 38, par.
12--13(a)(1) (now 720 ILCS 5/12--13(a)(1) (West
1994))). The trial court sentenced defendant to nine
years' imprisonment. Defendant now appeals his convic-
tion. We affirm.

BACKGROUND

On August 1, 1990, defendant was charged by com-
plaint with the offense of criminal sexual assault (Ill.
Rev. Stat. 1989, ch. 38, par. 12-13(a)(1)). Two weeks
later defendant was indicted on that same offense. The
indictment charged that on July 14, 1990, defendant, by
use of force, committed an act of sexual penetration by
inserting his penis into A.F.'s vagina.

Trial commenced on May 11, 1993, before Judge
Frederick Kapala and lasted until May 17, 1993. The
facts adduced at trial may be briefly stated. Additional
pertinent facts will be discussed in the context of the
issues raised on appeal. A.F., the complainant, testified
that on July 14, 1990, at 3 a.m., she started to walk to the
Penny Pincher [***3] Cafe (the cafe) in Rockford, Illi-
nois, to meet some friends. After walking three miles, a
red El Camino with a broken right headlight drove past
her, turned around, and pulled alongside her. The driver
of the vehicle, whom A.F. identified in court as defen-
dant, offered her a ride, which she accepted. As they
approached the cafe, defendant "punched the gas" and
drove past it. Defendant drove to a parking lot and told

A.F. that he was going to "make love to [her]." When A.F. tried to open her door, defendant told her "not to make him do it the hard way," because if she did, "he'd hurt [her] really bad." A.F. asked him if he was afraid of "going up for rape," and he said he was not because "he'd gone up lots of times before and never got caught." Defendant then hit her in the head, jumped on top of her, and removed her pants. After ordering her to remove her tampon, he inserted his penis into her vagina and ejaculated. Defendant then let her leave the car. As he drove away, she memorized the license plate number. A.F. stated it was 14CC2E, although the record reveals that the number was actually 1422 CE. A.F. then walked to the cafe and told some police officers, who happened to be [***4] there, that she had been raped. The police officers took her to the hospital. At the hospital, A.F. told the nurse that she had been raped.

A.F. also testified that on July 16, 1990, she went with her husband, Debra Shumaker, and Gerald Anderson to defendant's home. A.F.'s husband apparently knew that defendant was her assailant based on her description of him and his vehicle. He therefore [*947] wanted to "beat up" defendant. After their car got stuck in a ditch near defendant's home, a truck driven by defendant pulled up behind them. When defendant said something to them, A.F. turned around, pointed at him, and said, "He is the one that raped me." Defendant ran, but was caught and beaten by A.F.'s husband.

On cross-examination, A.F. stated that the distance from her home to the cafe was 8 to 10 miles. She stated that she touched the inside of the El Camino with her hands and that while inside the vehicle she tried to wipe off any fluids or menstrual blood on her. She admitted that she knew on July 20, 1990, that defendant had charged her with aggravated assault in relation to the July 16 incident. On redirect examination, A.F. testified that when she arrived at the cafe on July 14, 1990, [***5] she gave a description of her assailant to a police officer and told him that her assailant's vehicle was a red El Camino with a broken right headlight.

Officer Royal MacKenzie of the Rockford police department testified that at approximately 5 a.m., on July 14, 1990, A.F. approached him in the cafe and told him that she had been raped. Her blouse was torn [***380] and she was crying. She described her assailant and his vehicle, a red El Camino pickup truck with a broken headlight. She also provided the vehicle's license plate number. He then escorted her to SwedishAmerican Hospital.

Michelle Gillihan, a nurse at the hospital, testified that at approximately 5:45 a.m. on July 14, 1990, she met A.F., who told her that she had been raped. Gillihan then

performed a rape test examination on A.F. She did not notice any bruises on A.F.

Detective Bruce Scott of the Rockford police department testified that on July 20, 1990, he impounded defendant's vehicle, a red El Camino. The vehicle's right headlight did not work. Detective Scott also stated that when he served the criminal complaint on defendant in this case, defendant said, "yeah, but you can't fucking prove it." He acknowledged on cross-examination [***6] that when he impounded the vehicle, there was no indication that it had been recently cleaned.

Dr. Harold Deadman, supervisor of the Federal Bureau of Investigation's (FBI) DNA analysis unit, testified as an expert in forensic DNA analysis. According to Dr. Deadman, DNA (deoxyribonucleic acid) is a chemical substance present in the cellular material of all living things. Located in a body's chromosomes, DNA determines a person's characteristics. DNA is made of four types of subunits, which he described as being "like links in a chain." Although there are only four types of subunits, there are millions of individual subunits along the length of the chain. The sequence of the different subunits determines a person's characteristics. Except for identical twins, each person's DNA is unique.

[*948] Dr. Deadman testified that the DNA analysis unit examines evidence submitted in criminal cases by comparing the DNA extracted from an unknown source with DNA from a particular person. The unit attempts to identify an individual as being a contributor of a particular type of biological material, such as blood or seminal fluid. There are three general steps in DNA testing: (1) creating a DNA "profile" [***7] of a sample; (2) determining whether the profiles of different samples "match"; and (3) if the samples match, estimating the statistical probability of a random match.

The first step, creating a DNA "profile" of a sample, involves its own six-step process, known as "Restriction Fragment Length Polymorphism" (RFLP). Step 1 involves extracting the DNA from a sample. Step 2 involves cutting the extracted DNA into smaller fragments. The DNA is cut "by using chemical substances that subjects [sic] it to certain sequences that are present," thereby generating a large number of smaller fragments of DNA. In step 3, the DNA is separated by size. The DNA is placed in a gel; an electrical current is applied to the gel, forcing the DNA fragments to move according to their size. The larger fragments, which move more slowly, remain at the origin, while intermediate fragments spread throughout the gel. Once completed, the DNA fragments are arrayed across the gel according to their size. In step 4, the DNA fragments are transferred from the gel to a piece of nylon. When this is done properly, the fragments are arrayed on the nylon exactly as

they existed in the gel. Step 5 involves using radioactively [***8] charged probes to identify, locate, and measure the DNA fragments of concern to the test. In step 6, the probes are "visualized." A piece of x-ray film is placed on top of the probe, revealing DNA "bands" (pieces of DNA). DNA bands make up the DNA profile.

The second step requires interpreting the results of the RFLP procedure. Interpretation involves comparing DNA bands from known and unknown samples. A comparison may be made by visually inspecting and then measuring the DNA bands of the known and unknown samples. A "match" exists if the bands are consistent. A match between a known and unknown sample is not an absolute identification. A match is only a statement of consistency. That is, a match is a statement that the DNA in the unknown sample could have originated from the source of the known sample.

The third step involves estimating the statistical probability of a random match. Because a match is only a statement that the DNA in the crime scene sample could have [**381] originated from the defendant, the FBI estimates the statistical probability of a random match between the DNA sample taken from the crime scene and the DNA [**949] sample taken from the defendant. To do this, the FBI determines [***9] what part of the population would contain a DNA profile like that found in a particular case. In other words, the FBI estimates the frequency of the particular DNA test sample occurring in a population unit. In making this estimate, the FBI compares the DNA test samples to a previously constructed database. The FBI's databases are divided along racial lines. The Caucasian database, which was used in the present case, is a database of approximately 500-700 people, or between 1,000 and 1,500 DNA bands.

The FBI estimates the probability of a random match in the following manner. The bands in a particular category are added up and then divided by the total numbers of bands. The result is the "band frequency" for that population unit based on the FBI database. Once the frequencies of each probe are determined, they are multiplied together to determine the frequency of the DNA profile. This manner of multiplying the frequencies is known as the product rule. A more detailed explanation of the product rule may be found in *State v. Bible*, 175 Ariz. 549, 582-84, 858 P.2d 1152, 1185-86 (Ariz. 1993).

According to Dr. Deadman, the FBI's procedures have been criticized "primarily in the courtroom, [***10] by Defense experts in the courtroom." The FBI's procedures have not been criticized to any great extent at scientific conferences. Moreover, the scientific literature which deals with the issues of forensic DNA evidence is "almost overwhelmingly" in support of the FBI's procedures. Those publications that have criticized

the FBI's procedures are "very few," and they use "very little supporting data" to support their criticisms.

Using the FBI's procedures, Dr. Deadman concluded, to a reasonable degree of scientific certainty, that defendant's DNA "matched" the DNA recovered from the seminal fluid found on the underwear A.F. wore at the time of the attack. Dr. Deadman calculated that the probability of a random match was 1 in 60 million.

On cross-examination, Dr. Deadman testified that the database used in the present case is used for the entire United States, but that it includes samples only from California, Texas, Florida, and FBI trainees. While there may be some differences between ethnic groups within a population, those differences are not "meaningful or significant." Dr. Deadman conceded that it would be possible to get a different result in this case if the samples comprising [***11] the database were drawn from Illinois and that using a different database could result in a different probability of a random match. Dr. Deadman also conceded that a report by the National Research Council, Committee on DNA Technology in Forensic Science, DNA Technology in Forensic Science (1992) (NRC Report), stated that "questions have been [**950] raised about the adequacy of population data bases on which frequency estimates are based on the role of ratio and ethnic origin and frequency estimation."

The State rested at the conclusion of Dr. Deadman's testimony. In his own defense, defendant called Dr. Pravatichai Boonlayangoor to testify as an expert in forensic DNA analysis. Using the same test data as the FBI but a different method of calculating the probability of a random match, Dr. Boonlayangoor determined that the probability of a random match could be from 1 in 745 to 1 in 4,212. Dr. Boonlayangoor admitted that his method of calculation was not recommended in the NRC Report and was even more conservative. He also admitted that his method of calculation was used by no other scientist.

Kandie Dalcollo, defendant's wife, testified that between 2 and 3 a.m. on July 14, 1990, she [***12] heard defendant leave the house. She remained awake for the next 15 minutes, and during that time she did not hear her husband's car start. Mrs. Dalcollo next saw defendant at 6 a.m. that day. She admitted that she did not know where defendant was between 3:30 a.m. and 6 a.m. She described defendant as having a moustache and beard on July 14, 1990. Margaret Dalcollo, defendant's mother, testified that on July 14, 1990, at 5 a.m., she found defendant asleep in his [**382] car. She also testified that defendant's car, an El Camino, was not operable on July 14, 1990.

Defendant, a convicted thief, testified that on July 14, 1990, from approximately 2:30 to 5 a.m., he was asleep in his car. Between 5 and 5:10 a.m., his mother

woke him. According to defendant, his car was inoperable at that time. At the conclusion of defendant's testimony, the defense rested. After closing arguments, the jury returned a verdict of guilty.

DISCUSSION

Defendant has four principal contentions on appeal: (1) the trial court erred in admitting the DNA test results; (2) the trial court erred in denying defendant's motion to suppress identification evidence; (3) the prosecutor's comments in closing argument denied him [***13] a fair trial; and (4) he was not proved guilty beyond a reasonable doubt.

I

Defendant's first contention is that the trial court erred in admitting the DNA test results. Defendant posits two alternative arguments in support of this contention: (1) the trial court erred in refusing to conduct a Frye hearing (see *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013 (D.C. Cir. 1923)) on the admissibility of the DNA test results; and (2) the trial court erred in admitting the DNA test results.

[*951] A

[The following material is nonpublishable under *Supreme Court Rule 23*].

[The preceding material is nonpublishable under *Supreme Court Rule 23*].

B

Defendant next argues that the trial court erred in admitting the DNA evidence. Defendant apparently does not challenge whether the FBI's RFLP matching procedures are generally accepted in the relevant scientific community. Defendant instead makes one principal challenge to the admission of DNA test results in this case, namely, that the FBI's manner of determining the statistical probability of a random match of DNA profiles is not generally accepted in the relevant scientific community. Our subsequent analysis, therefore, will be limited [***14] to this one issue.

The admission of scientific evidence in Illinois is governed by the test set forth in *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013 (D.C. Cir. 1923). *People v. Eyles*, 133 Ill. 2d 173, 211, 139 Ill. Dec. 756, 549 N.E.2d 268 (1989); *People v. Baynes*, 88 Ill. 2d 225, 241, 58 Ill. Dec. 819, 430 N.E.2d 1070 (1981). But see *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 588, 125 L. Ed. 2d 469, 480, 113 S. Ct. 2786, 2794 (1993) (Frye test no longer applicable in federal trials). The classic statement of the test is found in Frye itself:

"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 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." *Frye*, 293 F. at 1014.

In other words, evidence is admissible [***15] when the scientific principle on which it rests has gained general acceptance in the relevant scientific community. *People v. Acri*, 277 Ill. App. 3d 1030, 1033, 214 Ill. Dec. 761, 662 N.E.2d 115 (1996). A reviewing court will not disturb a trial court's determination to admit evidence pursuant to the Frye standard absent an abuse of discretion. *Eyles*, 133 Ill. 2d at 211-12.

To date, our supreme court has not addressed whether DNA test results are admissible, although it has indicated it will in the appropriate case. See *Franson v. Micelli*, 172 Ill. 2d 352, 355, 217 Ill. Dec. 250, 666 N.E.2d 1188 (1996) (vacating, sua sponte, appellate court decision which held that the trial court erred in considering DNA evidence, where the trial court failed to enter a final appealable judgment); *People v. Moore*, 171 Ill. 2d 74, 98, 215 Ill. Dec. 75, 662 N.E.2d [***383] 1215 (1996) (holding that it need not decide the "interesting" issue of whether the FBI's DNA probability calculation method satisfied [*952] Frye because the admission of the DNA evidence was harmless error).

The Illinois appellate court, in contrast, has issued a multitude of opinions on this issue. See, e.g., *Franson v. Micelli*, 269 Ill. App. 3d 20, [***16] 206 Ill. Dec. 399, 645 N.E.2d 404 (1994), vacated on other grounds and appeal dismissed 172 Ill. 2d 352, 217 Ill. Dec. 250, 666 N.E.2d 1188 (1996); *People v. Heaton*, 266 Ill. App. 3d 469, 203 Ill. Dec. 710, 640 N.E.2d 630 (1994); *People v. Johnson*, 262 Ill. App. 3d 565, 199 Ill. Dec. 931, 634 N.E.2d 1285 (1994); *People v. Stremmel*, 258 Ill. App. 3d 93, 197 Ill. Dec. 177, 630 N.E.2d 1301 (1994); *People v. Watson*, 257 Ill. App. 3d 915, 196 Ill. Dec. 89, 629 N.E.2d 634 (1994); *People v. Miles*, 217 Ill. App. 3d 393, 160 Ill. Dec. 347, 577 N.E.2d 477 (1991); *People v. Lipscomb*, 215 Ill. App. 3d 413, 158 Ill. Dec. 952, 574 N.E.2d 1345 (1991). Before addressing defendant's arguments, we believe it is appropriate to analyze briefly these opinions.

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The fourth district first addressed the issue in *People v. Lipscomb*, 215 Ill. App. 3d 413, 158 Ill. Dec. 952, 574 N.E.2d 1345 (1991), and *People v. Miles*, 217 Ill. App. 3d 393, 160 Ill. Dec. 347, 577 N.E.2d 477 (1991). In *Lipscomb*, the trial court found that the RFLP analysis and the frequency procedures for determining the statistical probability of a random match were generally accepted in the relevant scientific communities. On appeal, [***17] the defendant argued that the trial court improperly applied the Frye test to DNA testing generally. According to the defendant, the trial court should have applied the Frye test to the specific procedures of DNA testing, such as the procedure for determining the statistical probability of a random match. The *Lipscomb* court rejected this argument. The court reasoned that Frye applied to new scientific principles and that the principle involved "is the general DNA forensic analysis" and not the procedures used within that framework. *Lipscomb*, 215 Ill. App. 3d at 432-33. The court then held that "any question concerning the specific procedures used by the company [performing DNA analyses] or expert goes to the reliability of the evidence and is properly considered by the jury in determining what weight to give to this evidence." *Lipscomb*, 215 Ill. App. 3d at 432.

In *Miles*, the defendant challenged on appeal the admissibility of the DNA test results on the ground that the probability statistics, as calculated by the product rule, were inadmissible. *Miles*, 217 Ill. App. 3d at 402. Relying on *Lipscomb*, the *Miles* court held that the DNA test results [***18] were admissible. The court reasoned that the *Lipscomb* court implicitly held that the process of generating probability statistics was an integral part of the DNA identification process and that, because this process satisfied the Frye test, probability statistics calculated thereby were admissible. *Miles*, 217 Ill. App. 3d at 405.

In *People v. Watson*, 257 Ill. App. 3d 915, 196 Ill. Dec. 89, 629 N.E.2d 634 (1994), the first district retreated from *Lipscomb* and *Miles*. In *Watson*, the State appealed the trial court's exclusion of DNA evidence on the ground it did not satisfy the Frye test. The *Watson* court initially agreed with *Lipscomb* [*953] and *Miles* that the theory underlying DNA profiling is generally accepted in the relevant scientific community. However, whereas the *Lipscomb* and *Miles* courts had then concluded that the procedures used when performing DNA analyses were admissible, the *Watson* court proceeded to subject each step in the DNA methodology to the Frye test. After doing so, the court concluded that the RFLP technique used for matching DNA profiles was generally accepted, but that the manner of calculating the statistical [***19] probability of a random match was not. *Watson*, 257 Ill. App. 3d at 929-30.

Soon after *Watson*, the second district issued *People v. Stremmel*, 258 Ill. App. 3d 93, 197 Ill. Dec. 177, 630 N.E.2d 1301 (1994). In *Stremmel*, the trial court ruled that the relevant scientific community generally accepted the reliability of the FBI's procedures and protocols to determine both the existence of a DNA match and the statistical probability [***384] of a random match. Relying on *Lipscomb* and *Miles*, and without any reference to *Watson*, the *Stremmel* court affirmed this ruling and rejected the defendant's argument that the actual testing procedures performed in a particular case were also subject to the Frye test. *Stremmel*, 258 Ill. App. 3d at 106.

The fourth district reentered the debate with *People v. Johnson*, 262 Ill. App. 3d 565, 199 Ill. Dec. 931, 634 N.E.2d 1285 (1994). In *Johnson*, the defendant argued that DNA evidence in general was inadmissible. Relying on *Lipscomb* and *Miles*, the *Johnson* court rejected this argument and held that DNA testimony, including testimony about the statistical probability of a random match, was admissible. *Johnson*, [***20] 262 Ill. App. 3d at 569. In doing so, the *Johnson* court noted the *Watson* court's disagreement with *Lipscomb* and *Miles*. *Johnson*, 262 Ill. App. 3d at 570.

In *People v. Heaton*, 266 Ill. App. 3d 469, 203 Ill. Dec. 710, 640 N.E.2d 630 (1994), the fifth district partially rejected *Watson*. In *Heaton*, relying solely on the NRC Report, the defendant argued that the DNA evidence was inadmissible because the product rule method used in calculating the statistical probability of a random match did not satisfy Frye. A divided court held that the trial court did not abuse its discretion in admitting DNA test results. While acknowledging a debate over the product rule, the *Heaton* court held that it would not rely on the NRC Report because it was never brought to the trial court's attention. *Heaton*, 266 Ill. App. 3d at 475-78. Justice Rarick dissented and argued that the court should conduct a broad review of the record. *Heaton*, 266 Ill. App. 3d at 480 (Rarick, J., dissenting). Justice Rarick then stated that the calculation of the statistical probability of a random match should be subjected to the Frye test and that, based on the NRC Report, the statistical [***21] probability analysis is not generally accepted in the relevant scientific community. *Heaton*, 266 Ill. App. 3d at 480-81 (Rarick, J., dissenting).

[*954] In *Franson v. Micelli*, 269 Ill. App. 3d 20, 206 Ill. Dec. 399, 645 N.E.2d 404 (1994), vacated on other grounds and appeal dismissed 172 Ill. 2d 352, 217 Ill. Dec. 250, 666 N.E.2d 1188 (1996), the first district continued to adhere to its previous holding in *Watson*.¹ In *Franson*, the defendant argued that the statistical probability evidence should not have been admitted because the procedures by which that evidence was derived were not generally accepted in the relevant scientific community. The *Franson* court held that the Frye test was appli-

cable to the procedures involved in the general DNA forensic analysis. *Franson*, 269 Ill. App. 3d at 29. The Franson court then held, after conducting a broad review of the record, that the manner of determining the statistical significance of a match of DNA profiles was not generally accepted. *Franson*, 269 Ill. App. 3d at 30.

1 Recently, the supreme court vacated Franson and dismissed the appeal on the ground that both it and the appellate court lacked jurisdiction to hear the appeal. However, we find much of the Franson court's reasoning instructive and therefore refer to it in our decision.

[**22] Having reviewed the principal Illinois cases on the admissibility of DNA evidence, we now shift our attention to the case at bar. Defendant urges us to conduct a broad review of the record and consider the NRC Report, even though he never presented this report to the trial court. Defendant argues that the NRC Report establishes that the product rule method for calculating the statistical probability of a random match does not satisfy the Frye test because it is not generally accepted within the relevant scientific community. As such, defendant argues, the trial court erred in admitting the DNA test results.

Analytically, defendant's argument compels us to answer three questions: (1) may we consider and rely upon legal and scientific commentaries when reviewing the trial court's determinations regarding the admissibility of DNA evidence, even if the commentaries were not originally before the trial court?; (2) are the procedures used to apply a scientific theory subject to the Frye test?; [**385] (3) if so, is the FBI's method of calculating the statistical probability of a random match generally accepted in the relevant scientific community? As we explain below, we answer each question [**23] in the affirmative.

(1)

The first question we must answer is whether we may consider and rely upon legal and scientific commentaries when reviewing the trial court's determinations regarding the admissibility of DNA evidence, even if the commentaries were not originally before the trial court. Defendant urges us to conduct a broad review of the record [**955] and consider materials such as the NRC Report in reviewing the trial court's determinations.

Generally, a reviewing court will not disturb a trial court's determination to admit evidence pursuant to the Frye standard absent an abuse of discretion. *Eyler*, 133 Ill. 2d at 211-12. Some courts interpret this standard of review so as to require a reviewing court to determine the issues on appeal based solely on the trial court record. See *Heaton*, 266 Ill. App. 3d at 476-77; *People v.*

Mehlberg, 249 Ill. App. 3d 499, 530-32, 188 Ill. Dec. 598, 618 N.E.2d 1168 (1993). We do not. Where the question of the general acceptance of a new scientific theory or technique is raised, the court is oftentimes asked to establish the law of the jurisdiction for future cases. *Watson*, 257 Ill. App. 3d at 923-24; *Heaton*, 266 Ill. App. [**24] 3d at 479-80 (Rarick, J., dissenting); accord *United States v. Porter*, 618 A.2d 629, 635 (D.C. App. 1992). This is certainly true in the present case. Thus, in recognition of the fact that the formulation of the law is a "quintessentially appellate function" (*Porter*, 618 A.2d at 635), we will engage in a broad review of the trial court's determination with respect to the general acceptance of forensic DNA analysis. See *Watson*, 257 Ill. App. 3d at 923-24; *Heaton*, 266 Ill. App. 3d at 479-80 (Rarick, J., dissenting). In doing so, we may consider the expert evidence presented in the trial court, judicial opinions from other jurisdictions, and any pertinent legal and scientific commentaries. See *Watson*, 257 Ill. App. 3d at 924.

We note that the position we adopt today--engaging in a broad review of the trial court's determination--accords with the practice of our supreme court when it has considered the admissibility of a scientific theory in a given case. See, e.g., *Eyler*, 133 Ill. 2d at 215 (adopting the reasoning and conclusion of *People v. Partee*, 157 Ill. App. 3d 231, 110 Ill. Dec. 845, 511 N.E.2d 1165 (1987), to hold that electrophoresis is generally accepted [**25] in the relevant scientific community; Partee, in turn, relied upon scientific commentaries that were apparently not before the trial court); *People v. Zayas*, 131 Ill. 2d 284, 289-90, 137 Ill. Dec. 568, 546 N.E.2d 513 (1989) (considering various legal and scientific commentaries to support conclusion that hypnotically enhanced testimony was inadmissible); *Baynes*, 88 Ill. 2d at 234-37 (considering and relying upon various scientific commentaries to support the conclusion that polygraph tests are inadmissible).

(2)

Having answered the first question in the affirmative, we must now answer the second: are the procedures used to apply a scientific theory subject to the Frye test? Under the Lipscomb/Miles line of cases, the procedure for calculating probability statistics is not subject to the Frye test. Rather, probability statistics are admissible because [**956] the DNA evidence in general satisfied the Frye test. As Miles explained:

"Implicitly, the [Lipscomb] court held the process of generating probability statistics is an integral part of the DNA identification process. Because the DNA identification process meets the Frye test and is admissible, [**26] probability statis-

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tics operated thereby are admissible."
Miles, 217 Ill. App. 3d at 405.

We disagree. In our view, application of the Frye test to determine the admissibility of DNA evidence requires that both the theory and the techniques or procedures implementing the theory must be generally accepted [***386] in the relevant scientific community. See *Franson*, 269 Ill. App. 3d at 30; *Watson*, 257 Ill. App. 3d at 929; accord *Bible*, 175 Ariz. at 586-87, 858 P.2d at 1189-90; *Lindsey v. People*, 892 P.2d 281, 290 (Colo. 1995); *Vargas v. State*, 640 So. 2d 1139, 1150 (Fla. App. 1994), rev'd on other grounds 667 So. 2d 175 (Fla. 1995); *Commonwealth v. Curnin*, 409 Mass. 218, 224-26, 565 N.E.2d 440, 444-45 (1991); *State v. Carter*, 246 Neb. 953, 982, 524 N.W.2d 763, 782 (1994); *State v. Vandebogart*, 136 N.H. 365, 376, 616 A.2d 483, 490 (1992); *Commonwealth v. Crews*, 536 Pa. 508, 522, 640 A.2d 395, 402 (1994); *State v. Cauthron*, 120 Wash. 2d 879, 888-89, 846 P.2d 502, 506-07 (1993). We reach this conclusion for two reasons.

First, Frye requires that the "thing" from which the deduction is made--e.g., the procedures upon which the DNA results [***27] are based--must be generally accepted. Undoubtedly, the theory behind DNA testing is generally accepted. Contrary to the position espoused by the Lipscomb/*Miles* line of cases, however, the procedures used to implement the theory are still subject to the Frye test. As the *Franson* court cogently explained:

"Under Frye, if the procedure or 'thing' upon which the DNA result was determined is not generally accepted, then the result is inadmissible. For instance, DNA testing to determine a 'match' may be well recognized, but the 'thing' upon which the result is based is the procedure used to arrive at the determination of whether there is a 'match.' Thus, if the procedures are not generally accepted, then the result is inadmissible under Frye. Similarly, although it may be generally accepted that statistical probabilities can be calculated based upon the 'matching' results, if the method used to calculate the statistical probabilities is not generally accepted as valid in the relevant scientific community, then the statistics should be inadmissible."
Franson, 269 Ill. App. 3d at 29-30.

Second, merely "because the DNA identification process meets the Frye [***28] test" does not mean that

"probability statistics operated thereby" are admissible. *Franson*, 269 Ill. App. 3d at 30, quoting [*957] *Miles*, 217 Ill. App. 3d at 405, 577 N.E.2d at 485. The procedures used to "match" DNA samples are separate and result in different findings than the procedures underlying probability statistics. The result of DNA identification procedures is the determination of whether the DNA samples "match." The result of statistical probability procedures is the determination of the frequency of a "match" in the relevant population. Thus, merely because DNA identification procedures may be generally accepted and the results admissible does not mean that subsequent statistical probabilities are admissible if the statistical probability procedures are not generally accepted. See *Franson*, 269 Ill. App. 3d at 30.

Accordingly, we hold that the Frye test requires that both the theory and the techniques or procedures implementing the theory must be generally accepted in the relevant scientific community. See *Franson*, 269 Ill. App. 3d at 30; *Watson*, 257 Ill. App. 3d at 929. This holding, however, should not be read as requiring that the specific procedures used in a particular case are also subject to the Frye [***29] test. See *Watson*, 257 Ill. App. 3d at 929; see also *Vandebogart*, 616 A.2d at 490 (Frye test does not include whether the testing laboratory performed the accepted scientific procedures in analyzing the forensic samples in a particular case). We have no quarrel with those cases which hold that any concerns with the specific procedures used in a particular case go to the reliability and weight of the evidence. See, e.g., *Stremmel*, 258 Ill. App. 3d at 106; *Miles*, 217 Ill. App. 3d at 402-03; *Lipscomb*, 215 Ill. App. 3d at 432.

(3)

We now arrive at the heart of the contention--whether the FBI's method of calculating the statistical probability of a random match is generally accepted in the relevant scientific community. Defendant maintains [***387] that the NRC Report and other scientific commentaries demonstrate that probability statistics are not generally accepted. He therefore asks us to reverse his conviction and remand the cause for a new trial.

In determining whether a novel scientific procedure is "generally accepted" in the scientific community, the issue is consensus versus controversy over a particular technique. *Porter*, 618 A.2d at 634. General acceptance [***30] does not require scientific unanimity. *Lindsey*, 892 P.2d at 289; *People v. Wesley*, 83 N.Y.2d 417, 423, 611 N.Y.S.2d 97, 100, 633 N.E.2d 451, 454 (1994). Moreover, the mere existence of a dispute does not preclude a finding that a procedure is generally accepted. *Lindsey*, 892 P.2d at 289; *People v. Soto*, 43 Cal. App. 4th 1783, 1801, 35 Cal. Rptr. 2d 846, 856 (1994). Rather, only significant [*958] disputes between quali-

fied experts will preclude a finding of "general acceptance." *Cauthron*, 120 Wash. 2d at 887, 846 P.2d at 505; *Porter*, 618 A.2d at 634; see *Acri*, 277 Ill. App. 3d at 1033-34 (reliability of uncorroborated alerts by accelerant-sniffing dogs in the field of arson investigation was not generally accepted; both sides on the issue were evenly split and adamant in their positions).

With these principles in mind, we now turn to whether the FBI's method of calculating the statistical probability of a random match is generally accepted in the relevant scientific community. As Dr. Deadman testified, a match is only a statement that the DNA in the crime scene sample could have originated from the defendant. The FBI therefore estimates, by using the product [***31] rule, the statistical probability of a random match between the DNA sample taken from the crime scene and the DNA sample taken from the defendant. In other words, the FBI estimates the frequency of the particular DNA test sample occurring in a population unit. In making this estimate, the FBI compares the DNA samples to a previously constructed population database.

According to the scientific literature, the product rule relies on two assumptions, both of which must exist for its calculations to be accurate. The first, known as "Hardy-Weinberg equilibrium," assumes that the members of the racial groups represented in the databases mate randomly within their group and thus mix the gene pool evenly. The second, known as "linkage equilibrium," assumes that the DNA bands identified by the RFLP procedures are not related to each other and thus are independent in a statistical sense. See generally R. Lewotin & D. Hartl, *Population Genetics in Forensic DNA Typing*, 254 *Science* 1745 (1991) (Lewotin & Hartl); see also *State v. Johnson*, 183 *Ariz.* 623, 627-28, 905 P.2d 1002, 1006-07 (*Ariz. App.* 1995); *Cauthron*, 120 Wash. 2d at 899-903, 846 P.2d at 512-14.

Although DNA test results [***32] have been admitted in criminal cases since 1988 (see *People v. Wardell*, 230 Ill. App. 3d 1093, 1101, 172 Ill. Dec. 478, 595 N.E.2d 1148 (1992)), the product rule was generally unchallenged until 1991. In December of that year, *Science*, a respected scientific journal with articles subject to peer review, published two articles which posited radically conflicting views of statistical probability calculations. Compare Lewotin & Hartl, at 1745 with R. Chakraborty & K. Kidd, *The Utility of DNA Typing in Forensic Work*, 254 *Science* 1735 (1991) (Chakraborty & Kidd). Four months later, the National Academy of Sciences published the results of a two-year study on the viability of DNA testing. See National Research Council, *Committee on DNA Technology in Forensic Science*, *DNA Technology in Forensic Science* (1992) (NRC Report).

[*959] We will not add to the already voluminous materials which have described the nature of the debate which developed as a result of the foregoing publications. Suffice it to say that the debate centered on the possibility of subgrouping among populations. Subgrouping is based on the premise that census populations designated "Caucasian," "Black," or "Hispanic" [***33] actually consist of multiple genetically diverse subpopulations. If subgrouping occurs, then some scientists and population geneticists opine that it may cause both Hardy-Weinberg and linkage disequilibrium, which would render statistical probability calculations inaccurate. See Lewotin & Hartl, at 1746. For the curious reader, a more detailed account of the debate is located in the following materials: *Watson*, 257 Ill. [***388] *App.* 3d at 929-33, citing *People v. Barney*, 8 Cal. App. 4th 798, 814-19, 10 Cal. Rptr. 2d 731, 740-43 (1992); *Lindsey*, 892 P.2d at 287, 293-95; *Bible*, 175 *Ariz.* at 584-86, 858 P.2d at 1187-89; NRC Report, at 74-75, cited in *Cauthron*, 120 Wash. 2d at 902-03, 846 P.2d at 514; Lewotin & Hartl, at 1745; Chakraborty & Kidd, at 1735.

Riding the crest of this alleged "bitter debate" (see L. Roberts, *Fight Erupts Over DNA Fingerprinting*, 254 *Science* 1721, 1723 (1991)), some courts have rejected testimony on probability statistics on the ground that the calculations were not generally accepted in the scientific community. See, e.g., *Bible*, 175 *Ariz.* at 585-86, 858 P.2d at 1188-89; *Barney*, 8 Cal. App. 4th at 820, 10 Cal. Rptr. 2d at 745; *Commonwealth [***34] v. Lanigan*, 413 *Mass.* 154, 162-63, 596 N.E.2d 311, 316 (1992). Other courts, including some in Illinois, have remanded the case for further consideration on whether the ceiling principle, a conservative method of estimating probabilities which attempts to account for population subgrouping, is generally accepted. See, e.g., *Franson*, 269 Ill. App. 3d at 30; *Watson*, 257 Ill. App. 3d at 935-36; *State v. Sivri*, 231 *Conn.* 115, 161, 646 A.2d 169, 192 (1994); *Porter*, 618 A.2d at 642; *Vandebogart*, 136 *N.H.* at 383, 616 A.2d at 494-95.

We need not decide whether these cases were properly decided. Even if the foregoing publications ignited a "bitter debate" in the scientific community, and thus demonstrated that the calculation of probability statistics was not generally accepted in the scientific community, the debate has clearly calmed in the last several years. This calming is attributable to two developments not considered by the foregoing cases.

The first is the recognition by scientists that more conservative methods to calculate statistical probabilities do not create a corresponding reduction in random match probability calculations. The NRC Report recommended [***35] that scientists use the ceiling principle, as [*960] opposed to the product rule, to calculate statisti-

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cal probabilities. However, Eric Lander, an early critic of the use of probability statistics, as well as a coauthor of the NRC Report, and Bruce Budowle, one of the principal architects of the FBI's DNA program, have observed that the use of this more conservative method does not create a corresponding reduction in random match probability calculations. See E. Lander & B. Budowle, DNA Fingerprinting Dispute Laid to Rest, 371 Nature 735 (1994).

The second development is the FBI's completion of an exhaustive worldwide population survey, a survey which was recommended by the NRC Report. See United States Department of Justice, Federal Bureau of Investigation, I-A VNTR Population Data: A Worldwide Study, (1993) (FBI Study), cited in *People v. Amundson*, 43 Cal. App. 4th 1503, 1521, 41 Cal. Rptr. 2d 127, 137 (1995) and *Lindsey*, 892 P.2d at 294. The study rebutted the assumption that population subgrouping affected DNA probability estimates to a defendant's disadvantage. FBI Study, at 2, cited in *Amundson*, 43 Cal. App. 4th at 1521, 41 Cal. Rptr. 2d at 137. Specifically, the study [***36] found, inter alia, that (1) subdivisions in a major population group do not substantially affect forensic estimates of the likelihood of a DNA profile; and (2) estimates of the likelihood of occurrence of a DNA profile using major population group databases (e.g., Caucasian, Black, and Hispanic) provide a greater range of frequencies than would estimates for subgroups of a major population category. FBI Study, at 2, cited in *Lindsey*, 892 P.2d at 294. Based on these findings, the study concluded that the estimate of the likelihood of occurrence of a DNA profile derived by the current practice of employing the product rule and using general population databases is reliable, valid, and meaningful, without for-

ensically significant consequences. FBI Study, at 2, cited in *Lindsey*, 892 P.2d at 294.

These developments clearly debunk the notion that a "bitter debate"--if even there was one--is still raging in the scientific community. Thus, we conclude that the FBI's calculation of statistical probabilities, as derived by the product rule, is generally accepted in the scientific community. Accord *Amundson*, 43 Cal. App. 4th at 1521, 41 Cal. Rptr. 2d [**389] at 138; *People v. Chandler*, [***37] 211 Mich. App. 604, 610-11, 536 N.W.2d 799, 803 (1995); *Lindsey*, 892 P.2d at 294. As such, the trial court did not err in admitting the DNA test results.

We note that our holding today is distinguishable from those reached in prior Illinois cases. In the Lipscomb/Miles line of cases, the courts did not consider the compelling materials we do today. Similarly, although the Watson and Franson courts considered some of these materials, they did not consider all of them.

[*961] II

[The following material is nonpublishable under *Supreme Court Rule 23*].

[The preceding material is nonpublishable under *Supreme Court Rule 23*].

CONCLUSION

For the foregoing reasons, the judgment of the circuit court of Winnebago County is affirmed.

Affirmed.

COLWELL and RATHJE, JJ., concur.



LEXSEE 22 P.3D 68

IN RE: Plaintiff: THE PEOPLE OF THE STATE OF COLORADO, v. Defendant:
MICHAEL EUGENE SHRECK.

Case No. 00SA105

SUPREME COURT OF COLORADO

22 P.3d 68; 2001 Colo. LEXIS 337; 2001 Colo. J. C.A.R. 1995

April 23, 2001, Decided

SUBSEQUENT HISTORY: [**1] As Modified May 14, 2001.

Subsequent appeal at *People v. Shreck*, 2004 Colo. App. LEXIS 1712 (Colo. Ct. App., Sept. 23, 2004)

PRIOR HISTORY: Boulder County District Court, No. 98CR2475. Honorable Daniel C. Hale, Judge.

DISPOSITION: RULE MADE ABSOLUTE.

COUNSEL: Ann B. Tomsic, Special Prosecutor, Arapahoe County District Attorney's Office, Englewood, Colorado, Attorney for Plaintiff.

David Kaplan, Colorado State Public Defender, Steven K. Jacobson, Deputy State Public Defender, Kristin Johnson, Deputy State Public Defender, Boulder, Colorado, Attorneys for Defendant.

Ken Salazar, Attorney General, Deborah Isenberg Pratt, Assistant Attorney General, Denver, Colorado, Attorneys for Amicus Curiae in Support of Plaintiff.

JUDGES: JUSTICE RICE delivered the Opinion of the Court.

OPINION BY: RICE

OPINION

[*70] EN BANC

JUSTICE RICE delivered the Opinion of the Court.

Original Proceeding Pursuant to C.A.R. 21.

The prosecution in this case initiated this original proceeding pursuant to C.A.R. 21, seeking relief from a

trial court order granting the defendant's motion to bar DNA evidence. The trial court held that under *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013, 1014 (D.C. Cir. 1923), the multiplex technique employed by the commercial [**2] testing kits used by the Colorado Bureau of Investigation ("CBI") in 1999 was not yet generally accepted at that time by the relevant scientific community. Thus, the trial court ruled that the DNA evidence at issue in this case, which was derived from those kits, was not admissible against the defendant. We issued a rule to show cause why the trial court's order should not be vacated, and the defendant responded.

We now hold that *CRE 702*, rather than *Frye*, governs a trial court's determination as to whether scientific or other expert testimony should be admitted. Such an inquiry should focus on the reliability and relevance of the proffered evidence and requires a determination as to (1) the reliability of the scientific principles, (2) the qualifications of the witness, and (3) the usefulness of the testimony to the jury. We also hold that when a trial court applies *CRE 702* to determine the reliability of scientific evidence, its inquiry should be broad in nature and consider the totality of the circumstances of each specific case. In doing so, a trial court may consider a wide range of factors pertinent to the case at bar. The factors mentioned in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593-94, 125 L. Ed. 2d 469, 113 S. Ct. 2786 (1993), [**3] and by other courts may or may not be pertinent, and thus are not necessary to every *CRE 702* inquiry. In light of this liberal inquiry, a trial court should also apply its discretionary authority under *CRE 403* to ensure that the probative value of the evidence is not substantially outweighed by unfair prejudice. Finally, we hold that under *CRE 702*, a trial court must issue specific findings as it applies the *CRE 702* and *403* analyses.

We further hold that under *CRE 702*, the multiplex testing techniques at issue in this case were sufficiently reliable to warrant admission of the DNA evidence derived from their use. Accordingly, we make the rule absolute and direct the trial court to vacate its order barring such evidence.

I. SCIENTIFIC BACKGROUND

We described the scientific principles and techniques underlying DNA typing in *Fishback v. People*, 851 P.2d 884, 885 (Colo. 1993). We now review those principles and techniques in the context of the particular method of DNA typing at issue in this case.

Within the nucleus of each human cell are twenty-three pairs of chromosomes composed of deoxyribonucleic acid ("DNA"), which contains the coded information that [*71] provides [**4] the genetic material determining the physical structure and characteristics for each individual. No two individuals, except identical twins, have the same DNA structure. A DNA molecule is shaped like a double helix, which resembles a twisted ladder. The sides of the ladder are composed of phosphate and sugar molecules and the rungs are composed of a pair of organic compounds called bases. Two bases form a single rung called a base pair. The order in which these base pairs appear in the ladder is the genetic code of that individual. There are approximately three billion base pairs in a human being, 99% of which are the same in each person. However, certain sections of DNA vary from person to person. These areas are called polymorphisms. DNA typing concerns the examination of two types of polymorphisms: length and sequence.

One method of detecting and measuring length variations is called restriction fragment length polymorphism ("RFLP") analysis. The RFLP procedure isolates DNA in a blood sample so that certain polymorphisms can be located in the DNA. RFLP is a widely accepted and scientifically validated method of testing that has generally been found to be admissible in state and [**5] federal courts. *United States v. Hicks*, 103 F.3d 837, 846-47 (9th Cir. 1996); *United States v. Chischilly*, 30 F.3d 1144, 1153-56 (9th Cir. 1994); *United States v. Lowe*, 954 F. Supp. 401, 416 (D. Mass. 1996); *Fishback*, 851 P.2d at 893.

Polymerase chain reaction ("PCR") is a process by which DNA fragments too small to be suitable for RFLP analysis can be analyzed. Under the PCR process, these DNA fragments are duplicated many times, thus allowing very small samples to be accurately tested. PCR also permits testing in a relatively short time in comparison to prior methods that required the decay of radioactive materials. Finally, unlike RFLP testing, which destroys the sample, PCR processing allows a technician to reproduce

and verify test results by creating a larger sample for testing.

The D1S80 test is a hybrid of the PCR and RFLP methods. It detects fragment length polymorphisms once the DNA fragment has been amplified through the PCR procedure.

Another form of PCR testing involves the use of locations on the DNA strand containing short tandem repeats ("STR") of baseline patterns. STR testing reveals length differences [**6] between chromosomes on different people with the same base pair sequences. There are thirteen locations at which the number of STRs are known to vary from person to person. Thus, if all thirteen locations of the known and questioned sample are identical, a match is considered to have been made.

When STR loci are amplified through the PCR process separately and run on a separate gel, the system is called "monoplex." Multiplex systems add more than one set of PCR primers to a reaction so as to be able to amplify several loci together and run them simultaneously. Monoplex systems and multiplex systems that amplify and run three loci simultaneously, ("triplex"), have been in use for many years.

The commercial kits used to perform the STR testing at issue in this case were manufactured by Perkins Elmer Biosystems ("PE"). These kits, called AmpFLSTR Profiler Plus ("Profiler Plus") and AmpFLSTR Cofiler ("Cofiler"), employ a combination sixplex and nineplex system that is able to read all thirteen locations at the same time.¹ In January 1999, when they were used in this case, the kits were relatively new to the market.

1 The Profiler Plus kit reads nine loci while the Cofiler kit reads six loci, two of which are also read by the Profiler Plus kit.

[**7] FACTS AND PROCEDURAL HISTORY

The defendant in this case has been in and out of jail since 1983. In April 1990, he was on parole and living in the Boulder area when a University of Colorado student was sexually assaulted. Although a rape kit was used on the victim, the crime was never solved. In 1998, the case was reopened and the CBI performed a DNA analysis using [*72] several PCR-based tests on the rape kit samples. A 1991 blood sample from the defendant was analyzed against the rape kit results. The CBI concluded that the probability that the contributor to the rape kit sample was not the defendant was one in 11,000. An analysis of a new blood sample from the defendant revealed identical results.

Several months later, the CBI performed more tests on the samples, this time using the Profiler Plus and Cofiler kits. By combining the Profiler Plus and Cofiler

results with the earlier tests, the CBI determined that the defendant could not be excluded as a contributor to the rape kit sample. The CBI also determined that the probability that the contributor was not the defendant but a random third person was one in 5.3 quadrillion.² Based on the DNA results, a positive photo line-up identification [**8] by the victim, and the fact that the defendant had been on parole and living in the area at the time of the crime, the defendant was arrested and charged with second degree kidnapping, two counts of sexual assault in the first degree, two counts of criminal attempt to commit murder in the first degree, assault in the second degree, and as a habitual criminal.

2 5.3 quadrillion = 5,300,000,000,000,000 = 5.3 x 10¹⁵.

The defendant moved to bar the use of the DNA evidence at trial on the grounds that (1) PCR and the PCR-based tests employed in this case were not generally accepted as reliable by the relevant scientific community; (2) STR tests in general and the STR multiplex technique employed by the Profiler Plus and Cofiler kits were not generally accepted; and (3) the methods of collection, preservation and handling of the samples, and the statistical methods used to determine the probability of a match were not generally accepted.

Applying the *Frye* standard as adopted in Colorado by *People v. Anderson*, 637 P.2d 354, 358 (Colo. 1981), [**9] and as explained in *People v. Lindsey*, 892 P.2d 281, 288-89 (Colo. 1995), and *Fishback v. People*, 851 P.2d 884, 890 (Colo. 1993), the trial court held that admissibility of the DNA evidence at issue required a showing that the technologies and methods used were generally accepted in the relevant scientific community. After reviewing the evidence, rulings from other jurisdictions, and scientific commentary and journals, the trial court concluded that PCR and the PCR-based tests used in this case, as well as the handling and statistical methods used, were generally accepted in the scientific community. The court also concluded that although PCR-based STR testing is different from other PCR-based tests, it is generally accepted as to multiplex and triplex applications.

The court, however, ruled that because the multiplex system at issue in this case involves a combination nineplex and sixplex system using new loci and primers, it differs from previous STR tests in a critical way, thus triggering a new *Frye* analysis. The trial court determined that the evidence of validation and peer review offered by the prosecution failed to meet guidelines published [**10] by the Technical Working Group on DNA Analysis Methods ("TWGDAM"). Thus, the court concluded that the multiplex technique employed by the Profiler Plus and Cofiler systems is not generally ac-

cepted and that the DNA evidence resulting from its use is therefore inadmissible. Alternatively, the trial court concluded under *Daubert*, that the Profiler Plus and Cofiler systems were not sufficiently reliable under *CRE 702* to warrant admission of the DNA evidence derived from their use.

The prosecution petitioned for a writ in the nature of prohibition pursuant to *C.A.R. 21*. We issued a rule to show cause why the trial court's order should not be vacated, and the defendant responded. We now hold that *CRE 702* governs a trial court's determination as to whether scientific evidence should be admitted. Under *CRE 702*, we hold that the multiplex STR testing techniques at issue in this case are sufficiently reliable and relevant to warrant admission. Accordingly, we make the rule absolute and direct the trial court to vacate its order barring the DNA evidence derived from these tests.

III. ANALYSIS

We have not previously addressed the admissibility of PCR or STR-based DNA testing, [**73] or [**11] the specific multiplex testing systems at issue here. Thus, this case presents us with the opportunity to address these matters of first impression. In doing so, we consider the appropriate standard governing the admissibility of scientific evidence. Our review includes an analysis of relevant Colorado case law, similar cases in other jurisdictions, and academic commentary.

A. Standard of Review

Under *C.A.R. 21*, we may, in our discretion, grant relief when (1) the trial court is proceeding without or in excess of its jurisdiction, or (2) it has abused its discretion, and (3) when no other adequate remedy exists. *C.A.R. 21*; *People v. District Court*, 898 P.2d 1058, 1060 (Colo. 1995). In this case, the prosecution's ability to present its case has been impaired by the exclusion of the DNA evidence in question. *Id.* Because double jeopardy would bar a retrial if the defendant were acquitted, no other adequate remedy exists. *People v. District Court*, 664 P.2d 247, 251 (Colo. 1983). As discussed below, we hold that the trial court erred in finding that the DNA evidence derived from the multiplex STR systems at issue in this case was inadmissible, [**12] and that its exclusion of the evidence was an abuse of discretion. Thus, relief under *C.A.R. 21* is appropriate here.

B. Admissibility of Scientific Evidence Generally

Prior to 1993, the widely accepted standard for admitting novel scientific evidence in both federal and state courts was the standard articulated in *Frye*. *Daubert*, 509 U.S. at 585 (noting that, "In the 70 years since its formulation in the *Frye* case, the 'general acceptance' test has been

the dominant standard for determining the admissibility of novel scientific evidence at trial."). This standard requires that "the thing from which [expert testimony is deduced] be sufficiently established to have gained general acceptance in the particular field to which it belongs." *Frye*, 293 F. at 1014. Applying this standard, the *Frye* court concluded that the systolic blood pressure deception test had not yet gained enough recognition among scientific authorities to warrant admission of its results. *Id.*

Most courts have interpreted *Frye* as requiring general acceptance of both (1) the underlying theory supporting the scientific conclusion and, (2) the techniques [**13] and experiments employing that theory.³ The court in *People v. Castro*, 144 Misc. 2d 956, 545 N.Y.S.2d 985, 986 (N.Y. Sup. Ct. 1989), however, held that a third requirement should apply in the complex area of DNA identification: that the actual testing procedures employed properly apply the accepted scientific techniques in analyzing the forensic samples at issue. Other courts have held that questions concerning testing procedures and the accuracy of particular test results go to the weight, rather than admissibility of the evidence. *See, e.g., Chischilly*, 30 F.3d at 1154; *United States v. Bonds*, 12 F.3d 540, 563 (6th Cir. 1993); *United States v. Shea*, 957 F. Supp. 331, 341 (D.N.H. 1997), *aff'd*, 159 F.3d 37 (1st Cir. 1998).

3 *United States v. Yee*, 134 F.R.D. 161, 194 (N.D. Ohio 1990); *Fishback*, 851 P.2d at 891; *State v. Vandebogart*, 136 N.H. 365, 616 A.2d 483, 490 (N.H. 1992); *State v. Ford*, 301 S.C. 485, 392 S.E.2d 781, 783 (S.C. 1990).

[**14] In 1993, the United States Supreme Court held in *Daubert v. Merrell Dow Pharmaceuticals, Inc.* that *Frye's* general acceptance test had been superseded by the adoption of *Federal Rule of Evidence 702*.⁴ 509 U.S. at 587. The Court reasoned that *Frye's* "rigid general acceptance requirement is at odds with the liberal thrust of the Federal Rules and their general approach of relaxing the traditional barriers to opinion testimony." *Daubert*, 509 U.S. at 588. The *Daubert* Court held that admissibility [*74] of scientific evidence under the Federal Rules of Evidence requires that the trial judge ensure that the evidence be both relevant and reliable. *Daubert*, 509 U.S. at 589. The Court thus held that under *Rule 702*, the reasoning or methodology underlying the testimony must be scientifically valid, and that such reasoning or methodology may properly be applied to the facts of the case. *Daubert*, 509 U.S. at 592. The Court then set forth a non-exclusive list of factors, including general acceptance, to guide a trial court in making this determination. *Daubert*, 509 U.S. at 593-94. The Court concluded its analysis by noting that the "inquiry envi-

sioned by *Rule* [**15] 702 is . . . a flexible one," and that the focus of the inquiry should be scientific validity as it pertains to evidentiary relevance and reliability. *Daubert*, 509 U.S. at 594.

4 Former *Federal Rule of Evidence 702* 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." *Fed. R. Evid. 702* (amended Dec. 2000 to add: "a witness qualified . . . may testify . . . if (1) 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.").

Recently, the United States Supreme Court expanded *Daubert's* general holding concerning the trial judge's gatekeeping function to testimony based not only on scientific knowledge, but also to testimony based on technical and "other specialized" knowledge. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 142, 143 L. Ed. 2d 238, 119 S. Ct. 1167 (1999). The Court stressed, however, that the inquiry was a flexible one, and held that the factors listed in *Daubert* were [**16] neither exclusive nor mandatory. *Id.*

C. Admissibility of Scientific Evidence in Colorado

Before reaching the relative merits of *Frye* and *Rule 702* for determining the admissibility of scientific evidence, we review our previous treatment of these standards in Colorado. The *Frye* standard was first adopted in Colorado in *People v. Anderson*, 637 P.2d at 358. In *Anderson*, this court held that polygraph results and the testimony of polygraph examiners were per se inadmissible in a criminal trial because the scientific theory or technique of the polygraph was not sufficiently advanced to permit its use at trial as competent evidence of credibility. *Id.*

We limited the applicability of *Frye*, however, in *People v. Hampton*, 746 P.2d 947, 951 (Colo. 1987), where we applied *CRE 702*, rather than *Frye*, to determine the admissibility of rape trauma syndrome evidence. There, we reasoned that *Frye* was only applicable to novel scientific devices and processes involving the manipulation of physical evidence, and that *Frye* had only been applied in Colorado to polygraph tests. *Hampton*, 746 P.2d at 950-51. Thus, we held [**17] that *CRE 702*, rather than *Frye*, governed the admission of testimony regarding rape trauma syndrome. *Id.*

Similarly, in *Campbell v. People*, 814 P.2d 1, 7 (Colo. 1991), we applied CRE 702, rather than *Frye*, in determining whether eyewitness identification evidence should be admitted. In that case, we explicitly held that *Frye* was only applicable to cases involving novel scientific devices or processes involving the evaluation of physical evidence. *Id.* at 8. Because no such scientific device or process was at issue in *Campbell*, we held that CRE 702's more liberal standard for admissibility should have been applied to the eyewitness identification evidence. *Id.*

We first addressed the admissibility of DNA evidence in Colorado in *Fishback v. People*, where we held that DNA evidence, unlike the evidence at issue in *Hampton* and *Campbell*, is "precisely the sort of scientific evidence which requires application of the *Frye* test." *Fishback*, 851 P.2d at 890. In concluding that the *Frye* test governed our inquiry, we reasoned that the highly technical and sophisticated techniques involved in DNA typing, and its relative [**18] novelty at the time, qualified it as "a novel scientific process involving the evaluation of physical evidence." *Id.* We also held that general acceptance of both the underlying theory or principle, and of the techniques used to apply that principle was required under *Frye*. *Fishback*, 851 P.2d at 891. Applying this standard, we concluded that the theory underlying DNA typing, the techniques employed in RFLP analysis, and the statistical techniques employed in that case were generally accepted among the relevant scientific communities. *Fishback*, 851 P.2d at 892-93.

In *Lindsey v. People*, we again considered the admissibility of DNA evidence in Colorado courts. 892 P.2d at 281. At issue in that case was the statistical method used to analyze DNA results. *Lindsey*, 892 P.2d at 285. Although we acknowledged that the United States Supreme Court had abandoned *Frye*'s general [*75] acceptance test in *Daubert*, we concluded that we were not bound by *Daubert*'s non-constitutional construction of the Federal Rules of Evidence. *Lindsey*, 892 P.2d at 288. Thus, we applied *Frye*, as interpreted in *Fishback*, to hold that the DNA statistical frequency analysis [**19] employed in that case was generally accepted. *Lindsey*, 892 P.2d at 288-95. In doing so, we noted that general acceptance could be considered broadly to mean accepted in a reasonably inclusive manner, and including a consideration of rulings from other jurisdictions and the general state of science. *Lindsey*, 892 P.2d at 289. We expressly declined, however, to evaluate the relative merits of *Frye* and CRE 702 in determining the admissibility of scientific evidence, noting that the issue was not before us in that case. *Lindsey*, 892 P.2d at 288.

In *Brooks v. People*, 975 P.2d 1105, 1106 (Colo. 1999), we declined to apply either *Frye* or *Daubert* to the

determination as to whether testimony on the subject of scent tracking evidence was admissible. In doing so, we reasoned that the evidence in question did not involve the type of scientific devices, processes, or theories that are properly subject to *Frye* scrutiny. *Brooks*, 975 P.2d at 1111-12. We were also unwilling to apply *Daubert* for the first time in that case, because we found that the scent-tracking evidence was experience-based specialized knowledge that was not dependent on scientific [**20] explanation, remarking that *Daubert* itself limited its holding to the scientific realm. *Id.* at 1113; see *Daubert*, 509 U.S. at 590 n.8. We noted that the decision in *Kumho* applied *Daubert* to technical and other specialized knowledge and that it provided that the *Daubert* factors were not exclusive. However, we opined that it was preferable to avoid debating whether or to what extent *Daubert* was applicable and held instead that CRE 702 and CRE 403 governed our determination as to whether the experience-based knowledge at issue in that case was admissible. *Brooks*, 975 P.2d at 1115.

A review of our previous treatment of *Frye* indicates that we have not fully endorsed its general acceptance standard as the appropriate test for determining the admissibility of scientific evidence in Colorado. After initially adopting *Frye* in the context of *Anderson*, which, like *Frye*, concerned the admissibility of polygraph evidence, we later limited its applicability in *Hampton*, 746 P.2d at 951, and in *Campbell*, 814 P.2d at 7, to novel scientific devices or processes involving the evaluation [**21] of physical evidence.

Although we later applied *Frye* in both *Fishback* and *Lindsey* to determine the admissibility of DNA evidence, we did so without evaluating the relative merits of *Frye* and CRE 702.⁵ In *Brooks*, we applied the rules of evidence, specifically Rules 702 and 403, rather than *Daubert* or *Frye* to determine the admissibility of experience-based scent-tracking evidence. 975 P.2d at 1106.

5 In *Fishback*, we noted that the parties did not seriously dispute the applicability of *Frye* in determining the admissibility of DNA typing evidence. *Fishback*, 851 P.2d at 891 (noting also, however, that the notion that *Frye* was superseded by CRE 702 lacked merit because CRE 702 became effective in January 1980 and we adopted *Frye* in *Anderson*, which was decided in November 1981). Similarly, in *Lindsey*, we expressly stated that, "We do not consider the relative merits of the *Frye* test or our corollary state rules of evidence for the simple reason [that] the issue is not now before us." *Lindsey*, 892 P.2d at 288-89 (noting also that *Frye*'s general acceptance test is "not far removed from evaluation required under FRE 702" in that under CRE 702, a court must

still screen the evidence to ensure its reliability, which may include consideration of the evidence's general acceptance).

[**22] In order to determine whether the DNA evidence derived from the multiplex STR technique at issue here was properly barred, we must first address the proper standard governing the admissibility of scientific evidence in Colorado. Because we have never addressed the relative merits of *Frye* and *CRE 702*, we now undertake that analysis in an effort to clearly set forth the standard for admitting scientific evidence in Colorado.⁶

6 In the absence of such a clear standard, the trial court below applied both a *Frye* and a *Daubert* analysis in determining the admissibility of the DNA evidence at issue. See *Fishback*, 851 P.2d at 896 (Mullarkey, J., concurring in the result only) (noting that, in light of the trial court's analysis under both *Frye* and *CRE 702*, "the time has come for this court to set forth clearly the standard by which novel scientific evidence should be assessed").

[*76] Proponents of *Frye*'s general acceptance test argue that it insulates juries from unreliable evidence [**23] that has not yet been found reliable by a sufficient number of experts. Joseph G. Petrosinelli, Note, *The Admissibility of DNA Typing: A New Methodology*, 79 *Geo. L.J.* 313, 317 (1990). Another justification for the *Frye* test is that it provides a method by which courts can assess the reliability of novel scientific expert testimony. *United States v. Downing*, 753 F.2d 1224, 1235 (3d Cir. 1985). Finally, proponents of *Frye* also argue that the general acceptance test safeguards against the possible prejudicial effects of testimony based upon questionable scientific evidence. *Id.*

Frye's general acceptance test has also, however, been heavily criticized on several grounds. Lawrence B. Ebert, *Frye after Daubert: The Role of Scientists in Admissibility Issues as Seen through Analysis of the DNA Profiling Cases*, The University of Chicago Law School Roundtable, 219 (1993); Petrosinelli, 79 *Geo. L.J.* at 318; Paul C. Giannelli, *The Admissibility of Novel Scientific Evidence: Frye v. United States, a Half-Century Later*, 80 *Colum. L. Rev.* 1197, 1208-23 (1980). Generally, critics have been concerned with *Frye*'s vagueness and [**24] its conservatism. *Downing*, 753 F.2d at 1236.

Commentators have found vagueness and ambiguity under *Frye* in determining, for example, (1) precisely what must be generally accepted, (2) the relevant scientific community, (3) how much agreement constitutes general acceptance, and (4) the extent to which *Frye* applies. Ebert, *supra*, at 225; Petrosinelli, 79 *Geo. L.J.* at

320; Giannelli, 80 *Colum. L. Rev.* at 1208-23. Such ambiguity yields inconsistent results and creates uncertainty in decision-making. *Fishback*, 851 P.2d at 896-97 (Mullarkey, J., concurring in the result only).⁷

7 Courts have found that *Frye*'s ambiguity provides an opportunity to manipulate the terms "scientific community" and "general acceptance" in order to reach a desired result. *Downing*, 753 F.2d at 1236.

Furthermore, while some critics have argued that the *Frye* inquiry is too malleable,⁸ others have concluded that the *Frye* standard is too rigid and that it unduly restricts [**25] the admission of probative evidence from a jury's consideration. See, e.g., *Downing*, 753 F.2d at 1236-37 (noting that some have argued that under *Frye*, courts may be required to exclude much probative and reliable information from the jury's consideration, thereby unnecessarily impeding the truth-seeking function of litigation); *United States v. Sample*, 378 F. Supp. 44, 53 (E.D. Pa. 1974) (noting that general acceptance is a proper requirement for taking judicial notice of scientific facts, but should not be a criterion for the admissibility of scientific evidence); *People v. Leahy*, 8 Cal. 4th 587, 882 P.2d 321, 330 (Cal. 1994) (acknowledging that a reliable, readily provable technique could remain unknown and untested by the relevant scientific community, thus delaying its use in the courtroom). We agree that *Frye*'s rigidity may exclude evidence with strong support within the community but that may fall short of "general acceptance" under *Frye*. *Fishback*, 851 P.2d at 897 (Mullarkey, J., concurring in the result only); *Lindsey*, 892 P.2d at 296 (Mullarkey, J., concurring in the result [**26] only).

8 *Castro*, 545 N.Y.S.2d at 987.

We also find that this rigidity is ill-suited for determining the admissibility of scientific evidence, which, by its nature, is ever-evolving. Under *Frye*, once a scientific principle or discovery becomes generally accepted, it forever remains accepted, despite improvements or other developments in scientific technologies. *Fishback*, 851 P.2d at 897 (Mullarkey, J., concurring in the result only); *Lindsey*, 892 P.2d at 296 (Mullarkey, J., concurring in the result only). Conversely, because it will take time for any scientific technique to become generally accepted, the *Frye* test restricts the admissibility of reliable evidence that may not yet qualify as "generally accepted" under *Frye*. *Brooks*, 975 P.2d at 1112 (noting that *Frye* fails to "address the tough questions that arise on the cutting edge of science, [in that it] requires that the courts wait until science itself determines the validity [**27] of the scientific proposition in question."); [**77] *Downing*, 753 F.2d at 1236-37; Petrosinelli, 79 *Geo. L.J.*

at 320 (describing this problem with the *Frye* test as a "cultural lag"). Thus, we conclude that *Frye*'s general acceptance test, particularly when viewed rigidly, is unsuitable as the sole dispositive standard for determining the admissibility of scientific evidence in Colorado.⁹

9 As discussed above, although our decisions in *Fishback* and *Lindsey* relied on *Frye*'s general acceptance test to determine the admissibility of the DNA evidence at issue in those cases, we did not specifically evaluate the merits of *Frye* in relation to *CRE 702*. To the extent that these decisions are relied upon to argue that *Frye* is the appropriate standard governing the admissibility of scientific evidence, we disapprove.

We therefore hold that the rules of evidence, particularly *CRE 702*¹⁰ and *CRE 403*, represent a better standard, because their flexibility is consistent with a liberal [**28] approach that considers a wide range of issues. See *Downing*, 753 F.2d at 1237 (noting that the language of *Rule 702*, the spirit of the rules of evidence, and the problems with applying *Frye* "suggest the appropriateness of a more flexible approach to the admissibility of . . . scientific evidence").

10 *CRE 702* is identical to the former federal rule of the same number. See *supra* note 4.

The focus of a *Rule 702* inquiry is whether the scientific evidence proffered is both reliable and relevant. *Daubert*, 509 U.S. at 589; see *Brooks*, 975 P.2d at 1114 (holding that under *CRE 702*, evidence that is reasonably reliable and that will assist the trier of fact should be admitted). In determining whether the evidence is reliable, a trial court should consider (1) whether the scientific principles as to which the witness is testifying are reasonably reliable, and (2) whether the witness is qualified to opine on such matters. *Brooks*, 975 P.2d at 1114. In [**29] determining whether the evidence is relevant, a trial court should consider whether the testimony would be useful to the jury. *Id.*

A trial court's reliability inquiry under *CRE 702* should be broad in nature and consider the totality of the circumstances of each specific case. *Brooks*, 975 P.2d at 1114 (noting that "the relevant factors applicable to a *CRE 702* inquiry will likely vary depending on the particular subject matter at hand"); *Campbell*, 814 P.2d at 7-8 (holding that the trial court retains its broad discretion to evaluate on a case-by-case basis whether the testimony in question would assist the trier of fact to understand the evidence or to determine a fact in issue); see also *Kumho*, 526 U.S. at 150 (holding that a trial court's gatekeeping inquiry under *Rule 702* must be tied to the facts of a particular case).

Given the flexible, fact-specific nature of the inquiry, we decline to mandate that a trial court consider any particular set of factors when making its determination of reliability. Instead, we hold that the *CRE 702* inquiry contemplates a wide range of considerations that may be pertinent to the evidence at [**30] issue. *Downing*, 753 F.2d at 1238 ("The reliability inquiry that we envision is flexible and may turn on a number of considerations, in contrast to the process of 'nose-counting' that would appear to be compelled by a careful reading of *Frye*.").

By way of illustration, however, we recite here the wide range of issues other courts have considered when making a *Rule 702* determination. For example, in *Daubert*, the Court articulated the following nonexclusive list of general observations that a trial court might consider: (1) whether the technique can and has been tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) the scientific technique's known or potential rate of error, and the existence and maintenance of standards controlling the technique's operation; and (4) whether the technique has been generally accepted. 509 U.S. at 593-94. The Third Circuit has articulated yet other considerations: (1) the relationship of the proffered technique to more established modes of scientific analysis; (2) the existence of specialized literature dealing with the technique; (3) the non-judicial uses to which the technique [**31] are put; (4) the frequency and type of error generated by the technique; and (5) whether such evidence has been offered in previous cases to support [**78] or dispute the merits of a particular scientific procedure. *Downing*, 753 F.2d at 1238-39.

We hold that a trial court making a *CRE 702* reliability determination may, but need not consider any or all of these factors, depending on the totality of the circumstances of a given case. A trial court may also consider other factors not listed here, to the extent that it finds them helpful in determining the reliability of the proffered evidence.

Our determination that a trial court may, but need not consider the factors listed in *Daubert* is consistent with the United States Supreme Court's reasoning in *Kumho Tire Co. v. Carmichael*: "The factors identified in *Daubert* may or may not be pertinent in assessing reliability, depending on the nature of the issue, the expert's particular expertise, and the subject of his testimony." 526 U.S. at 150. The Supreme Court in *Kumho* further held that:

we can neither rule out, nor rule in, for all cases and for all time the applicability of the factors mentioned [**32] in *Daubert*, nor can we now do so for subsets of

cases categorized by category of expert or by kind of evidence.

Too much depends on the circumstances of the particular case at issue. *Id.*¹¹

11 Commentators have also criticized *Daubert's* list of factors for its "amorphous structure, [in that it creates] various laundry lists of factors [that] are combined in arbitrary ways by nonexperts to produce unknown probabilities of accuracy to be balanced against unmeasured prejudices." Ebert, *supra*, at 230.

Such reasoning is also consistent with our previous declination to "give any special significance to the *Daubert* factors," in the context of considering evidence we considered to be experience-based specialized knowledge. *Brooks*, 975 P.2d at 1114. In *Brooks*, we held that it was preferable to avoid discussing "whether or to what extent a court should apply the *Daubert* factors," and concluded instead, that the proper focus should be on "whether the evidence is reasonably [**33] reliable information that will assist the trier of fact." *Id.*

Any concerns that invalid scientific assertions will be admitted under this liberal standard are assuaged by *Rule 702's* overarching mandate of reliability and relevance. See *Daubert*, 509 U.S. at 595. Such concerns are also mitigated by "vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof." *Id.* at 596. In addition, a trial court making a *CRE 702* determination must apply its discretionary authority under *CRE 403* to ensure that the probative value of the evidence is not substantially outweighed by the danger of unfair prejudice, confusion of the issues, undue delay, waste of time, or needless presentation of cumulative evidence. *Id.*; *Campbell*, 814 P.2d at 8; *Hampton*, 746 P.2d at 951 n. 8. Finally, a trial court's *CRE 702* determination must be based upon specific findings on the record as to the helpfulness and reliability of the evidence proffered. *Brooks*, 975 P.2d at 1114; *Campbell*, 814 P.2d at 8. The trial court must also issue specific findings as to its [**34] consideration under *CRE 403* as to whether the probative value of the evidence is substantially outweighed by its prejudicial effect. *Brooks*, 975 P.2d at 1114; *Campbell*, 814 P.2d at 8.

To summarize, we conclude that *CRE 702*, rather than *Frye*, represents the appropriate standard for determining the admissibility of scientific evidence.¹² We hold that under this standard, the focus of a trial court's inquiry should be on the reliability and relevance of the scientific evidence, and that such an inquiry requires a determination as to (1) the reliability of the scientific principles; (2) the qualifications of the witness; and (3)

the usefulness of the testimony to the jury. We also hold that when a trial court applies *CRE 702* to determine the reliability of scientific evidence, its inquiry should be broad in nature and consider the totality of the circumstances of each specific case. In doing so, a [*79] trial court may consider a wide range of factors pertinent to the case at bar. The factors mentioned in *Daubert* and by other courts may or may not be pertinent, and thus are not necessary to every *CRE 702* inquiry. In light of this liberal standard, [**35] a trial court should also apply its discretionary authority under *CRE 403* to ensure that the probative value of the evidence is not substantially outweighed by unfair prejudice. Finally, we hold that under *CRE 702*, a trial court must issue specific findings as it applies the *CRE 702* and *403* analyses.

12 We decline to limit the applicability of *CRE 702* to only the novel scientific evidence governed previously by *Frye*. Nothing in the text of the rule requires such a limitation, and our holding is consistent with that of the United States Supreme Court in *Daubert*, which expressly applied its holding to all scientific evidence. *Daubert*, 509 U.S. at 593 n. 11.

D. Application of *CRE 702* to Evidence at Issue

Having determined that *CRE 702* represents the proper standard, we now turn to the issue of whether the evidence derived from the DNA testing techniques at issue in this case is admissible under that standard. The trial court below did not have the benefit of our ruling [**36] and instead employed a thorough *Frye* analysis to conclude that the evidence was inadmissible. Alternatively, the trial court applied the *Daubert* factors to reach the same result.¹³ Thus, a determination of admissibility under our new standard is required.

13 The trial court analyzed the evidence under the *Daubert* factors without any discussion of *CRE 702's* reliability or relevance prongs. After a brief discussion of each *Daubert* factor, the trial court concluded that several of them were not met and therefore, the evidence was inadmissible under *Daubert*.

Because the record in this case is sufficient for a determination of admissibility under *CRE 702*, we need not remand the case to the trial court. Instead, we conclude that, under *CRE 702's* liberal standard for admissibility, the evidence derived from the PE kits at issue here is admissible.

As discussed above, admissibility under *CRE 702* is appropriate when (1) the scientific principles at issue are reasonably reliable, (2) the witness [**37] is qualified to opine on such principles, and (3) the testimony will be

useful to the jury. In this case, the parties do not question the qualification of the witness, nor do they dispute that the evidence will assist the jury. Thus, our main concern is whether the PCR-based multiplex STR system from which the evidence here was derived is sufficiently reliable.

We begin by discussing the admissibility of PCR and STR-based DNA testing, as we have not previously addressed this issue.¹⁴ The majority of courts in other jurisdictions that have considered the issue have held that DNA evidence derived from the PCR testing method satisfies the standards for admissibility under either *Frye* or *Rule 702*.¹⁵ Indeed, the National Research Council's Committee on Forensic DNA Science has concluded that the molecular technology on which PCR is [*80] based is thoroughly sound, and that the results are highly reproducible when appropriate quality-control methods are followed. *Shea*, 957 F. Supp. at 338-39.

14 The trial court determined, based on the evidence before it, and rulings from other jurisdictions, that DNA evidence derived from PCR-based STR testing is generally accepted under *Frye* and is thus admissible. As discussed below, we agree that such evidence is admissible, but make our determination under *CRE 702*.

[**38]

15 *Shea*, 957 F. Supp. at 339 (holding that because PCR is based on sound scientific methods and has been generally accepted in both forensic and non-forensic settings, it readily satisfies *Rule 702*'s reliability requirement); *Harmon v. State*, 908 P.2d 434, 440 (Alaska Ct. App. 1995) (holding that under *Frye*, there seems to be little question concerning the scientific acceptance of the theory underlying PCR DNA typing), *overruled on other grounds by*, *State v. Coon*, 974 P.2d 386, 391 (Alaska 1999); *People v. Wright*, 62 Cal. App. 4th 31, 72 Cal. Rptr. 2d 246, 250 (Cal. Ct. App. 1998) (holding that DNA evidence derived from PCR testing was admissible under *Frye*); *People v. Pope*, 284 Ill. App. 3d 695, 672 N.E.2d 1321, 1327, 220 Ill. Dec. 309 (Ill. App. Ct. 1996) (holding that PCR-based methods of DQ alpha typing and polymarker typing for DNA identification are generally accepted under *Frye*); *State v. Hill*, 257 Kan. 774, 895 P.2d 1238, 1247 (Kan. 1995) (finding no error in the trial court's determination that PCR amplification evidence satisfied *Frye*); *State v. Moore*, 268 Mont. 20, 885 P.2d 457, 475 (Mont. 1994) (upholding trial court's finding that PCR testing is sufficiently reliable under *Rule 702* for forensic purposes), *overruled on other grounds by*, *State v. Gollehon*, 274 Mont. 116, 906 P.2d 697, 700 (Mont. 1995);

Watts v. State, 733 So. 2d 214, 223 (Miss. 1999) (holding that PCR testing produces reliable results); *State v. Dishon*, 297 N.J. Super. 254, 687 A.2d 1074, 1086 (N.J. Super. Ct. App. Div. 1997) (holding that PCR was reliable because it was found to be generally accepted under *Frye*); *People v. Morales*, 227 A.D.2d 648, 643 N.Y.S.2d 217, 219 (N.Y. App. Div. 1996) (holding that PCR method had gained general acceptance under *Frye*); *Campbell v. State*, 910 S.W.2d 475, 478-79 (Tex. Crim. App. 1995) (holding that underlying theory of PCR DNA testing is valid under *Rule 702*).

[**39] Similarly, as the trial court has acknowledged, the National Institute of Standards and Technology ("NIST") has determined that there are several advantages of using STRs over conventional techniques, and that the use of STRs for genetic mapping and identity testing has become widespread among DNA typing laboratories. John M. Butler & Dennis J. Reeder, *Short Tandem Repeat DNA Internet Database*, <http://www.cstl.nist.gov/biotech/strbase/intro.htm>. As a result, many courts have found that DNA evidence derived from STR-based testing is admissible either under *Frye*'s general acceptance test or under *Rule 702*'s reliability test.¹⁶ The wide acceptance of PCR and STR testing among scientists and courts in various jurisdictions indicates that the use of such systems in DNA analysis is reliable. Furthermore, the evidence in the record demonstrates that unlike RFLP testing, which destroys the sample, PCR processing allows for easy replication of test results by amplifying the sample. We are therefore convinced that DNA evidence derived from PCR-based testing, and specifically such evidence derived from the STR method is sufficiently reliable under *CRE 702* to warrant admission in Colorado. [**40]¹⁷

16 *People v. Allen*, 72 Cal. App. 4th 1093, 85 Cal. Rptr. 2d 655, 659-60 (Cal. Ct. App. 1999) (holding that STR testing is generally accepted under *Frye*); *State v. Roth*, 2000 Del. Super. LEXIS 219, at *5 (Del. Super. Ct. May 12, 2000) (holding that single-source STR DNA evidence is reliable under *Daubert*); *State v. Rokita*, 316 Ill. App. 3d 292, 299, 249 Ill. Dec. 363, 736 N.E.2d 205, 210 (Ill. App. Ct. 2000) (noting that STR-based testing is now generally accepted in the relevant scientific community); *Commonwealth v. Rosier*, 425 Mass. 807, 685 N.E.2d 739, 743 (Mass. 1997) (holding that PCR-based tests, including STR, are scientifically valid); *State v. Jackson*, 255 Neb. 68, 582 N.W.2d 317, 325 (Neb. 1998) (holding that the trial court correctly determined that PCR-based STR DNA testing used in that case was generally accepted).

17 See *Brooks*, 975 P.2d at 1114 (holding that evidence is admissible if it is reasonably reliable and will assist the trier of fact).

[**41] The evidence at issue in this case was derived from a PCR-based STR multiplex system.¹⁸ Specifically, the Profiler Plus and Cofiler kits at issue here employed a combination sixplex and nineplex system. Having determined that PCR and STR-based testing are reliable under *CRE 702*, the issue before us now is whether the specific multiplex testing performed in this case is sufficiently reliable under *CRE 702* to warrant admission of the evidence derived from their use.

18 As discussed above, multiplex systems add more than one set of PCR primers to a reaction so as to be able to amplify and run several loci simultaneously. In contrast, monoplex systems run each STR locus separately.

We agree with the trial court's conclusion that, in general, evidence derived from multiplex testing should be admitted. However, we reach this conclusion by applying *CRE 702*, rather than *Frye*. In doing so, we conclude, based on the scientific evidence presented under the totality of circumstances in this case, that multiplex testing [**42] is sufficiently reliable to warrant such admission. Evidence in the record of numerous studies concerning multiplex testing, widespread dissemination of multiplex information, and popular use of multiplex systems supports our conclusion.

According to NIST, multiplex, which involves adding more than one set of PCR primers to the reaction in order to target multiple locations, is an ideal technique for DNA typing because the probability of identical alleles in two individuals decreases with an increase in the number of polymorphic loci examined. Butler, *supra* at <http://www.cstl.nist.gov/biotech/strbase/multiplx.htm>. The NIST website indicates that monoplex and multiplex STRs are used extensively in the forensic field, and the site lists over 900 published articles detailing the use of STRs in population studies, medical research and diagnosis, and in the forensic field.

Indeed, the trial court acknowledged that one advantage to multiplexing is its ability to offer greater discrimination. The trial court also noted that multiplexing requires less material, fewer tests and thus is ideal in the [**81] forensic setting and saves time and money. In addition, because fewer tests are required, [**43] the risk of contaminating samples is reduced. While testing multiple loci in one test can be problematic because adding more than one set of PCR primers to a reaction may cause primers for one locus to complex with those of other loci, the reproducibility of test results under this process mitigates this risk. Furthermore, the numerous

studies concerning multiplex testing and evidence in the record of widespread dissemination of multiplex information support its reliability.

The record indicates that the prosecution submitted fourteen studies addressing the consistency and reliability of the PE kits and their forensic use. Because the majority of the studies were conducted in foreign countries and because they were published in a book that was not well-known, the trial court concluded that they were not sufficiently peer reviewed. The trial court similarly dismissed a study performed in the United States by a well-respected expert in the field, and another validation study included by PE in its user's manual. The record also indicates that information about the multiplex method had been widely disseminated through numerous poster sessions and symposia. Although the trial court found [**44] that this failed to establish validation under strict TWGDAM guidelines and thus indicated no general acceptance under *Frye*, we reach a different conclusion under *CRE 702*. We find that the evidence in the record of numerous studies concerning multiplex, widespread dissemination of multiplex information, and popular use of multiplex systems indicates that multiplex systems are reliable under *CRE 702*.

The trial court acknowledged that triplexing, which is a form of multiplexing, is generally accepted. However, it nonetheless held that the sixplex and nineplex systems at issue in this case were not sufficiently validated or peer reviewed, and thus evidence derived from their use was inadmissible. We disagree.

As a preliminary matter, we disapprove of the trial court's distinction between the sixplex and nineplex systems at issue in the present case and other multiplex systems not at issue here that have been widely accepted by the scientific community.¹⁹ Such a fine distinction is not required under *CRE 702*'s liberal standard for admissibility. See *Daubert*, 509 U.S. at 594 ("The inquiry envisioned by *Rule 702* is, we emphasize, a flexible one."); *Bonds*, 12 F.3d at 565 [**45] (holding that a *Rule 702* inquiry is "a flexible and more lenient test that favors the admission of any scientifically valid expert testimony").

19 Indeed, while concluding that only monoplex and triplex STR systems are generally accepted, the trial court noted that the NIST website provides a list of fifty-two validation studies including validations of multiplex STRs, and lists of core STR loci, including monoplex, triplex, tetraplex, quintuplex, pentaplex, and heptaplex loci.

We also conclude that questions as to the reliability of the particular type of multiplex kit go to the weight of the evidence, rather than its admissibility. *State v. Russell*, 125 Wn.2d 24, 882 P.2d 747, 768 (Wash. 1994)

(holding that general acceptance under *Frye* of PCR kit was not required because the kit is simply one tool for carrying out generally accepted PCR methodology); see also *Hicks*, 103 F.3d at 848 (holding that challenges to laboratory protocols used in PCR testing do not weigh against [**46] the admissibility of PCR); *Shea*, 957 F. Supp. at 340 (concluding that concerns about handling and quality control procedures affect the weight that should be given to evidence, rather than its admissibility). Finally, we are persuaded that the multiplex systems at issue in this case are sufficiently reliable by their acceptance by several other courts that have considered the issue.

Although our research reveals no appellate court decisions discussing the admissibility of DNA evidence derived from a multiplex system, the parties have submitted copies of several trial court rulings from other jurisdictions that have admitted DNA evidence derived from the very multiplex STR systems at issue here. *State v. Lynch*, No. CR 98-11390 (Ariz. Super. Ct. Aug. 17, 1999) (ruling that Profiler Plus and Cofiler kits were generally accepted under *Frye*); *State v. Hill*, No. 232982 (Cal. Super. Ct. Apr. 18, 2000) (ruling that issue as to whether [*82] PE kit is generally accepted goes to weight, not admissibility and concluding that evidence derived from such kit is admissible under *Frye*); *State v. Bertsch*, No. 94F07255 (Cal. Super. Ct. Oct. 20, 1999) (ruling that PE multiplex [**47] kits were admissible under *Frye's* general acceptance test); *Commonwealth v. Gaynor*, No. 98-0965-0966 (Mass. Super. Ct. Apr. 13, 2000) (ruling that evidence derived from Profiler Plus and Cofiler kits was admissible under *Daubert*); *State v. Dishmon*, No. 99047345 (Minn. Dist. Ct. Mar. 2, 2000) (ruling that evidence derived from Profiler Plus and Cofiler kits was admissible under *Frye*).

For example, a Minnesota District Court found recently in *State v. Dishmon* that evidence obtained using the Profiler Plus and Cofiler kits was admissible. *Dishmon*, No. 99047345, slip op. at 13. That court concluded that because PCR-STR typing met the *Frye* test, general acceptance of the specific kits used was not required. *Id.* at 8. In the alternative, the court held that evidence presented in that case indicated that the Profiler Plus and Cofiler kits were generally accepted. *Id.* at 9.

Similarly, a Massachusetts court held recently that evidence derived from the Profiler Plus and Cofiler kits was reliable under *Daubert*. *Gaynor*, No. 98-0965-0966, slip op. at 2. That court reasoned, "Because the more recent testing consists of essentially a refinement in [**48] the STR system of analysis, which has been determined to be generally accepted in the scientific community, I find the recent test results to be reliable." *Id.* The court also determined that specific concerns about

the Profiler Plus and Cofiler kits themselves were issues of weight, rather than admissibility. *Id.* at 5.

We are aware of only one trial court that has found the evidence derived from the Profiler Plus and Cofiler kits to be inadmissible. The Vermont District Court held in *State v. Pfenning* that evidence derived from the Profiler Plus kit was inadmissible because the kit had not been sufficiently validated or subjected to peer review under *Daubert*. No 57-4-96 (Vt. Dist. Ct. Apr. 6, 2000). Because we have determined that compliance with the *Daubert* factors is not determinative as to the question of admissibility, we are not persuaded by *Pfenning* because its analysis focuses on a particular factor under *Daubert*, holding that the absence of that factor defeats admissibility. See *Kumho*, 526 U.S. at 151 (noting that, "It might not be surprising in a particular case . . . that a claim made by a witness has never been the subject of [**49] peer review . . ."); *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 155 (3d Cir. 1999) (holding that, given the liberal thrust of the rules of evidence and the flexible nature of the *Daubert* inquiry, published studies on general causation are not required for admission of a medical expert's testimony).

Thus, after considering the totality of the circumstances in this case, we conclude that the evidence derived from the PE sixplex and nineplex STR systems is admissible under *CRE 702* because (1) multiplex systems are generally reliable; (2) questions as to the reliability of a specific type of multiplex kit go to the weight of the evidence, rather than its admissibility; and (3) the specific multiplex kits used in this case have been deemed reliable by other courts. We also find that the probative value of the evidence derived from the kits used is not substantially outweighed by the danger of unfair prejudice, confusion of the issues, undue delay, waste of time, or needless presentation of cumulative evidence. Therefore, the evidence at issue here meets the requirements of *CRE 403* and should be admitted. Accordingly, we make our rule to show cause absolute and order [**50] the trial court to vacate its order barring such evidence.

IV. CONCLUSION

We hold that *CRE 702*, rather than *Frye*, is the appropriate standard for determining the admissibility of scientific evidence in Colorado. We hold that under this standard, the focus of a trial court's inquiry should be on whether the scientific evidence is reasonably reliable and whether it will assist the trier of fact, and that such an inquiry requires a determination as to (1) the reliability of the scientific principles, (2) the qualifications of the witness, and (3) the usefulness of the testimony to the jury. We also hold that [*83] when a trial court applies *CRE 702* to determine the reliability of scientific evidence, its inquiry should be broad in nature and consider

the totality of the circumstances of each specific case. In doing so, a trial court may consider a wide range of factors pertinent to the case at bar. The factors mentioned in *Daubert* and by other courts may or may not be pertinent, and thus are not necessary to every *CRE 702* inquiry. In light of this liberal standard, a trial court should also apply its discretionary authority under *CRE 403* to ensure that the probative value of the [**51] evidence is not substantially outweighed by unfair prejudice. Finally, we hold that under *CRE 702*, a trial court must issue specific findings as it applies the *CRE 702* and *403* analyses.

Applying this standard, we hold that DNA evidence derived from PCR-based testing is admissible under *CRE 702*. Similarly, we hold that evidence derived from STR systems, including STR multiplex systems, is also admissible under *CRE 702*. Finally, we conclude that the evidence at issue in this case, which was derived from kits employing a combination sixplex and nineplex system, is sufficiently relevant and reliable under *CRE 702* to warrant admission. Accordingly, we make our rule to show cause absolute and we order the trial court to vacate its order barring this evidence.



LEXSEE 131 F. SUPP. 2D 1347

BRIDGET GUTHRIE SIHARATH, Plaintiff, v. SANDOZ PHARMACEUTICALS CORPORATION, Defendant. BONNIE JOYCE RIDER and WALTER ANTHONY RIDER, Plaintiffs, v. SANDOZ PHARMACEUTICALS CORPORATION, a Delaware Corporation, SANDOZ LTD., a Swiss Corporation, and SANDOZ PHARMA LTD., a Swiss Corporation, Defendants.

CIVIL ACTION FILE NO. 1:95-CV-965-TWT, CIVIL ACTION FILE NO. 1:95-CV-3068-TWT

UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF GEORGIA, ATLANTA DIVISION

131 F. Supp. 2d 1347; 2001 U.S. Dist. LEXIS 5767; CCH Prod. Liab. Rep. P16,102

March 1, 2001, Decided

March 1, 2001, Filed

DISPOSITION: **[**1]** Defendant's Motion to Exclude and for Summary Judgment on Issues of Medical Causation Under Daubert v. Merrell Dow Pharmaceuticals, Inc. [Doc. 68], GRANTED. Defendant's Motion for Partial Summary Judgment on Warning Claims [Doc. 69-1], DENIED AS MOOT. Defendant's Motion for Partial Summary Judgment on Fraud and Negligent Misrepresentation [Doc. 69-2], DENIED AS MOOT. Defendant's Renewed Motion for Summary Judgment on the Statute of Limitations [Doc. 69-2], DENIED AS MOOT. Defendant's Motion for Oral Argument on its Renewed Motion for Summary Judgment on the Statute of Limitations [Doc. 126], DENIED AS MOOT. Defendant's Motion for Leave to Amend its Answer to Plead Federal Preemption [Doc. 133-1], DENIED AS MOOT. Defendant's Motion for a Briefing Schedule [Doc. 133-2], and DENIED AS MOOT. Defendant's Motion for Oral Argument on its Federal Preemption Defense [Doc. 133-3] DENIED AS MOOT. Defendant's Motion to Exclude and for Summary Judgment on Issues of Medical Causation Under Daubert v. Merrell Dow Pharmaceuticals, Inc. [Doc. 116] GRANTED. Defendant's Motion for Partial Summary Judgment on Warning Claims [Doc. 117-1], DENIED AS MOOT. Defendant's Motion for Partial **[**2]** Summary Judgment on Fraud and Negligent Misrepresentation [Doc. 117-2], DENIED AS MOOT. Defendant's Motion for Leave to Amend its Answer to Plead Federal Preemption [Doc. 177-1], DENIED AS MOOT. Defendant's Motion for a Briefing Schedule [Doc. 177-2], and DENIED AS MOOT. Defendant's

Motion for Oral Argument on its Federal Preemption Defense [Doc. 177-3]. DENIED AS MOOT.

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JUDGES: THOMAS W. THRASH, JR., United States District Judge.

OPINION BY: THOMAS W. THRASH, JR.

OPINION

[*1349] ORDER

These are two complex products liability actions. In each case, a postpartum woman suffered a stroke after taking a prescription drug manufactured by the Defendant. In its simplest form, the question presented is did the drug cause the strokes? Or, is the temporal association of taking the drug and a [**4] subsequent stroke merely coincidental? To begin to answer those questions, the Court must address the recurring issue of what is the quantity and quality of scientific evidence that a plaintiff must present on the issue of medical causation in a world of imperfect scientific knowledge.

Although the cases have not been consolidated, the motions and documentary evidence filed, the expert testimony, and the issues raised are identical in both cases. Consequently, the Court addresses the pending motions of both cases in this single Order. *Siharath v. Sandoz Pharmaceuticals Corporation*, No. 1:95-CV-965-TWT, ("Siharath") is before the Court on Defendant's Motion to Exclude and for Summary Judgment on Issues of Medical Causation Under *Daubert v. Merrell Dow Pharmaceuticals, Inc.* [Doc. 68]. *Rider v. Sandoz Pharmaceuticals Corporation*, No. 1:95-CV-3068-TWT, ("Rider") is likewise before the Court on Defendant's Motion to Ex-

clude and for Summary Judgment on Issues of Medical Causation Under *Daubert v. Merrell Dow Pharmaceuticals, Inc.* [Doc. 116].

I. BACKGROUND

Parlodel(R) is manufactured by Defendant Sandoz Pharmaceuticals Corporation --now Novartis Pharmaceuticals Corporation. [**5] Corporation. ¹ In 1980, the drug was approved for use to suppress postpartum lactation. Approximately 9 million women in the United States have taken the drug to suppress postpartum lactation. On September 20, 1989, Plaintiff Bridget Guthrie Siharath gave birth by Caesarean section to her second child. At the time, she was 17 years-old. She was unable to breast feed the child because she had taken pain medication. To suppress lactation, her doctor prescribed Parlodel(R). Ms. Siharath took regular doses of Parlodel(R) from the evening of September 20, 1989, until the morning of September 25, 1989. Later in the day on September 25, Ms. Siharath suffered three seizures and a subarachnoid hemorrhagic stroke. Her treating physicians were unable to diagnose the cause of the seizures or the stroke. No unusual trauma resulted from the Caesarean section. There was no indication that she suffered from eclampsia, a toxic blood condition associated with pregnancy that causes seizures and sometimes coma. Ms. Siharath did not smoke. Although she did have a history of suffering migraine headaches, no evidence existed that her migraine history was related to the stroke. Her treating physicians also [**6] could not say that Ms. Siharath's stroke was caused by the spasm or constriction of the arteries and veins ("vasospasm" and "vasoconstriction" respectively). While taking Parlodel(R), Ms. Siharath regularly ingested pseudoephedrine, a nasal decongestant. It is possible that pseudoephedrine can react with ergot alkaloids, the class of drugs of which Parlodel(R) is a member. Pseudoephedrine taken at minimal doses, however, is unlikely alone to cause hemorrhagic strokes. Ms. Siharath was hospitalized from September 25 to October 7, 1989. On March 10, 1995, she filed this pharmaceutical products liability action in negligence and strict liability, alleging that Parlodel(R) caused her seizures and stroke. She seeks compensatory and punitive damages. ²

¹ For convenience, the company and its subsidiaries named in *Rider* will be referred to as "Defendant."

² The case was assigned to the undersigned on May 19, 2000.

[*1350] Plaintiff Bonnie Joyce Rider gave birth to a daughter on December 2, 1993. The child was delivered [**7] by Caesarean section. At the time, Ms. Rider was 39 years old. On December 5, she was prescribed

Parlodel(R) to suppress lactation. She took the medicine from then until December 8, 1993. On December 9, 1993, Ms. Rider began having difficulty moving her right leg and arm. She was admitted to the hospital with complaints of abrupt onset of headache and weakness of the right leg and arm. During her hospitalization, Ms. Rider intermittently complained of involuntary jerking movements of the right leg. Ms. Rider was given a computerized tomography ("CT") scan, which revealed that she had suffered an acute intracranial hemorrhagic stroke. A magnetic resonance imaging ("MRI") performed the following day confirmed that she had suffered a left parietal hemorrhage. No unusual trauma occurred as a result of the Caesarean section, and there was no indication that Ms. Rider suffered from eclampsia. Ms. Rider had smoked at various times, but no evidence suggested that smoking alone had caused the stroke. Her doctor concluded that her stroke was caused by vasospasm. On November 28, 1995, she and her husband, Walter Anthony Rider, filed this pharmaceutical products liability action in negligence [**8] and strict liability, alleging that Parlodel(R) caused her seizures and stroke. The Riders seek compensatory and punitive damages.³

3 This action also was assigned to the undersigned on May 19, 2000.

After a preliminary review of the voluminous record, the Court held a status conference on August 2, 2000, and at that time granted Defendant's request for an evidentiary hearing on its Daubert objections to Plaintiffs' expert testimony on medical causation. Each side was given five hours for direct and cross examination of witnesses and one hour for argument.⁴ The Court on December 18-20, 2000, held a three-day Daubert hearing at which it heard evidence and argument from both sides regarding medical causation. At the hearing, Plaintiffs presented testimony from two of their experts, Dr. Maurice N.G. Dukes and Dr. Kenneth Kulig. Defendant presented testimony from three of its experts, Dr. James Martin, Dr. Karl Engelman and Dr. David Buchholz. Both sides took full advantage of the opportunity to cross [**9] examine the other side's experts. In addition to the Daubert hearing, the Court has reviewed the massive volume of documentary evidence (in all, about 575 exhibits, depositions and affidavits) that relates to Plaintiffs' expert testimony on medical causation. The Court's ruling is based on both the testimony from the Daubert hearing and the substantial documentary evidence in the record.

4 Without reasonable time limits, the hearing would have been completely unmanageable due to the volume of documents and potential testimony. The time limits focused the experts and the attorneys upon what was important. The Court is

convinced that it has as good (if not a better) understanding of the issues after three intense days than it would have if the hearing had lasted three months. The time allocated for the hearing was used efficiently because no evidentiary objections were allowed. See *Federal Rules of Evidence 104(a)* ("Preliminary questions concerning the qualification of a person to be a witness . . . shall be determined by the court, subject to the provisions of subsection (b). In making its determination it is not bound by the rules of evidence except those with respect to privileges.").

[**10] II. SUMMARY JUDGMENT STANDARD

Summary judgment is appropriate only when the pleadings, depositions, and affidavits submitted by the parties show that no genuine issue of material fact exists and that the movant is entitled to judgment as a matter of law. *Fed. R. Civ. P. 56(c)*. The court should view the evidence and any inferences that may be drawn in light most favorable to the nonmovant. *Adickes v. S.H. Kress and Co.*, 398 U.S. 144, 158-159, 26 L. Ed. 2d 142, 90 S. Ct. 1598 (1970). The party seeking summary judgment must first identify grounds that show the absence [**1351] of a genuine issue of material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323-24, 91 L. Ed. 2d 265, 106 S. Ct. 2548 (1986). The burden then shifts to the nonmovant, who must go beyond the pleadings and present affirmative evidence to show that a genuine issue of material fact does exist. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 257, 91 L. Ed. 2d 202, 106 S. Ct. 2505 (1986).

III. DISCUSSION

A. INTRODUCTION

Defendant contends that Plaintiffs' experts must be excluded from testifying in this case on the grounds that their expert testimony on medical causation is inadmissible. Expert testimony is admissible only if it satisfies the standards that the United [**11] States Supreme Court articulated in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594, 125 L. Ed. 2d 469, 113 S. Ct. 2786 (1993); accord *General Elec. Co. v. Joiner*, 522 U.S. 136, 146, 139 L. Ed. 2d 508, 118 S. Ct. 512 (1997); *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 141, 143 L. Ed. 2d 238, 119 S. Ct. 1167 (1999). The Supreme Court in *Daubert* explained that *Federal Rule of Evidence 702* allows the admission of expert testimony only if: (1) the expert is competent and qualified to testify regarding the matters that he intends to address; (2) the methodology by which the expert reaches his conclusions is sufficiently reliable; and (3) the expert, through scientific, technical or specialized expertise, provides

testimony that assists the trier of fact to understand the evidence or determine a fact in issue. *Daubert*, 509 U.S. at 590-91; accord *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1309 (11th Cir. 1999); *City of Tuscaloosa v. Harcross Chems., Inc.*, 158 F.3d 548, 562 (11th Cir. 1998).

The first element is competence. The expert must be qualified in his field of expertise. The proponent of expert testimony bears the burden of establishing its admissibility. *Wells v. Ortho Pharm. Corp.*, 615 F. Supp. 262, 295 (N.D. Ga. 1985), [**12] aff'd, mod. in part, and remanded on other grounds, 788 F.2d 741, 747-48 (11th Cir. 1986). "The burden of laying the proper foundation for the admission of the expert testimony is on the party offering the expert, and admissibility must be shown by a preponderance of the evidence." *Allison*, 184 F.3d at 1306. Where the burden has not been satisfied, *Federal Rule of Evidence* 702 precludes expert testimony. See *United States v. Paul*, 175 F.3d 906, 912 (11th Cir. 1999) (witness' review of literature in area outside his field "did not make him any more qualified to testify as an expert . . . than a lay person who read the same articles"); *City of Tuscaloosa*, 158 F.3d at 563 ("Portions of [plaintiffs' expert's] testimony lie outside of his competence as a statistician . . . , thus requiring the exclusion of those portions of [his] data and testimony . . .").

The second element of admissibility is reliability. To be considered reliable, expert testimony on scientific issues must be supported by "scientific knowledge." "The adjective 'scientific' implies a grounding in the methods and procedure of science. Similarly [**13] the word 'knowledge' connotes more than subjective belief or unsupported speculation." *Daubert*, 509 U.S. at 590. The Supreme Court in *Daubert* identified four factors to assist courts in determining whether testimony meets the standard of reliable scientific knowledge: (1) whether the expert's theory can and has been tested; (2) whether it has been subjected to peer review; (3) the known or expected rate of error; and (4) whether the theory or methodology employed is generally accepted in the relevant scientific community. *Daubert*, 509 U.S. at 593. These factors, however, are not exhaustive. At its core, the "scientific knowledge" inquiry seeks to determine whether there is "some objective, independent validation of the expert's methodology." *Moore v. Ashland Chem., Inc.*, 151 F.3d 269, 276 (5th Cir. 1998); accord *Michigan Millers Mut. Ins. Corp. v. Benfield*, 140 F.3d 915, 921 (11th Cir. 1998). "Thus, the proponent of the testimony [**1352] does not have the burden of proving that it is scientifically correct, but that by a preponderance of the evidence, it is reliable." *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1312 (11th Cir. 1999). [**14]

The final element of admissibility, set forth in *Daubert*, is an appropriate relevance, or "fit," between

the expert's opinion and the facts of the case. *Daubert*, 509 U.S. at 591; *United States v. Gilliard*, 133 F.3d 809, 812 (11th Cir. 1998); *United States v. Smith*, 122 F.3d 1355, 1358-59 (11th Cir. 1997). Scientific testimony does not assist the trier of fact unless the testimony has a valid scientific connection to the pertinent inquiry. *Daubert*, 509 U.S. at 591. There is no "fit" where there is "simply too great an analytical gap between the data and the opinion offered," as when an expert offers animal studies showing one type of cancer in laboratory mice to support causation of another type of cancer in humans. *General Elec. Co. v. Joiner*, 522 U.S. 136, 146, 139 L. Ed. 2d 508, 118 S. Ct. 512 (1997).

In this case, Plaintiffs seek to admit the testimony of five medical experts to support their *prima facie* requirement of establishing medical causation. To survive Defendant's Motions for Summary Judgment, Plaintiffs must produce evidence that would allow a reasonable jury to find to a reasonable degree of medical certainty [**15] that Parlodel(R) is (1) capable of causing stroke and (2) that Parlodel(R) did in fact cause their strokes. See, e.g., *Joiner v. General Elec. Co.*, 864 F. Supp. 1310, 1319 (N.D. Ga. 1994) ("When medical causation is at issue, plaintiffs must prove causation to a 'reasonable degree of medical certainty.'"), rev'd on other grounds, 78 F.3d 524, 534 (11th Cir. 1996), rev'd on other grounds, 522 U.S. 136, 146-47, 139 L. Ed. 2d 508, 118 S. Ct. 512 (1997); accord *Parrott v. Chatham County Hosp. Auth.*, 145 Ga. App. 113, 115, 243 S.E.2d 269 (1978). The first element has been termed "general causation" while the second element has been termed "specific causation." *Wheat v. Sofamor, S.N.C.*, 46 F. Supp. 2d 1351, 1357 (N.D. Ga. 1999). "General causation is the capacity of a product to cause injury; specific causation is proof that the product in question caused the injury of which the plaintiff complains." *Id.*

Defendant contends that three of Plaintiffs' five experts are not qualified to testify. Defendant also contends that the testimony of all five of Plaintiffs' experts is inadmissible because their testimony is neither scientifically reliable nor relevant. [**16] Defendant contends that Plaintiffs' experts' testimony fails to meet the *Daubert* standards for admissibility because Plaintiffs' experts (1) have failed to provide any evidence, either published or unpublished, that Parlodel(R) increases one's risk of stroke; (2) rely on uncontrolled and unreliable spontaneous reports and anecdotal case reports as the basis for their opinions; and (3) cannot show that their opinions have an acceptable error rate or are otherwise generally accepted.

Plaintiffs' five experts are as follows. Dr. Kenneth Kulig is a physician who is board certified in toxicology and emergency medicine. He is licensed to practice medicine in Colorado. A practicing physician for more

than 20 years, Dr. Kulig received his undergraduate degree from Michigan State in 1972, followed by a M.D. degree from Wayne State Medical School in Detroit in 1978. He completed an internship in internal medicine and a residency in emergency medicine. He then obtained a two-year fellowship in clinical toxicology at the University of Colorado. Thereafter, he became affiliated with both Denver General Hospital and the Rocky Mountain Poison Center. In 1991, he joined Porter Adventist Hospital [**17] in Denver where he established a private practice, served as Chairman of its Department of Medicine, and remains to this day as both Chairman of the Pharmacy and Therapeutics Committee and Director of the Porter Regional Toxicology Center. Dr. Kulig also is an associate clinical professor in the Division of Emergency Medicine and Trauma at the University of Colorado [*1353] Health Sciences Center. Dr. Kulig's affidavit states that he has published almost 150 journal articles, including one article related to Parlodel(R). Defendant in its briefs does not contest Dr. Kulig's qualifications in the field of toxicology. It contests only the reliability and relevance of his proposed testimony.

Dr. Dennis Petro is a board-certified neurologist. He received his M.D. degree at Pennsylvania State University. He completed a residency in neurology at Hershey Medical Center in Hershey, Pennsylvania. He became employed by the Food and Drug Administration ("FDA") in Rockville, Maryland, in 1977. While at the FDA, Dr. Petro reviewed drug applications relevant to neurologic disorders, specifically analgesics and drugs of abuse. At the time Dr. Petro began his employment with the FDA, Parlodel(R) was an investigative [**18] drug. After leaving the FDA, Dr. Petro became employed by the New York State Department of Health, but still continued part-time employment with the FDA as a consultant. Later he worked on the development of neurologic drugs while employed by Wyeth Laboratories and then Pfizer Pharmaceuticals. Thereafter, Dr. Petro joined the Nassau County Medical Center on Long Island, New York, to run its Neurologic Department Research Program. From there, he joined Fidia Pharmaceutical Corporation in Washington, D.C. Dr. Petro eventually left Fidia and became a consultant in new drug development. Since 1980, he has served as a member of the American Heart Association's Stroke Council. He also has published at least 16 medical articles in peer-reviewed journals. Defendant does not contest Dr. Petro's qualifications in the field of neurology. It contests only the reliability and relevance of his proposed testimony.

Dr. Subir Roy is a reproductive endocrinologist who serves as a professor in the Department of Obstetrics and Gynecology at the University of Southern California ("USC") School of Medicine. He received his M.D. degree at the University of North Carolina at Chapel Hill.

He completed both [**19] an internship and residency in obstetrics and gynecology at the Los Angeles County-University of Southern California Medical Center in Los Angeles, California. He then obtained a fellowship in gynecologic endocrinology and infertility from USC and has remained with USC ever since. Dr. Roy served on the FDA's Fertility and Maternal Health Drugs Advisory Committee when it considered the safety of Parlodel(R) in 1989. In October 1998, he was appointed to a four-year term on the FDA's OB/GYN Devices Advisory Committee. He is board certified by the American Board of Obstetrics and Gynecology. He has been a consultant to such publications as the American Journal of Obstetrics and Gynecology, The Journal of Reproductive Medicine, Obstetrics and Gynecology, and the Journal of the American Medical Association. He himself has published more than 60 peer-reviewed articles. Nevertheless, Defendant contends that Dr. Roy is not qualified by education or experience to render an expert opinion in this case. It also contests the reliability and relevance of his proposed testimony.

Dr. Anthony Guarino is a pharmacologist and toxicologist. He received his Ph.D. in pharmacology in 1966 from the [**20] University of Rhode Island. From 1972 to 1980, Dr. Guarino served as the Chief of the Laboratory of Toxicology at the National Cancer Institute in Bethesda, Maryland. From March 1980 to August 1984, he served as a review scientist for the FDA, where he conducted pharmacology and animal toxicology reviews of drugs being offered for clinical investigation and FDA approval. He was responsible for determining, primarily on the basis of animal study data that pharmaceutical manufacturers submitted, whether drugs could be introduced to humans safely and ultimately whether they should be approved for widespread commercial marketing and use. Since 1985, Dr. Guarino has been an adjunct professor of pharmacology at the University of South Alabama College of Medicine in Mobile, Alabama. He also has consulted in the field of drug development [*1354] in recent years. He has served on the editorial boards of three professional journals, including Regulatory Toxicology and Pharmacology. He has reviewed manuscripts for another 15 medical, chemical and environmental publications and has himself published more than 100 articles in his field. Nevertheless, Defendant contends that Dr. Guarino is not qualified [**21] by education or experience to render an expert opinion in this case. It also contests the reliability and relevance of his proposed testimony.

Dr. Maurice N.G. Dukes considers himself to be an adverse drug reaction scientist. No board certification exists for this discipline. Dr. Dukes received his medical degree from St. John's College in England in 1956 and a law degree from Cambridge University in 1957. Follow-

ing graduation in 1957, Dr. Dukes accepted employment with Richardson-Merrell Pharmaceuticals in its Netherlands office. From 1961 to 1972, he worked at Organon Pharmaceuticals International, eventually obtaining the positions of research manager and assistant research director. In 1972, he became Vice Chairman of the Netherlands National Drug Regulatory Commission, that country's functional equivalent of the FDA. He remained in that position until 1982. Between 1978 and 1982, Dr. Dukes also served as Deputy Member of the European Economic Community's ("EEC") Committee for Proprietary Medicinal Products. In 1982, he left those positions to head the pharmaceuticals program for the World Health Organization's ("WHO") European Regional Office. He left that position in 1991 but [**22] continues to consult with the WHO and the World Bank on drug policy. Additionally, Dr. Dukes served between 1985 and 1997 as a professor of drug policy studies at the University of Groningen in the Netherlands. He now serves as an adviser in drug policy studies at the University of Oslo in Oslo, Norway. For years, Dr. Dukes has edited the two internationally recognized standard treatises on drug side effects. Since 1975, he has been the editor-in-chief of Meyler's Side Effects of Drugs. From 1977 to 1996, he served as editor-in-chief of the Meyler's complement, Side Effects of Drugs Annual. He is also the editor-in-chief of the International Journal of Risk and Safety in Medicine and has authored such books as *The Effects of Drug Regulation* (1985) and *Responsibility for Drug-Induced Injury* (1988 & 2d ed. 1998). He also has authored some 240 papers and journal articles on such issues as pharmaceutical products, drug policy, adverse reactions and drug economics. He remains active in the development and establishment of adverse reaction monitoring systems, particularly in Central and Eastern Europe, Africa, and Southeast Asia. Dr. Dukes has never been a licensed, [**23] practicing physician in the United States or any other country. Principally, for that reason, Defendant contends that Dr. Dukes is not qualified by education or experience to render an expert opinion in this case. It also contests the reliability and relevance of his proposed testimony.

Having reviewed the depositions, affidavits, other documentary evidence, and, in the cases of Dr. Kulig and Dr. Dukes, having observed and considered their testimony at the Daubert hearing, the Court concludes that Drs. Kulig, Petro, Roy, Guarino, and Dukes are all well qualified by education and experience to provide an opinion on medical causation in this case. Indeed, Dr. Dukes -- whom Defendant most strenuously challenges -- is an exceptionally qualified expert on the issue of adverse drug reactions. The fact that he has chosen to spend his professional life in the world of public policy and academics instead of clinical practice in no way reduces his expertise in the field of adverse drug reaction science.

Defendant's argument to the contrary minimizes the contributions made to medical science by those who accept the call of public service and selflessly remain in that service throughout the [**24] duration of their careers.

The opinion of Plaintiffs' experts regarding medical causation in these cases is that [*1355] Parlodel(R) caused Plaintiffs' seizures and hemorrhagic strokes. The argument underlying their conclusion of medical causation is the following causal chain: (1) Parlodel(R)'s active ingredient, bromocriptine, prevents lactation from occurring by blocking the hormone that causes it. (2) Bromocriptine is a member of the ergot alkaloid class of drugs. (3) With respect to circulation, ergot alkaloids can cause vasoconstriction (narrowing of the blood vessels) and hypertension (high blood pressure). (4) Vasoconstriction can lead to seizures and even ischemic stroke (strokes caused by decreased blood flow to the brain). (5) If vasoconstriction can lead to ischemic strokes, it also likely causes hemorrhagic strokes (strokes caused by a rupture to the vessel). (6) Parlodel(R), therefore, caused Plaintiffs' hemorrhagic strokes.

Plaintiffs' experts admit that bromocriptine does not always act as a vasoconstrictor. They contend that bromocriptine can cause two seemingly anomalous circulation effects, depending on one's "vascular tone." If one's arterial resistance is low, Plaintiffs' [**25] experts admit that bromocriptine can cause vasodilation (widening of the blood vessels) and hypotension (low blood pressure). Vasodilation and hypotension are admittedly inconsistent with their theory of causation. If, however, one's arterial resistance is high, Plaintiffs' experts contend that bromocriptine, like other ergot alkaloids, can cause vasoconstriction and hypertension, which can lead to seizures and stroke. The "vascular tone" of Plaintiffs' cerebral arteries at the time of their strokes is completely unknown.

In short, the chain of Plaintiffs' argument is that Parlodel(R)'s active ingredient is bromocriptine, which is an ergot alkaloid. Ergot alkaloids are a class of drugs that can cause hypertension, seizures and ischemic strokes and, therefore, likely cause hemorrhagic strokes, also. The question before the Court is whether their methodology in constructing this causal chain is based on scientific knowledge that is sufficiently relevant and reliable to assist the trier of fact; or whether Plaintiffs' causal chain instead includes "leaps of faith" and is no more than a hypothesis not adequately supported by the scientific method. See *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 745 (3d Cir. 1994) [**26] ("Daubert's requirement that the expert testify to scientific knowledge -- conclusions supported for good grounds for each step of the analysis -- means that any step that renders the analysis unreliable under the *Daubert* factors renders the expert's testimony unreliable.") (emphasis in original);

Allison v. McGhan Med. Corp., 184 F.3d 1300, 1314 (11th Cir. 1999) ("Daubert decisions in other courts warn against leaping from an accepted scientific premise to an unsupported one.").

In *Daubert*, the Supreme Court "listed four noninclusive factors courts should consider in determining reliability under *Rule 702*: (1) whether the theory or technique can be tested; (2) whether it has been subjected to peer review; (3) whether the technique has a high known or potential rate of error; and (4) whether the theory has attained general acceptance within the scientific community." *Allison*, 184 F.3d at 1312 (citing *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 593-94, 125 L. Ed. 2d 469, 113 S. Ct. 2786 (1993)). Sorting through the mass of material submitted in this case, a few things are clear. The theory of the Plaintiffs' experts has not been validated by [**27] testing except to the limited extent that the animal studies and epidemiological studies discussed below are considered tests. The theory has not been subjected to peer review except to the limited extent discussed below with respect to statements in medical treatises. The rate of error is unknown. The theory has not attained general acceptance within the scientific community unless the removal of the indication for suppression of lactation by the Food and Drug Administration ("FDA") discussed below constitutes such acceptance. Applying the *Daubert* criteria literally, the testimony of Plaintiffs' experts [*1356] should be excluded as unreliable and irrelevant. Nevertheless, given that the *Daubert* criteria are noninclusive, the Court must go forward and address the issue of whether there is other data relied upon by Plaintiffs' experts that satisfies the necessity for reliable and relevant scientific knowledge.

B. EPIDEMIOLOGICAL STUDIES

The central question in this pharmaceutical products liability case, just as in *Daubert*, is the issue of medical causation. The starting point of the *Daubert* analysis must be consideration of the factors identified by the Supreme Court [**28] in that case to determine reliability and relevance. The first of these is whether the theory of causation has been tested. Epidemiology is the medical science devoted to determining the cause of disease in human beings. Epidemiologists employ cohort studies, case-control studies, and ecological studies to determine whether individuals exposed to an agent have a greater risk of developing the disease in question. Bailey, et al., "Reference Guide on Epidemiology," Reference Manual on Scientific Evidence 340-45(2000). In epidemiological terms, the difference in risk of getting the disease is the "relative risk." A relative risk of 1.0 means that the agent has no effect on the incidence of disease. When the relative risk reaches 2.0, the agent is responsible for an equal number of cases of disease as all other background

causes. A relative risk of 2.0 implies a 50 percent likelihood that an exposed individual's disease was caused by the agent in question. See, e.g., *Hall v. Baxter Healthcare Corp.*, 947 F. Supp. 1387, 1403 (D. Or. 1996); Reference Manual at 348-49. Thus, in the world of epidemiology, the threshold for concluding that an agent was more likely [**29] than not the cause of a disease is a relative risk greater than 2.0.

The existence of relevant epidemiological studies can be a significant factor in proving general causation in toxic tort cases. *Hall*, at 947 F. Supp. at 1403. Indeed, epidemiological studies provide "the primary generally accepted methodology for demonstrating a causal relation between a chemical compound and a set of symptoms or disease." *Conde v. Velsicol Chem. Corp.*, 804 F. Supp. 972, 1025-26 (S.D. Ohio 1992), *aff'd*, 24 F.3d 809, 814 (6th Cir. 1994). Plaintiffs do not dispute this point. (Transcript of *Daubert* Hearing, at 192) (recounting statement previously made by Dr. Kulig that epidemiological studies are the most important source for establishing causation).

Four epidemiological studies have been conducted to investigate a possible association between Parlodel(R) and stroke. The first study at issue is Kenneth Rothman, An Epidemiologic Evaluation of the Possible Relation Between Bromocriptine, Puerperal Seizures and Strokes (Epidemiologic Resources, Inc. Sept. 30, 1988) (Defendant's Motion to Exclude and for Summary Judgment, *Siharath v. Sandoz [**30] Pharms. Corp.*, Ex. 10.) [Doc. 68]; (Defendant's Motion to Exclude and for Summary Judgment, *Rider v. Sandoz Pharms. Corp.*, Ex. 10.) [Doc. 116]. In the hearing, this was referred to as the ERI study. The ERI study, commissioned by Defendant, is the only epidemiologic study using case controls and cohorts that has sought to determine whether a causal relationship exists between Parlodel(R) and stroke. This study reviewed hospital records of 280,096 postpartum women. Out of a total of 107 postpartum strokes in this population, only one occurred in a woman who had taken Parlodel(R). Of the 77 controls, only one had been exposed to Parlodel(R). The resulting relative risk calculation, at 8.4, was deemed not statistically reliable by the study's investigators. Even Dr. Kulig admitted, "I'm not going to say that this shows the drug causes stroke." (Transcript of *Daubert* Hearing, at 177.)

Realizing this limitation of the ERI study, Plaintiffs' experts emphasize instead their opinion that the study shows that Parlodel(R) does cause "late-occurring seizures" -- seizures occurring more than 72 hours after delivery. Plaintiffs allege that the relative risk factor of Parlodel(R) [*1357] for [**31] late-occurring seizures is 2.86. This allegation, however, ignores the fact that there were only three cases of late-occurring seizure in the study where the patient took bromocriptine. And in

two of those cases, the patients also had been given ergonovine, which neither Plaintiff in this case ingested. Indeed, the study concluded that although there is a positive association between bromocriptine and seizures among those who also received ergonovine, there is "a weak *negative* association among those who did not receive ergonovine." Rothman, *An Epidemiologic Evaluation*, at 23 (emphasis added). Dr. Kulig may be correct when he says that the ERI study was not well-conducted and does not unequivocally establish that Parlodel(R) is not dangerous for postpartum women. (Transcript of Daubert Hearing, at 178.) But the conclusion cannot be drawn from the ERI study that Parlodel(R) causes hemorrhagic stroke in postpartum women. Consequently, the Court must agree with Defendant that the ERI study is inadequate to advance Plaintiffs' theory of causation.

The second study is HCIA Inc., *Postpartum Complications and Parlodel(R)* (October 1995). (Defendant's Motion to Exclude and [*32] for Summary Judgment, *Siharath v. Sandoz Pharms. Corp.*, Ex. 12.) [Doc. 68]; (Defendant's Motion to Exclude and for Summary Judgment, *Rider v. Sandoz Pharms. Corp.*, Ex. 12.) [Doc. 116]. This study, also commissioned by Defendant, is commonly referred to as the HCIA study. The study analyzed 533,816 delivery records from 128 hospitals. It tracked postpartum complications and correlated complications with Parlodel(R) use. The estimated relative risk for stroke associated with bromocriptine use was 1.088, with a confidence interval ("CI") from 0.448 to 2.643. Similarly, the estimated relative risk for seizures associated with bromocriptine use was 1.071, with a CI from 0.406 to 2.829. See Reference Manual at 360 ("A confidence interval is a range of values calculated from the results of a study, within which the true value is likely to fall; the width of the interval reflects random error.") For both preexisting and non-preexisting hypertensive women, the study concluded that there existed *anegative* association. As Plaintiffs contend and Defendant admits, the HCIA study may possess methodological flaws that prevent a court from determining that Parlodel(R) definitely [*33] does not cause seizures and stroke, but the study certainly does not support Plaintiffs' theory of causation that Parlodel(R) does cause seizures and hemorrhagic stroke.

The third study is R.M.C. Herings and B.H.C. Stricker, *Bromocriptine and Suppression of Postpartum Lactation*, *Pharmacy World & Sci.* 17:133-37 (1995). (Defendant's Motion to Exclude and for Summary Judgment, *Siharath v. Sandoz Pharms. Corp.*, Ex. 13.) [Doc. 68]; (Defendant's Motion to Exclude and for Summary Judgment, *Rider v. Sandoz Pharms. Corp.*, Ex. 13.) [Doc. 116]. This study is often referred to as the Herings-Stricker study. In this study, investigators compared hospital admission and drug use of 2,130 women to identify

the existence of ischemic heart disease, hypertension, and cerebrovascular events such as stroke before, during and after use of Parlodel(R) for postpartum lactation. The study found that no women whatsoever were admitted to hospitals for any of these conditions during the presumed exposure period or in the following two months. Plaintiffs question the methodology of this study on a number of grounds, including that the sample size was too small for an accurate epidemiological study. [*34] That may be, but the study also does not support Plaintiffs' theory that Parlodel(R) causes hemorrhagic stroke and seizures.

The fourth study is Andrea D. Witlin, et al., *Postpartum Stroke: A Twenty-Year Experience*. (Defendant's Motion to Exclude and for Summary Judgment, *Siharath v. Sandoz Pharms. Corp.*, Ex. 11.) [Doc. 68]; (Defendant's Motion to Exclude [*1358] and for Summary Judgment, *Rider v. Sandoz Pharms. Corp.*, Ex. 11.) [Doc. 116]. This study was accepted for publication by the *American Journal of Obstetrics and Gynecology* but the offer was later withdrawn. The study, however, has been subjected to some peer review. It concluded that postpartum women who take bromocriptine are less likely to experience stroke than patients who are exposed to the drug. Indeed, the study concluded that, with a relative risk of 0.12, they are eight times less likely to suffer postpartum stroke. One of the study's authors, however, conceded in a deposition for the Rider case that "this study was not designed to address whether bromocriptine causes stroke or not." (Deposition of Dr. Baha M. Sibai, at 146.)

In short, neither the ERI study, the HCIA study, nor the Herings-Stricker study [*35] shows any statistically significant relationship between Parlodel(R) and stroke. The unpublished Witlin study found that bromocriptine was negatively associated with postpartum stroke, but it is unpublished and questions surround its actual intended purpose. As Dr. Kulig stated, "there is no good epidemiology on the subject." (Transcript of Daubert Hearing, at 281.) Plaintiffs' experts concede that no epidemiological study shows a statistically significant association between Parlodel(R) and stroke. The epidemiological studies either show no relationship or a negative relationship between the drug and stroke. Unable to rely upon the epidemiological studies as support for their causation opinions, Plaintiffs' experts predictably are critical of the conclusion that the studies prove Parlodel(R) is safe for postpartum women. None of the epidemiological studies are perfect; all have their flaws. It is important to recall, however, that the burden is on Plaintiffs to show that well-conducted epidemiological studies do show a statistically significant relationship between Parlodel(R) and seizures and stroke. It is not Defendant's burden to show the lack of such relationship.

Plaintiffs' [**36] well-taken criticisms of the epidemiological studies does not satisfy their burden of proof. See *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp. 2d 1015, 1044 (E.D. Mo. 2000) ("In the absence of their own epidemiological evidence supporting the conclusions of their experts that Parlodel(R) can cause an ICH [intracranial hemorrhage], the best plaintiffs can do is attack defendant's studies."); *Brumbaugh v. Sandoz Pharm. Corp.*, 77 F. Supp. 2d 1153, 1156 (D. Mont. 1999) ("The plaintiff criticizes certain aspects of these studies, but she produced no epidemiological study, or other reliable scientific proof that does make the causal link between Parlodel and her condition, or any related condition. Plaintiff's lawyers attack on defendant's studies does not meet the law's requirements. She must come forward with reliable scientific evidence of her own to defeat a summary judgment motion when her case is based on the expert's proof."). No evidence has been offered of an increase in postpartum strokes after the drug was approved for suppression of lactation; no evidence has been offered of a decrease in postpartum strokes after the approval for suppression [**37] of lactation was withdrawn. Reference Manual at 345 ("Another epidemiologic approach is to compare disease rates before and after a point in time when some event of interest took place.") The absence of epidemiological support raises the question of whether the causation opinions of Plaintiffs' experts are merely speculative and not based on scientific knowledge.

The lack of epidemiological studies supporting Plaintiffs' claims creates a high bar for Plaintiffs to surmount with respect to the reliability requirement, but it is not automatically fatal to Plaintiffs case. If other reliable scientific knowledge exists, Plaintiffs may overcome this evidentiary gap in their case. Epidemiological evidence is not the only legally sufficient proof for establishing a *prima facie* case of medical causation. In a pre-Daubert case, the Eleventh Circuit stated that:

[A] cause-effect relationship need not be clearly established by animal or epidemiological [*1359] studies before a doctor can testify that, in his opinion, such a relationship exists. As long as the basic methodology employed to reach such a conclusion is sound, such as use of tissue samples, standard tests, and patient [**38] examination, products liability law does not preclude recovery until a "statistically significant" number of people have been injured or until science has had the time and resources to complete sophisticated laboratory studies of the chemical.

Wells v. Ortho Pharm. Corp., 788 F.2d 741, 745 (11th Cir. 1986) (quoting *Ferebee v. Chevron Chem. Corp.*, 237 U.S. App. D.C. 164, 736 F.2d 1529, 1535-36 (D.C. Cir. 1984). Additionally, in *Allison v. McGhan Medical Corporation*, 184 F.3d 1300, 1316 (11th Cir. 1999), a post-Daubert case, the Eleventh Circuit analyzed all other proffered evidence even after it concluded that the plaintiff had not presented adequate epidemiological studies.

Epidemiology often is difficult to conduct. Additionally, ethical issues abound. "One cannot ethically experiment on human beings, exposing them to near certainty of some number of deaths, simply to satisfy some evidentiary standard." *Globetti v. Sandoz Pharms. Corp.*, 111 F. Supp. 2d 1174, 1180 (N.D. Ala. 2000). Consequently, this Court looks not only to the existence of epidemiology but also the other forms of causation evidence that Plaintiffs offer in totality [**39] to support their case. As the Eleventh Circuit has stated, although an individual item of evidence alone may not suffice to establish causation, it may serve as one component, that when added to others, does prove causation:

Opinions of any kind are derived from individual pieces of evidence, each of which by itself might not be conclusive, but when reviewed in its entirety are the building blocks of a perfectly reasonable conclusion, one reliable enough to be submitted to a jury along with the tests and criticisms cross-examination and contrary evidence would supply.

Joiner v. General Elec. Corp., 78 F.3d 524, 531 (11th Cir. 1996), rev'd on other grounds, 522 U.S. 136, 146-47, 139 L. Ed. 2d 508, 118 S. Ct. 512 (1997).

C. CASE REPORTS

In the absence of statistically significant epidemiological studies to support their general causation theories, Plaintiffs' experts rely most heavily on case reports. Case reports are a form of anecdotal evidence where one event is reported as following another. Reference Manual at 91. Defendant's response to the reliance upon case reports is twofold. First, it contends that the specific case reports relied upon by Plaintiffs [**40] are not cases where Parlodel(R) caused hemorrhagic stroke in postpartum women. Second, it contends that case reports in general do not satisfy the requirements of the scientific method sufficient to establish general causation. Following much thought and careful review of the case reports,

relevant case law, and numerous scholarly articles, the Court agrees on both counts.

Dr. Duker, Plaintiffs' principal adverse drug reactions expert, emphasized in his affidavit a number of Sandoz case reports as evidence for his opinion that Parlodel(R) causes strokes:

The most damning answer of all to Defendant's argument lies in the fact which I have detailed already, namely that Sandoz (both in Switzerland and the U.S.A.) had over a long period made use of precisely the evidence and methods which I have [been] using and had relied on them. From the records, one can see precisely what the general conclusions of Sandoz['s] own adverse reaction staff regarding Parlodel were when they had made use of these methods to examine specific reports. They were quite clear. Having examined the specific facts and circumstances implicated in individual reports of bromocriptine-associated adverse [**41] experiences, and without any references whatsoever to or reliance upon evidence from formal epidemiological studies, the DMC [Sandoz's Drug Monitoring Centre] at Basel concluded that [*1360] several adverse reactions -- including, but not limited to, strokes, hypertensive crises, seizures, and myocardial infarctions -- were *probably caused by use of Parlodel (bromocriptine mesylate)*. When one turns back to the original DER's [drug experience reports] received by Sandoz which had led them to this conclusion one can see how firmly founded the conclusion was.

(Affidavit of M.N.G. Duker, M.D., M.A., LL.M., at PP 36-37 (emphasis in original).) After looking at the adverse reaction reports themselves, the Court must conclude that this is a considerable overstatement of the case. This should be apparent from a brief examination of the reports relied upon by Dr. Duker.

In paragraph 36 of his affidavit, Dr. Duker states that Sandoz concluded that bromocriptine had probably caused an ischemic stroke in a woman five days after she began taking the drug. This woman, however, (1) was 62 years old; (2) was not postpartum; (3) had suffered from hypertension for 12 years; (4) suffered from [**42] acromegaly, a life-threatening pituitary disease that Dr. Duker admits can lead to stroke; (5) was taking bro-

mocriptine to reduce the size of a tumor (an approved indication); and (6) was also taking cortisone. (Plaintiffs' Ex. 125.) The case report emphasizes that her stroke was "probably due to hypotension," not hypertension. The initial adverse drug report states only that it was possible, not probable, that the adverse event was due to Parlodel(R). A subsequent, more detailed analysis in the case report likewise states that causality "is difficult to ascertain" and that it is only "possible" that Parlodel(R) "may be related to ischaemic cerebral infarction." Additionally, even if it can be said that bromocriptine probably caused this woman's stroke, it should be noted that this is the only stroke that Sandoz's Drug Monitoring Centre has ever concluded as "probably" having been caused by bromocriptine. Dr. Duker has written that "sometimes an adverse development may be a complication of the primary disease which is being treated rather than a complication of drug therapy." M.N.G. Duker, et al., *Responsibility for Drug-Induced Injury: A Reference Book for Lawyers, the Health Professions* [**43] and *Manufacturers* 43 (2d ed. 1998). This case report may be a good example of this process.

Dr. Duker refers in paragraph 37 of his affidavit to a 23 year old German woman who took Parlodel(R) for three months and suffered from hypertension and cerebellar incoordination. As Defendant's counsel elicited from Dr. Duker on cross-examination at the Daubert hearing, however, this patient was not postpartum; was taking Parlodel(R) to treat a pituitary adenoma, which itself can lead to hypertension and incoordination; and suffered from multiple sclerosis, a condition for which cerebellar incoordination is a classic symptom. (Plaintiffs' Ex. 57.) Also, the adverse event report stated only that it was "possible" that Parlodel(R) was causally related to her hypertension and incoordination. Mere possibility does not establish medical causation. Although an adverse case report is not required to "rule out" every other possibility to have some reliability, it should do more than just fail to rule out the alleged cause. It should provide a source for "ruling in" the alleged cause. A finding that Parlodel(R) "probably" caused a particular adverse event may add needed evidence to a causation [**44] theory. A finding that it only "possibly" caused the adverse event does not.

Dr. Duker refers next in paragraph 37 of his affidavit to a 22 year old French woman who took Parlodel(R) to suppress postpartum lactation. She later developed hypertension and convulsions. (Plaintiffs' Ex. 60.) Dr. Duker, however, fails to mention in his affidavit that the patient was hypertensive before delivery; that her hypertension decreased after taking Parlodel(R); and that she suffered from postpartum eclampsia, which can lead to seizures and stroke. See generally Steven J. Kittner, et al., *Pregnancy and the Risk of Stroke*, *New Eng. J. Med.*

768-74 (1996) [*1361] (discussing 28.3 relative risk of stroke for pregnant women compared with non-pregnant women).

Dr. Dukes also refers to a 20 year old Arkansas woman who took Parlodel(R) to suppress postpartum lactation and later developed hypertension. Dr. Dukes says that her symptoms improved after being taken off the drug, but the case report notes that she continued to suffer from hypertension for another four to five days. (Plaintiffs' Ex. 61.) This fact raises questions about the dechallenge (stopping use of the drug by the patient) aspect of this report, [**45] which is what Dr. Dukes emphasizes. Dr. Dukes discussed additional case reports in his affidavit. Defense counsel effectively discredited these additional case reports as evidence of a relationship between Parlodel(R) and postpartum stroke. See Transcript of Daubert Hearing, at 108-19 (referring to Plaintiffs' Exs. 126, 127, 25& 168). Thus, Defendant has raised serious questions about Dr. Dukes' analysis of these case reports.

Additionally, Dr. Dukes stated during the Daubert hearing that the value of adverse drug reports varies greatly, depending on the quantity, nature and content of the reports. (Transcript of Daubert Hearing, at 20.) He explained that in determining whether a sufficient quantity exists, one should ask how many reports have been received. In determining the nature of the reports, one should ask whether the reactions are what one might expect of the drug, the drug type and the dosage. In determining whether the content of the reports is sufficient, Dr. Dukes provided a chart at the hearing listing four questions that can assist in this analysis:

(1) Are at least some of the events described in full detail?

(2) Is the time course of the [**46] reaction credible?

(3) If the time reaction is reversible, did it disappear when the drug was stopped, or "dechallenged"? If it was ethical to repeat the treatment ("rechallenge"), did the effect reappear?

(4) Are more obvious alternative causes present?

The adverse drug reports in this case lack the requisite quantity, nature and content. From 1980 to 1994, millions of women took Parlodel(R). The modest number of case reports associating the drug with stroke or even postpartum hypertension is not what would be expected if there was a significant increased risk. Only one report exists that links Parlodel(R) to a stroke, and in that case

the patient suffered from an underlying condition that itself can cause stroke. No other patient in any case reports suffered any form of stroke. The other patients instead suffered non-cerebral effects such as hypertension and myocardial infarction. Many of the case reports cited involved patients who were not postpartum. One case report involved a patient who was dechallenged but continued to suffer from hypertension for another four to five days. In short, Plaintiffs' have not pointed to a single case report involving a postpartum [**47] woman who suffered a hemorrhagic stroke. Accordingly, even if case reports could be used to establish general causation, the Court would have to conclude that they are insufficient to do so in this case. The case reports simply lack the quantity, nature and content that Dr. Dukes himself claims is necessary for case reports to provide reliable scientific information about causation.

The fact of the matter is that even if relevant case reports existed, they cannot establish general causation:

Case reports are not reliable scientific evidence of causation, because they simply describe[] reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation.

Casey v. Ohio Medical Prods., 877 F. Supp. 1380 at 1385; see also *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp. 2d 1015, (E.D. Mo. 2000) (concluding [*1362] in Parlodel(R) products liability case that case reports did not support the reliability of plaintiffs' expert testimony); *Hollander v. Sandoz Pharms. Corp.*, 95 F. Supp. 2d 1230, 1235-38 (W.D. Okla. 2000) [**48] (noting that "case reports have been repeatedly rejected as a scientific basis for a conclusion regarding causation"); *Brumbaugh v. Sandoz Pharm. Corp.*, 77 F. Supp. 2d 1153, 1157 (D. Mont. 1999) (concluding that testimony in Parlodel(R) case was inadmissible because the expert was relying only on case reports of possible adverse drug reactions); *In re Breast Implant Litig.*, 11 F. Supp. 2d 1217, 1228 (D. Colo. 1998) ("To the extent there are case or anecdotal reports noting various symptoms or signs in breast implanted women, without controls, these suggest only a potential, untested hypothesis that breast implants may be their cause."); *Willert v. Ortho Pharm. Corp.*, 995 F. Supp. 979, 981 (D. Minn. 1998) (concluding that case reports are not sufficient evidence of causation because they do not exclude other alternative explanations); *Pick*

v. American Med. Sys., 958 F. Supp. 1151, 1161-62 (E.D. La. 1997) (noting that "courts have frequently rejected case studies as an insufficient basis to decide causation when they lack control groups" and that "the individual reports cited must be shown to be independently reliable [**49] under Daubert before they can be admitted"); *Hall v. Baxter Healthcare*, 947 F. Supp. 1387, 1411 (D. Or. 1997) ("Case reports and case studies are universally regarded as an insufficient scientific basis for a conclusion regarding causation because case reports lack controls."); *Haggerty v. Upjohn Co.*, 950 F. Supp. 1160, 1165 (S.D. Fla. 1996) ("While case reports may provide anecdotal support, they are not a substitute for scientifically designed and conducted inquiry."), *aff'd*, 158 F.3d 588 (11th Cir. 1998); *Muzzey v. Kerr-McGee Chem. Corp.*, 921 F. Supp. 511, 519 (N.D. Ill. 1996) (stating that anecdotal reports may be an incentive for more careful investigation, but are not reliable bases to form a scientific opinion about a causal link); *Wade-Greaux v. Whitehall Labs.*, 874 F. Supp. 1441, 1453 (D.V.I. 1994) ("[Case] reports record nothing more than a temporal association between an exposure and a particular occurrence. Because of individual confounding factors, one cannot draw causation conclusions from such anecdotal data. Epidemiologists use their population studies to eliminate the chance associations [**50] and confounding factors, which inherently affect anecdotal reports, to determine whether a statistically significant positive association exists.")

Adverse reaction reports and other case reports are generated by the clinical process of "differential diagnosis." Differential diagnosis is a patient-specific process of elimination that medical practitioners use in an attempt to identify the "most likely" cause of a set of signs and symptoms from a list of possible causes. Differential diagnosis, however, does not by itself unequivocally prove the cause, even for the particular patient. Nor can the process establish general causation. *In re Breast Implant Litig.*, 11 F. Supp. 2d 1217, 1230-31 (D. Colo. 1998); see generally Michael B. Kent, Jr., *Daubert, Doctors and Differential Diagnosis: Treating Medical Causation Testimony as Evidence*, 66 Def. Couns. J. 525, 532 (1999) (discussing differential diagnosis and general causation). Indeed, differential diagnosis assumes that general causation has been proven for the entire list of possible causes that are eliminated one-by-one:

The process of differential diagnosis is undoubtedly important to the question [**51] of "specific causation." If other possible causes of an injury cannot be ruled out, or at least the possibility of their contribution to causation minimized, then the "more likely than not" threshold for proving causation may not be met. *But it*

*is also important to recognize that a fundamental assumption underlying this method is that the final, suspected "cause" remaining after this process of elimination must actually be capable of causing the injury. That is, the expert must "rule in" the other suspected cause [**1363] as well as "rule out" other possible causes. And, of course, expert opinion on this issue of "general causation" must be derived from scientifically valid methodology.*

Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1413 (D. Or. 1996) (quoting *Cavallo v. Star Enter.*, 892 F. Supp. 756, 771 (E.D. Va. 1995), *rev'd* on other grounds, 100 F.3d 1150, 1157-59 (4th Cir. 1996) (emphasis in *Hall*)). With respect to general causation, the relevant scientific field is epidemiology or toxicology and not clinical medicine.

Both of Plaintiffs' experts who testified at the Daubert hearing recognize the severe limitations of [**52] case reports and differential diagnosis in establishing general causation. Dr. Kulig admitted the limitations in the following exchange:

Q: As a matter of scientific methodology, Dr. Kulig, case reports do not establish general causation and you would never attempt to do so, true?

A: True.

Q: And as a matter of scientific methodology, Dr. Kulig, case series do not establish general causation and you would never attempt to do so, true?

A: True.

Q: And as a matter of scientific methodology, Dr. Kulig, differential diagnosis as applied to a specific patient cannot establish general causation?

A: In and of itself, I wouldn't establish it, but now you're getting closer.

(Transcript of Daubert Hearing, at 193.) Case reports can establish only specific causation. Testimony regarding specific causation, however, is irrelevant unless general causation is established. *Hall*, 947 F. Supp. at 1413. Accordingly, given the limits of case reports in establishing general causation, as recognized by Plaintiffs' experts, the Court must conclude that Plaintiffs' reliance upon

case reports as a substitute for epidemiology cannot withstand the [**53] scrutiny that Daubert requires.

The court in *Globetti v. Sandoz Pharmaceuticals Corporation*, 111 F. Supp. 2d 1174 (N.D. Ala. 2000) gave considerable weight to case reports and the differential diagnosis process in overruling a Daubert objection. A couple of comments are in order. First, that case involved an allegation that Parlodel(R) caused an acute myocardial infarction. A case can be made that the medical community in general accepts the theory that Parlodel(R) is a risk factor for acute myocardial infarction in the postpartum period. This alone may be sufficient to satisfy the Daubert standard. Second, there is a much greater leap of faith from accepting that bromocriptine is a vasoconstrictor to the conclusion that it causes hemorrhagic strokes than to the conclusion that it can cause arterial spasm. Finally, the Court believes that the weight given to case reports in this Order is more consistent with the weight of authority in general and in Parlodel(R) stroke cases specifically. To the extent that Globetti holds that case reports are sufficient to show that Parlodel(R) causes stroke, this Court finds it unpersuasive, particularly given the strong epidemiological [**54] evidence that pregnancy itself is a strong risk factor for stroke. See generally Steven J. Kittner, et al., Pregnancy and the Risk of Stroke, *New Eng. J. Med.* 768-74 (1996)(discussing 28.3 relative risk of stroke for pregnant women compared with non-pregnant women).

D. EFFECTS OF OTHER ERGOT ALKALOIDS

Plaintiffs' experts also rely on adverse effects of drugs other than bromocriptine, but within the same class, to support their hypothesis that Parlodel(R) causes seizures and stroke. They allege that the effects of bromocriptine are similar to those of other ergot alkaloids, a family of naturally occurring and semi-synthetic compounds. Defendant contends that this reliance raises serious questions of "fit." The Court agrees. In general, "testimony extending general conclusions about similar drugs does not meet Daubert's requirements of reliability." *Brumbaugh v. Sandoz Pharm. Corp.*, 77 F. Supp. 2d 1153, 1157 (D. Mont. 1999); accord *Schudel v. General Elec. Co.*, 120 F.3d 991, 996-97 (9th Cir. 1997); see generally Daniel J. Capra, The Daubert Puzzle, 32 *Ga. L. Rev.* 699, 715 (1998) ("One example of improper extrapolation [**55] is an expert's use of structure analysis."). Small differences in molecular structure often have significant consequences. *Schudel*, 120 F.3d at 996-97. Each ergot alkaloid has distinctive pharmacological properties, and bromocriptine differs physically from the other ergot alkaloids in several respects, most notably the addition of a bromine atom.

The chemical diversity of ergot alkaloids corresponds to the *diversity of the biological activities of these compounds*. It is probably correct to state that there are few chemical groups which comprise substances with such diversified actions Many ergot compounds show a considerable spectrum of pharmacologic actions and, if the doses necessary to obtain a specific effect are taken into account, exhibit a high degree of specificity (selectivity).

B. Berde & H.O. Schild, *Ergot Alkaloids and Related Compounds 2* (emphasis in original).

In *Mitchell v. Gencorp, Inc.*, 165 F.3d 778, 782 (10th Cir. 1999), the plaintiffs' experts sought to testify that exposure to the defendant's chemicals caused the decedent to develop chronic myelogenous leukemia. The plaintiffs' experts attempted [**56] to support their conclusion with various published works that link exposure to benzene and certain types of leukemia. The plaintiffs' experts, however, did not possess any information suggesting that the decedent had ever been exposed to benzene. Consequently, the plaintiffs' experts attempted to show the following relationship: (1) the defendant's products were chemically similar to benzene; (2) because the defendant's products and benzene are chemically similar, they should affect the body in similar ways; (3) benzene exposure causes certain types of leukemia; (4) because benzene exposure causes other types of leukemia, it is logical that it could cause chronic myelogenous leukemia as well; (5) the decedent's exposure to the defendant's products caused him to develop chronic myelogenous leukemia. The district court found that the plaintiffs' experts' opinions lacked sufficient scientific validation to withstand the demands of Daubert. The Tenth Circuit affirmed:

In analyzing the experts' opinions, we begin by noting that the record contains some testimony about the similarities between benzene and Defendant's products. Missing from this evidence is additional testimony [**57] explaining exactly what these similarities are and how the similarities cause the human body to respond to Defendant's chemicals in a manner similar to benzene. Nor does the literature Plaintiffs presented support the notion that chemicals similar to benzene will affect the body in a manner similar enough to cause the same response as benzene.

Id.

Likewise, Plaintiffs' experts in this case cannot show that bromocriptine, the active ingredient in Parlodel(R), affects the body in a manner similar to other ergot alkaloids. Plaintiffs' argument in this regard is as follows: Parlodel(R)'s active ingredient is bromocriptine. Bromocriptine is a semi-synthetic ergot alkaloid. Ergot alkaloids are a class of drugs that can cause vasoconstriction. Vasoconstriction can lead to hypertension, seizures and ischemic strokes. Hemorrhages are another type of stroke, so it is possible that they also are caused by Parlodel(R). As in Mitchell, this argument suffers from a number of flaws. As mentioned above, bromocriptine cannot be assumed to cause the same effects as other ergot alkaloids. Bromocriptine differs physically from the other ergot alkaloids in several respects, most notably [**58] the addition of a bromine atom. It is accepted in the scientific and medical community that bromocriptine is not always a vasoconstrictor. It can be a vasodilator depending upon vascular tone. No evidence exists that other ergot alkaloids cause such peculiar effects. This scientific fact supports both the finding that small [**1365] differences in chemical structure often have significant consequences and the conclusion that testimony about similar drugs often does not meet Daubert's requirements of reliability.

Additionally, even if scientific support did exist for the Plaintiffs' conclusion that bromocriptine acts like other ergot alkaloids, Plaintiffs have presented no evidence that ergot alkaloids cause hemorrhagic strokes. There is evidence only that they may cause ischemic strokes. See, e.g., Goldfrank's Toxicologic Emergencies 754 (6th ed. 1998) ("In more serious cases, severe peripheral vasoconstriction may produce ischemic changes including angina, myocardial infarction, cerebral ischemia, and mesenteric ischemia."). Dr. Kulig states that in his clinical experience drugs that cause ischemia can also cause hemorrhage, but he cites as examples only cocaine and methamphetamine, [**59] two highly dangerous drugs that no expert has claimed are similar to bromocriptine or any other ergot alkaloid. (Transcript of Daubert Hearing, at 166.) Furthermore, no epidemiology or even learned treatises link ergot alkaloids to hemorrhagic strokes. (Transcript of Daubert Hearing, at 212.) Significant physiological distinctions exist between ischemic and hemorrhagic strokes. Ischemic strokes are caused by lack of blood flow to the brain. Hemorrhagic strokes are caused by the rupture of a blood vessel in the brain. The treatises list only cerebrovascular ischemia among the cerebral risk factors for ergot alkaloids. For all of the above reasons, Plaintiffs' experts' argument that bromocriptine is akin to other ergot alkaloids has not been supported by sufficient reliable scientific evidence

in the record. Consequently, the Court cannot adopt Plaintiffs' conclusion that bromocriptine's effects can be extrapolated from the effects of other ergot alkaloids.

E. FOOD AND DRUG ADMINISTRATION DETERMINATIONS

Plaintiffs next contend that Food and Drug Administration findings and conclusions support their experts' causation opinions. On August 24, 1994, the FDA issued the following [**60] statement:

Since approval of bromocriptine for use in preventing physiological lactation, FDA has received a number of reports of serious and life-threatening adverse experiences (hypertension, seizures, and CVA's [cardiovascular accidents]) associated with the use of bromocriptine for this indication. FDA believes that the number of women experiencing such adverse experiences may well be greater than those reported to the FDA. The above evidence, in aggregate, calls into question bromocriptine's safety for use in postpartum women given that bromocriptine may be responsible for hypertension, seizures, and CVA's in a small but significant number of patients. Moreover, bromocriptine may be an additional risk factor in patients who are already at risk for seizures and stroke. In addition, a possible mode of action exists for these adverse events. In the general population, a risk factor for hypertensive crises and spasms is exposure to ergot alkaloids. Bromocriptine is a semi-synthetic ergot alkaloid.

* * *

FDA now has new information suggesting that therapeutic use of bromocriptine for the prevention of physiological lactation may lead to serious adverse experiences, [**61] including death and paralysis, in a small but significant number of patients. Patients at high risk of experiencing these serious adverse experiences cannot be adequately predetermined. In light of the limited benefit of using bromocriptine for the prevention of lactation, and the effectiveness and lack of serious adverse effects of conservative treatments such as breast binding with or without mild analgesics, the risk that bromocriptine may cause a serious adverse effect in a postpartum woman is un-

acceptable. Accordingly, the Director concludes that the potential risks associated with the use of bromocriptine for the prevention of physiological lactation [*1366] outweigh its limited benefits and bromocriptine is no longer shown to be safe for use in preventing physiological lactation.

59 Fed. Reg. 43347, 43351 (Aug. 24, 1994).

Plaintiffs contend that this statement by the FDA supports the reliability of their experts' testimony. Plaintiffs' contention, however, ignores the lower standard of proof for agency determinations based upon a risk-utility analysis than the standard of proof required for the imposition of tort liability.

The methodology employed by a [*62] government agency "results from the preventive perspective that the agencies adopt in order to reduce public exposure to harmful substances. The agencies' threshold of proof is reasonably lower than that appropriate in tort law, which traditionally makes more particularized inquiries into cause and effect and requires a plaintiff to prove that it is more likely than not that another individual has caused him or her harm."

Mitchell v. Gencorp, Inc., 165 F.3d 778, 783 n.3 (10th Cir. 1999) (quoting *Allen v. Pennsylvania Eng'g Corp.*, 102 F.3d 194, 198 (5th Cir. 1996)). In this case, the lower standard is reflected in the FDA's August 24, 1994, order itself. The August 24 order fails to state affirmatively that a connection exists between bromocriptine and the type of injuries suffered in these cases. Instead it states that the evidence received by the FDA only "calls into question bromocriptine's safety," that bromocriptine "may be an additional risk factor in patients who are already at risk for seizures and stroke," and that the FDA had obtained new evidence "suggesting that therapeutic use of bromocriptine for the prevention of physiological [*63] lactation may lead to serious adverse experiences . . ." 59 Fed. Reg. 43348, 43351 (Aug. 24, 1994) (emphasis added). This language does not suggest that the FDA concluded that bromocriptine causes seizures and stroke. It merely indicates that in light of the limited social utility of bromocriptine for suppression of lactation, the availability of alternative therapy, and reports of possible adverse effects, the drug should no longer be used

for that indication. As the federal districts courts in *Hollander v. Sandoz Pharmaceuticals Corp.*, 95 F. Supp. 2d 1230, 1234 n.9 (W.D. Okla. 2000), and *Glastetter v. Novartis Pharmaceuticals Corp.*, 107 F. Supp. 2d 1015, 1036 (E.D. Mo. 2000) noted, the FDA's decision was motivated not simply by concerns with bromocriptine, but also by the relative risks and benefits of available alternatives. Accordingly, Plaintiffs' reliance on this FDA action to show reliability is insufficient to satisfy the requirements of Daubert

F. ANIMAL STUDIES

Plaintiffs' experts also rely on animal studies to support their causation opinions. Defendant questions the reliability, or "fit," of these studies. Extrapolations [*64] from animal studies to human beings generally are not considered reliable in the absence of a credible scientific explanation of why such extrapolation is warranted. *Hall v. Baxter Healthcare Corp.*, 947 F. Supp. 1387, 1410 (D. Or. 1996); see also *Turpin v. Merrell Dow Pharms., Inc.*, 959 F.2d 1349, 1360 (6th Cir. 1992) (excluding testimony where the record failed to make clear how animal studies were sufficient to show that Bendectin causes birth defects); *Richardson v. Richardson-Merrell, Inc.*, 273 U.S. App. D.C. 32, 857 F.2d 823, 830 (D.C. Cir. 1988) (excluding animal studies of Bendectin because of the overwhelming body of contrary epidemiological evidence and the admissions of the expert that animal studies merely raise a suspicion of causation in humans); *Lynch v. Merrell-National Labs*, 830 F.2d 1190, 1194 (1st Cir. 1987) (excluding animal studies of Bendectin in the absence of significant confirmatory epidemiological data); *Viterbo v. Dow Chemical Co.*, 826 F.2d 420, 424 (5th Cir. 1987) (excluding evidence where there was only a single animal study and it showed a link to a disease completely different than plaintiff's diseases). [*65] The use of animal studies to prove causation in human beings has two distinct disadvantages. Reference Manual at 346. First, extrapolating from animals to humans is [*1367] difficult because "differences in absorption, metabolism, and other factors may result in interspecies variation in responses." *Id.*; (Transcript of Daubert Hearing, at 19 (recounting Dr. Dukes' statement that with animal studies "you don't really know what that means in the living subject")). Second, "the high doses customarily used in animal studies requires consideration of the dose-response relationship and whether a threshold no-effect dose exists." Reference Manual, at 346; (Transcript of Daubert Hearing, at 255-57 (stating Dr. Kulig's agreement that these two disadvantages exist and limit the reliability of animal studies)). To ensure that the expert's conclusion based on animal studies is reliable, there must exist "a scientifically valid link between the sources or studies consulted and the conclusion reached." *Cavallo v. Star Enter.*, 892

F. Supp. 756, 762 (*E.D. Va.* 1995), *aff'd* in part, *rev'd* in part on other grounds, 100 *F.3d* 1150, (4th Cir. 1996).

A few courts [**66] have been more amenable to the use of animal studies in proving causation, at least pre-Daubert. See *In re Paoli R.R. Yard PCB Litig.*, 916 *F.2d* 829, 853-54 (3d Cir. 1990) (questioning exclusion of animal studies by district court); *Villari v. Terminix Int'l, Inc.*, 692 *F. Supp.* 568, 571 (*E.D. Pa.* 1988) (allowing testimony based on animal studies because "a substantial portion of the scientific community relies on animal studies of this type in assessing health risks to humans"); *Marder v. G.D. Searle & Co.*, 630 *F. Supp.* 1087, 1094 (*D. Md.* 1986) ("There is a range of scientific methods for investigating questions of causation -- for example, toxicology and animal studies, clinical research, and epidemiology -- which all have distinct advantages and disadvantages."), *aff'd*, *Wheelahan v. G.D. Searle & Co.*, 814 *F.2d* 655 (4th Cir. 1987). Nevertheless, the basic requirement remains: there must exist a reliable scientific explanation of why such extrapolation is warranted. Summarizing, as Judge Nangle has written:

Although some courts have recognized the relevance of animal studies, in some toxic tort cases, they have [**67] tended to view such studies with suspicion, and several courts have specifically held that animal studies alone cannot prove causation in humans. "[Animal studies], singly or in combination, do not have the capability of proving causation in human beings in the absence of any confirmatory epidemiological data." One court has gone so far as to hold that animal studies "are of so little probative force and are so potentially misleading as to be inadmissible. They cannot be the predicate for an opinion under *Rule 703*." Nothing in the record persuades this Court to depart from the precedent set in Georgia federal district courts as well as in other circuits by viewing animal studies favorably.

Bell v. Swift Adhesives, Inc., 804 *F. Supp.* 1577, 1579-80 (*S.D. Ga.* 1992) (citations omitted). After careful review of the animal studies at issue in this case, the Court concludes that Plaintiffs have not met the necessary standard for reliability.

There are basically three animal studies relied upon by Plaintiffs as evidentiary support for their theory that Parlodel(R) causes hemorrhagic strokes. These studies are (1) a Sandoz study conducted on the hind limb of a dog [**68] to determine bromocriptine's vasoconstrictive

properties (Plaintiffs' Ex. 113); (2) a Sandoz study that assessed the effect of bromocriptine on the carotid artery of three mongrel dogs (Plaintiffs' Ex. 191); and (3) a group of Sandoz studies performed on pithed animals (Plaintiffs' Exs. 18, 19, 20, 21 & 210). As shown below, however, none of these studies establish that Parlodel(R) causes stroke in humans -- or even in animals, for that matter. Even Dr. Kulig stated that he "wouldn't make the leap to stroke." (Transcript of Daubert Hearing, at 254 (emphasis added)). Furthermore, all of these animal studies have methodological flaws that prevent any conclusion that they "fit" with Plaintiffs' causation theory.

The Bertholet and Sutter study of the "hind-limb" of a dog (Plaintiffs' Ex. 113) attempted to determine, by injecting bromocriptine [**1368] into the hind limb of a dog, whether bromocriptine acts as a vasoconstrictor and, if so, at what point vasoconstriction takes place. Some of the experts in this case refer to this study as the "inversion point study" since it sought to determine at what vascular resistance bromocriptine changes, or "inverts," from a vasodilator to a vasoconstrictor. [**69] Plaintiffs contend that the study shows that Parlodel(R) is a vasoconstrictor. They admit, though, that the study does not demonstrate that Parlodel(R) causes stroke. (Transcript of Daubert Hearing, at 259.) The study also suffers from numerous other methodological flaws that raise serious questions about its reliability. First, the study did not attempt to measure any effects in the dog's cerebral blood vessels. Second, while not dispositive, it is noteworthy that the drug caused vasoconstriction at 1,250 times the human dosage of bromocriptine. One could not possibly achieve this blood level in a human. (Transcript of Daubert Hearing, at 342.) Third, Plaintiffs' experts admit that they "do not know how the dog's hind limb artery resistance compares to a human's hind limb artery resistance." (Transcript of Daubert Hearing, at 260.) Fourth, Plaintiffs cannot say whether dogs and humans have similar inversion points or even whether humans have inversion points at all. (Transcript of Daubert Hearing, at 261.) Consequently, the Court must conclude that this study is not sufficiently reliable to make up for the absence of epidemiological studies.

The "carotid artery" study [**70] (Plaintiffs' Ex. 191) attempted to determine the effects of bromocriptine on the carotid artery of a dog. Plaintiffs emphasize that the study concluded that bromocriptine is capable of increasing vascular resistance by 177 percent. (Transcript of Daubert Hearing, at 157-58.) Plaintiffs contend that this fact clearly establishes that bromocriptine is a vasoconstrictor. Plaintiffs' experts, however, admit that this study does not demonstrate that bromocriptine causes stroke. (Transcript of Daubert Hearing, at 262.) The most they can say is that a drug that can cause vasoconstriction of the carotid artery should be "high on the suspi-

cious drug list" for causing stroke. (Transcript of Daubert Hearing, at 262.) Suspicion, however, does not constitute the reasonable degree of medical certainty required to establish *prima facie* causation. Additionally, Defendant has provided a very persuasive argument that this study is of limited significance. According to Defendant, the study shows only that vascular resistance increased, not that blood vessels constricted or dilated. Any number of other factors could have caused the change in blood flow. Simply put, a change in resistance [**71] may occur regardless of a change in the artery. Analogizing to decreased pressure that one might experience in the shower when additional water faucets are turned on, Defendant's expert Dr. Engelman explained how in the carotid artery study the dog's cardiac output already was rapid, blood pressure dropped, and consequently the flow into the carotid artery dropped, resulting in an increase in resistance. Dr. Engelman convincingly explained that Plaintiffs' experts' simply conclude that the increase in resistance was caused by vasoconstriction, but that was not necessarily the case at all. All anyone really knows is that there was an increase in resistance in the study. The reason is unknown. That vasoconstriction occurred is simply a hypothesis, not an actual scientific finding.

Furthermore, Defendant noted that the flow probe in the study was placed only at the common carotid artery before it branches, with one branch going to the brain and the other going to the rest of the head. Consequently, there was no way for the researchers to measure the flow in either of these two branches. Dr. Engelman explained that typically when blood pressure falls, the body seeks to preserve blood [**72] flow to the heart and the brain. One, therefore, would have expected in this study for the carotid artery branch to the rest of the head to have contracted to preserve blood flow to the brain via the other branch. Because of the manner in which the carotid artery study was conducted, [*1369] there is no way to determine whether vasoconstriction occurred whatsoever in the branch to the brain. (Transcript of Daubert Hearing, at 335-41.) In short, the carotid artery study appears so flawed that it cannot be said to provide scientific knowledge on the effect of blood flow to the brain in dogs, much less humans.

Plaintiffs also contend that a number of studies conducted on pithed animals (Plaintiffs' Exs. 18, 19, 20, 21 & 210) show that bromocriptine can cause severe vasoconstriction. Pithed animals have had their central nervous system obliterated. The pithed animal studies at issue include rats, mice, dogs, cats and rabbits. Plaintiffs argue that vasoconstriction in these experiments was so severe that the tails of rats and mice became deprived of blood and fell off, as did the ear margins of dogs. Nevertheless, Plaintiffs' experts admit that they do not know whether these tests are predictive [**73] of human outcomes.

(Transcript of Daubert Hearing, at 265.) It also is true that pithing an animal causes dramatic effects that otherwise would not be seen. As Defendant's expert, Dr. Engelman, testified, a pithed animal is one in which the brainstem is destroyed by inserting a probe or needle into the *foramen magnum* (the hole at the back, lower portion of the skull) and then moving the probe back and forth and up and down until the lower portion of the brain has been destroyed. This portion of the brainstem is the area where regulatory reflexes control the body's cardiovascular system. Consequently, destroying this regulatory mechanism renders an animal extremely sensitive to any change in blood pressure. Any drug that might affect blood pressure, whether to increase or decrease it, will thus magnify that change tremendously. (Transcript of Daubert Hearing, at 334.) Plaintiffs' expert, Dr. Dukes, has written that "animal studies can sometimes prove embarrassingly [sic] misleading, even where matters as serious as effects on pregnancy . . . are concerned." M.N.G. Dukes et al., *Responsibility for Drug-Induced Injury: A Reference Book for Lawyers, the Health Professions* [**74] and *Manufacturers* 38 (2d ed. 1998). The methodology of using pithed animals to determine cardiovascular effects such as blood pressure seems less than reliable. Given the possible magnifying effects of pithing on blood pressure, the pithed animal studies are of limited, if any, utility. Because causation must be based on scientific knowledge allowing for a reasonable degree of medical certainty rather than mere "leaps of faith," the Court must conclude that the animal studies do not assist Plaintiffs in satisfying the requirements of Daubert.

G. LEARNED TREATISES

Plaintiffs also rely on a number of medical treatises that they contend support their causation theory. Plaintiffs cite medical treatises stating the following:

(1) "In the Physician's Desk Reference . . . there is well-documented evidence of strokes in women receiving bromocriptine for post-partum breast milk suppression . . ." M.D.B. Stephens, ed., *Detection of New Adverse Drug Reactions* 383.

(2) "Drug interactions and use after pregnancy can induce life-threatening responses," "severe HT [hypertension] with stroke has been reported after use for suppression of lactation," and "[a] possible [**75] early identifying symptom in patients who are at risk for severe reaction to bromocriptine in the postpartum period is headache, which may occur hours to days before the development of hyperten-

sion, seizures, stroke, or myocardial infarction." Williams & Wilkins Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning 26 tbl. 1-34, 867 & 868.

(3) "Adverse effects [for bromocriptine] which occur more rarely, but which are serious . . . include unusual and continuing headache, vision changes, seizures, or strokes." USP, Material Safety Data Sheet (1995).

[*1370] (4) "Many postpartum patients who developed stroke and/or seizures in association with bromocriptine therapy complained of constant and often progressively severe headaches hours to days prior to the acute event." American Hospital Formulary Service Drug Information 2560 (1995).

These excerpts from the treatises, however, do not provide sufficient support for Plaintiffs' causation theory. The statements in the treatises are clearly based on case reports and, therefore, provide no more support than the case reports themselves. See *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp. 2d 1015, 1034 n.18 (E.D. Mo. 2000) [*76] ("Indeed, as defendant notes, all the texts, treatises, and journals cited by plaintiffs appear based upon the accumulated case reports or individual case reports. The Court does not believe that texts and treatises that draw an 'association' between Parlodel and vasoconstriction based upon case reports make such texts and treatises any more reliable than the case reports on which they rely."). They do not add any additional scientific knowledge. For example, the statement in Ellenhorn's Medical Toxicology that bromocriptine use after pregnancy can cause "life threatening responses" cites as authority a journal article authored by Dr. Kullig, Bromocriptine-associated headache: Possible life-threatening sympathomimetic interaction, 78 *Obstetrics and Gynecology* 941-43 (1991) (Plaintiffs' Ex. 516). This article is nothing more than a case report. Additionally, the Court notes that one of the treatises that discusses bromocriptine but fails to state that the drug causes stroke is Meyler's Side Effects of Drugs, which is edited by Plaintiffs' expert Dr. Dukes. In any event, the Court concludes that Plaintiffs' reliance on learned treatises is insufficient to make up for the lack [*77] of reliable epidemiological studies. To the extent that the court reached a different conclusion in *Globetti v. Sandoz Pharmaceuticals Corporation*, 111 F. Supp. 2d 1174 (N.D. Ala. 2000), this Court finds it unpersuasive and contrary to the weight of authority.

H. TOTALITY OF THE EVIDENCE

Plaintiffs have produced an enormous mass of evidence about Parlodel(R). Prior to Daubert, the Court in all likelihood would have said that it is the function of the jury to evaluate the relevance and reliability of Plaintiffs' expert testimony. The command of Daubert, however, is that scientific testimony must be based upon scientific methodology. In concluding that Parlodel(R) causes seizures and hemorrhagic strokes, Plaintiffs' experts have not relied upon reliable scientific methodology. This would be a different case if there was at least some support for the causal hypothesis in the peer-reviewed epidemiological literature, a predictable chemical mechanism, general acceptance in learned treatises and other scientific literature of a causal relationship, a plausible animal model, and dozens of well-documented case reports involving postpartum women with no other risk factors for [*78] stroke. In such a case, the totality of the evidence would be enough to satisfy the demands of Daubert. In this case, no epidemiological studies support Plaintiffs' causation theory. Plaintiffs have not established that all ergot alkaloids cause vasoconstriction and strokes. Although the FDA has removed its indication of Parlodel(R) for postpartum lactation, this decision was based upon a risk-utility analysis rather than a finding using scientific methodology that Parlodel(R) causes strokes. The standard by which the FDA deems a drug harmful is much lower than is required in a court of law. The FDA's lesser standard is necessitated by its prophylactic role in reducing the public's exposure to potentially harmful substances. The animal studies that Plaintiffs rely on do not "fit" because the reliability of extrapolating them to the human situation has been forcefully and effectively challenged by Defendant. The excerpts from learned treatises that Plaintiffs cite are merely based on case reports and, therefore, provide no more assistance [*1371] than the case reports themselves. The case reports do not establish that Parlodel(R) causes hemorrhagic stroke in postpartum women. Additionally, [*79] case reports do not establish general causation. In short, none of the types of evidence that Plaintiffs offer -- individually or collectively -- establish a *prima facie* case that Parlodel(R) causes stroke. Cf. *Wells v. Ortho Pharm. Corp.*, 788 F.2d 741, 744 (11th Cir. 1986) ("Plaintiffs presented several epidemiological studies that indicated an association between spermicide use and deleterious effects on the fetus."). As Plaintiffs' expert, Dr. Dukes, has written, one cannot lump together lots of hollow evidence in an attempt to determine what caused a medical harm. (Transcript of Daubert Hearing, at 67 (recounting statement in Dr. Dukes' book *Responsibility for Drug-Induced Injury*)). Dr. Dukes has also stated that the "culmination of elements of evidence will clearly only lead to a valid result if the various elements of proof

which are brought together each have some individual validity in and among themselves." Id.

Plaintiffs' causal chain also is seriously flawed. The chain of Plaintiffs' argument is that Parlodel(R)'s active ingredient is bromocriptine, which is an ergot alkaloid, and ergot alkaloids are a class of drugs that can cause hypertension, [**80] seizures and ischemic strokes and, therefore, likely cause hemorrhagic strokes. Three scientifically unwarranted "leaps of faith" exist in this causal chain. First, a serious question exists whether bromocriptine is like other ergot alkaloids since it generally causes hypotension rather than hypertension. Second, even if Parlodel(R) can occasionally cause hypertension, Plaintiffs have not established that it can cause hypertension so severe as to cause seizures and stroke in humans. Third, even if Parlodel(R) can cause hypertension severe enough to cause stroke in humans, Plaintiffs have not shown that it causes hemorrhagic stroke. Plaintiffs have identified no epidemiological or animal studies, or even case reports, where Parlodel(R) was deemed to have caused a hemorrhagic stroke. Additionally, all medical evidence presented in this case on other ergot alkaloids establishes only that they may cause *ischemic* stroke. As discussed, ischemic strokes and hemorrhagic strokes are distinct and have different *modi operandi*. Ischemic strokes are caused by a reduction in blood flow to the brain. Hemorrhagic strokes are caused by a rupture to a blood vessel in the brain. Perhaps there [**81] is a reasonable extrapolation of ischemic strokes to hemorrhagic strokes, but Plaintiffs never fully explained it on their own or even when the Court raised the issue during the Daubert hearing. (Transcript of Daubert Hearing, at 39, 85, 165-66.) As Judge Becker of the Third Circuit has explained, expert testimony must be supported by "good grounds" at each step of the causal chain; and any step that renders their analysis unreliable also renders the testimony inadmissible. *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 745 (3d Cir. 1994). In this case, "there is simply too great an analytical gap between the data and the opinion proffered." *General Electric Co. v. Joiner*, 522 U.S. 136, 146, 139 L. Ed. 2d 508, 118 S. Ct. 512 (1997).

In short, Plaintiffs' case is not based on reasonable medical certainty, or "probabilities." It instead is based merely on "possibilities." This fact is vividly shown by the following exchange:

Q: Is it your opinion to a reasonable probability that Parlodel caused seizures in the case of Ms. Siharath?

A: No, I [Dr. Kulig] just said it was a possibility. I didn't want to rule it out.

(Transcript of Daubert Hearing, at 267.) [**82] The inability of Dr. Kulig -- as well as Plaintiffs' other experts -- to answer this question in the affirmative requires this Court to exclude the experts' testimony and grant summary judgment in favor of Defendant. Experts must do something more than just "rule out" other possible causes. They must explain how they were able to "rule in" the product in question. If all an expert does is rule out other possible causes, he or she may fail to [*1372] account for other potential (and sometimes unknown or unthought of) causes. When an expert only rules out causes, the trier of fact knows only what did not cause the harm. This does not necessarily aid the trier of fact in determining what did cause the harm-- and that is what the law requires in tort cases, especially those that involve allegedly toxic products.

As Defendant's expert, Dr. Buchholz explained at the Daubert hearing, doctors every day seek to determine causes of injury and illness and make patients healthier. In their eternal quest for "the answer," however, doctors sometimes believe that they have found a cause when they have not necessarily done so. Doctors in their day-to-day practices stumble upon coincidental occurrences [**83] and random events and often follow human nature, which is to confuse association and causation. They are programmed by human nature and the rigors and necessities of their clinical practices to conclude that temporal association equals causation, or at least that it provides an adequate proxy in the chaotic and sometimes inconclusive world of medicine. This shortcut aids doctors in their clinical practices because their most important objective day-to-day is to help their patients and "first, do no harm," as their Hippocratic oath requires. Consequently, "they make a leap of faith. And then in retrospect they build a bridge constructed of other anecdotal evidence, in some cases totally unrelated about heart attacks in older men and things like that and animal data, a bridge to help lead others across the chasm." (Transcript of Daubert Hearing, at 429.) The Court does not question Dr. Kulig's honest conviction that Parlodel(R) causes stroke or think that he is deliberately peddling "junk science." The Court also does not question that the methodology Dr. Kulig discussed at the Daubert hearing serves him well every day in the clinical practice of medicine. Dr. Kulig obviously [**84] is an exceptionally qualified practitioner, and the Court found him to be a very credible witness in this regard. Unfortunately, his clinical impression is not the sort of scientific methodology that Daubert demands.

Basically, Plaintiffs seek to survive Defendant's Motions to Exclude and for Summary Judgment by emphasizing that they have employed the same methodology as is applied by doctors throughout the world in their clinical practices. Plaintiffs argue that they have used the best

methodology available for this case. That may be so, but their methodology does not satisfy the requirements of Daubert. They have not provided sufficient, reliable scientific evidence to support a jury finding of legal causation. As Dr. Bucchholz explained:

I make clinical decisions all the time in the practice of medicine, Your Honor. I'm forced to because I have to take care of patients who are sick, and I have to decide what I think is going on, which most of the time I can't do based on scientific evidence because it doesn't exist or epidemiologic data because they don't exist.

So I make a judgment, a clinical decision about causation based on what's the background incidence [**85] of what just happened?. Because if it's more than negligible, then any association may well be by chance. What's the plausible mechanism? It helps to have a mechanism. The more detailed and specific, the better. What's the quality of the case reports or clinical experience, not just the quantity, but the quality in terms of how specific is the association? How consistent is the association?

Does the -- do the individual cases suggest that this mechanism that I might postulate has actually played out? Is there evidence of mechanism working along the way? And then finally, you have to do a differential diagnosis. What are the other possible explanations realizing in that differential that there is a large number of situations like stroke where you are going to wind up with an indeterminate diagnosis.

*That is clinical decision making that I go through on a routine basis, but it is [**1373] not scientific methodology.* Scientific methodology involves formulating a question or hypothesis and then testing it in such a way as to minimize bias in its founding, enabling a statistical analysis, publishing that if you can get it published through peer review, others replicating or refuting [**86] it. That's the type of process, that's not what I do as a doctor in formulating conclusions on causation in a daily basis.

(Transcript of Daubert Hearing, at 396-97 (emphasis added).)

Plaintiffs' counsel and their expert witnesses have done the best they could with the data available from the scientific literature and the Defendant's internal studies. If Daubert established a "best efforts" test, they unquestionably would have passed that test. Nevertheless, it appears that their "testimony is based more on personal opinion than on scientific knowledge." *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1319 (11th Cir. 1999). To steal a phrase from Judge Jones, their opinions are "educated guesses dressed up in evening clothes." *Hall v. Baxter Healthcare Corp.*, 947 F. Supp. 1387, 1407 (D. Or. 1996). To the extent that the court in *Globetti v. Sandoz Pharmaceuticals Corporation*, 111 F. Supp. 2d 1174, 1179 (N.D. Ala. 2000) held that Daubert is satisfied by presenting the "best scientific evidence available as a practical matter," this Court must respectfully disagree. Daubert demands reliable and relevant scientific opinion based [**87] upon reliable scientific methodology rather than mere "subjective belief or unsupported speculation." *Allison*, 184 F.3d at 1319, n. 23. The ultimate conclusion of the Court is that no expert can express such an opinion given the current state of scientific knowledge about Parlodel(R) and stroke.

Finally, the Court should not be too eager to make leaps of faith from a pharmaceutical manufacturer's basic research. Defendant continually researched whether an association exists between Parlodel(R) and hypertension, seizures, myocardial infarctions, and strokes. It attempted to determine whether the correlation of these conditions and Parlodel(R) use was a causal occurrence or rather only a chance occurrence. They never were able to establish causation. If this Court were to lower the Daubert standard based on anecdotal, temporal evidence obtained from Sandoz case reports, unfounded extrapolations, and leaps of faith, the Court would create an unintended disincentive for pharmaceutical companies to engage in ongoing research as to their products' safety and efficacy. Such an "ostrich in the sand" approach would in the long run make pharmaceutical products more risky, [**88] not safer.

In an attempt to prohibit the presentation of "junk science" to the trier of fact, perhaps Daubert has raised the bar for admissibility of expert testimony too high. Maybe there should be a middle ground between the Daubert standard and a standard that would allow sympathetic plaintiffs with catastrophic injuries to recover against pharmaceutical manufacturers based upon nothing more than speculation and conjecture. It is not, however, for this Court to seek that middle ground. This Court's duty is to apply the law as it exists today. And Daubert requires reliable science to support scientific opinion. "Striking the appropriate balance may some-

times be a difficult task." *Allison*, 184 F.3d at 1321. In some cases, no reliable science exists. Unfortunately for Plaintiffs, it appears to the Court that this is one of those cases. As Judge Posner has written, "the courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it." *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996). A court cannot determine causation in a case such as this one until science has done so. "Scientific [**89] conclusions are subject to perpetual revision. Law, on the other hand, must resolve disputes finally and quickly." See *Allison*, 184 F.3d at 1322 (11th Cir. 1999) (quoting *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 597, 125 L. Ed. 2d 469, 113 S. Ct. 2786 (1993)). That Parlodel(R) can and did cause the Plaintiffs' [*1374] strokes "is not a natural inference that a juror could make through human experience." *Allison*, 184 F.3d at 1320. "Thus, medical expert testimony was essential to prove causation in this case." *Id.* Consequently, the Court must grant Defendant's Motions to Exclude and for Summary Judgment as to the Plaintiffs' negligence and strict liability claims.

IV. CONCLUSION

For the reasons set forth above, the Court in *Siharath* GRANTS Defendant's Motion to Exclude and for Summary Judgment on Issues of Medical Causation Under *Daubert v. Merrell Dow Pharmaceuticals, Inc.* [Doc. 68], DENIES AS MOOT Defendant's Motion for Partial Summary Judgment on Warning Claims [Doc. 69-1], DENIES AS MOOT Defendant's Motion for Partial Summary Judgment on Fraud and Negligent Misrepresentation [Doc. 69-2], DENIES AS MOOT Defendant's Renewed Motion for Summary [**90] Judgment on the Statute of Limitations [Doc. 69-2], DENIES AS MOOT Defendant's Motion for Oral Argument on its Renewed Motion for Summary Judgment on the Statute of Limitations [Doc. 126], DENIES AS MOOT Defendant's Motion for Leave to Amend its Answer to Plead Federal Preemption [Doc. 133-1], DENIES AS MOOT Defendant's Motion for a Briefing Schedule [Doc. 133-2], and

DENIES AS MOOT Defendant's Motion for Oral Argument on its Federal Preemption Defense [Doc. 133-3]. The Clerk is directed to enter judgment for the Defendant.

Similarly, the Court in *Rider* GRANTS Defendant's Motion to Exclude and for Summary Judgment on Issues of Medical Causation Under *Daubert v. Merrell Dow Pharmaceuticals, Inc.* [Doc. 116], DENIES AS MOOT Defendant's Motion for Partial Summary Judgment on Warning Claims [Doc. 117-1], DENIES AS MOOT Defendant's Motion for Partial Summary Judgment on Fraud and Negligent Misrepresentation [Doc. 117-2], DENIES AS MOOT Defendant's Motion for Leave to Amend its Answer to Plead Federal Preemption [Doc. 177-1], DENIES AS MOOT Defendant's Motion for a Briefing Schedule [Doc. 177-2], and DENIES AS MOOT Defendant's Motion for Oral Argument on its Federal [**91] Preemption Defense [Doc. 177-3]. The Clerk is directed to enter judgment for the Defendants.

SO ORDERED, this 1 day of March, 2001.

THOMAS W. THRASH, JR.

United States District Judge

JUDGMENT

This action having come before the court, Honorable Thomas W. Thrash, Jr., United States District Judge, for consideration of defendants' motions to exclude and for summary judgment on issues of medical causation under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, and the court having granted said motions, it is

Ordered and Adjudged that the plaintiffs take nothing; that the defendants recover its costs of this action, and the action be, and the same hereby, is **dismissed**.

Dated at Atlanta, Georgia, this 5th day of March, 2001.