reference is made in either the policy or the endorsement to identify the papers as related, the endorsement will be considered part of the policy. Section 27–14–1 of the Code of Alabama, which defines an insurance policy as including "all clauses, riders, endorsements and papers attached, or issued, and delivered for attachment thereto and made a part thereof," also supports this reading of *Greene*.

Here, the endorsement was physically attached to the policy that defendants received. A "20–Day Right to Examine" afforded defendants sufficient time to review the policy, including all attachments, and confirm that it conformed to their expectations. *See Rager*, 712 So.2d at 335 (relying on a 10–day right to examine). By not returning the policy to MetLife or otherwise objecting, defendants agreed to its terms. The fact that defendants never signed the endorsement does not preclude them from being bound by it. *See id.* at 335 (rejecting insured's argument that unsigned endorsement was invalid).

Greene also requires that sufficient reference be made in *either* the policy or the endorsement to identify the papers as related. *See Greene*, 700 So.2d at 1357 (citing 43 Am. Jr.2d *Insurance* § 296 (1982)). Though not specifically mentioned in the policy itself, the endorsement here specifically referenced the policy to which it was attached. It stated that any "claim or controversy relating in any way to the sale, servicing, validity . . . *of this policy* . . . must be submitted to final and binding arbitration." R2–27–Ex1 (Policy) (emphasis added). This language clearly indicates that the endorsement relates to the insurance policy to which it was physically attached and was intended to be included with it.

The endorsement here also conformed exactly to the terms for modification set forth in the policy. Those terms require that any changes to the policy be issued in writing and signed by MetLife's President, Vice–President, or Secretary in order to be valid. The endorsement here was attached to the policy, in writing, and signed by Christine N. Markussen, Vice–President and Secretary of MetLife.

For the foregoing reasons, we REVERSE the judgment of the district court and REMAND with instructions to grant MetLife's petition to compel arbitration.

Bonnie Joyce RIDER, Walter Anthony Rider, her spouse, Plaintiffs–Appellants,

v.

SANDOZ PHARMACEUTICALS CORPORATION, a Delaware Corporation, Sandoz Ltd., a Swiss Corp., Sandoz Pharma Ltd., a Swiss Corporation, Defendants–Appellees.

Bridget Guthrie Siharath, Plaintiff–Appellant,

v.

Sandoz Pharmaceuticals Corporation, a Delaware Corporation, Defendant–Appellee.

Nos. 01–11965, 01–11966.

United States Court of Appeals, Eleventh Circuit.

June 24, 2002.

Patients in two cases who suffered hemorrhagic strokes after taking bromocriptine drug postpartum brought products

liability action against drug manufacturer. Manufacturer moved to exclude patients' expert testimony on issue of causation. The United States District Court for the Northern District of Georgia, Nos. 95-03068-CV-TWT-1, 95-00965-CV-TWT-1, Thomas W. Thrash, J., 131 F.Supp.2d 1347, granted motion. Patients appealed. The Court of Appeals, Roney, Circuit Judge, held that expert testimony on causation was inadmissible under *Daubert*.

Affirmed.

1. Products Liability ⚿83

While epidemiological studies may be powerful evidence of causation in a pharmaceutical products liability action, the lack thereof is not fatal to the plaintiff's case.

2. Products Liability ⚿83

By themselves, case reports of patients who suffered injuries subsequent to ingesting a drug cannot prove causation in a pharmaceutical products liability action, though they may support other proof of causation.

3. Evidence ⚿557

Dechallenge/rechallenge data reports provided by patients' experts were not reliable evidence under *Daubert* to prove causation, in products liability action alleging that bromocriptine drug taken postpartum caused patients to suffer hemorrhagic strokes; subjects of reports did not suffer strokes, but experienced different symptoms, including headaches and paralysis.

4. Evidence ⚿555.10, 557

Expert testimony offered by patients, who took manufacturer's bromocriptine drug postpartum, to show that drug caused them to suffer hemorrhagic strokes was insufficiently reliable under *Daubert* to be admissible in products liability action against manufacturer; evidence that other drugs in same chemical family caused vasoconstriction did not prove that drug at issue did also, animal studies in which bromocriptine demonstrated vasoconstrictive properties in dogs and other animals could not be extrapolated to humans, and evidence that bromocriptine caused ischemic stroke was not reliable to prove that drug caused hemorrhagic stroke. Fed.Rules Evid.Rule 702, 28 U.S.C.A.

Bert Black, Diamond, McCarthy, Taylor & Finley, Dallas, TX, Ellen Relkin, Weitz & Luxenberg, P.C., New York City, for Plaintiffs–Appellants.

Joe G. Hollingsworth, Katharine R. Latimer, Scott S. Thomas, Spriggs & Hollingsworth, Washington, DC, Lawrence J. Myers, Smith Moore LLP, Atlanta, GA, for Defendants–Appellees.

Appeals from the United States District Court for the Northern District of Georgia.

Before ANDERSON, HULL and RONEY, Circuit Judges.

RONEY, Circuit Judge:

This case involves an issue that has repeatedly come before federal courts: whether expert testimony purporting to link the drug Parlodel with hemorrhagic stroke is admissible to prove causation. Bridget Siharath and Bonnie Rider (plaintiffs) brought this action, alleging that their postpartum hemorrhagic strokes were caused by ingestion of Parlodel. Defendant Sandoz Pharmaceuticals Company (Sandoz), maker of Parlodel, moved to suppress the testimony of the plaintiffs' expert witnesses and for summary judgment. The district court held that the plaintiffs' expert testimony was not sufficiently reli-

able to meet the standards established by *Daubert v. Merrell Dow Pharm.,* 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993), and granted summary judgment in favor of Sandoz. Plaintiffs appeal. We affirm.

At the outset, we should point out that this decision does not affirm the interpretation that the appellants and some of the amici give to the district court's opinion at *Siharath v. Sandoz Pharm. Corp.,* 131 F.Supp.2d 1347 (N.D.Ga.2001). The appellants argue that the district court did not follow the law as prescribed by the *Daubert* trilogy, as hereafter set forth, misunderstood the scientific basis for the opinions sought to be introduced by plaintiffs, and overlooked critical evidence. In our judgment this is a grossly distorted understanding of the decision of the district court and is unsupported in the record. This opinion should be read with the understanding that in our view, with due consideration of alleged incidental problems with the opinion itself, the district court correctly applied the principles established in the *Daubert* trilogy, without modification, and considered all of the voluminous evidence in the record and all of the evidence taken at a three-day hearing, whether or not specifically mentioned in the opinion. The district court was unable to find sufficiently reliable scientific evidence to support a decision that bridged the gap between the conclusion that Parlodel caused other injuries, which might include ischemic stroke, and the conclusion that Parlodel was a probable cause of the hemorrhagic strokes suffered by plaintiffs. We have reviewed the opinion, noted a problem or two with the opinion itself, considered the arguments in the briefs of both appellants and amici, and reviewed the record, and conclude that under an unmodified application of the *Daubert* trilogy, a proper consideration of every piece of evidence offered, and a study of the expert opinions themselves, the district court did not abuse its discretion in denying the admission of the testimony of the five expert witnesses offered by the plaintiffs to prove causation in this case.

I. Background

Bridget Siharath and Bonnie Rider both took the drug Parlodel to suppress lactation after childbirth. The active ingredient in Parlodel is bromocriptine, an ergot alkaloid compound. Both women subsequently suffered hemorrhagic strokes.

Siharath and Rider filed suit against Sandoz, alleging that Parlodel caused their hemorrhagic strokes. After discovery, Sandoz moved, *in limine,* to exclude the opinions and testimony of the plaintiffs' experts on causation, and for summary judgment. Because the motions, documentary evidence, experts, and issues were the same in both cases, the district court addressed the motions together. The district court held a *Daubert* hearing to determine whether the evidence was admissible.

The district court, in a three-day hearing, examined the evidence presented in great detail and found that the plaintiffs' claims were based on speculation and conjecture rather than the scientific method. The court drew a careful distinction between clinical process, in which conclusions must be extrapolated from incomplete data, and the scientific method, in which conclusions must be drawn from an accepted process, and concluded that the plaintiffs' experts were relying on the former. Accordingly, the district court excluded the evidence and granted summary judgment in favor of Sandoz. A detailed summary of the facts is fully set forth in the published district court opinion, *Siharath v. Sandoz Pharm. Corp.,* 131 F.Supp.2d 1347 (N.D.Ga.2001). This appeal followed.

II. The Legal Standard

Toxic tort cases, such as this one, are won or lost on the strength of the scientific evidence presented to prove causation. For many years the standard for admissibility of such evidence was the "general acceptance" test set forth in *Frye v. United States,* 293 F. 1013 (D.C.Cir.1923). When the Federal Rules of Evidence were enacted in 1975, a question arose as to whether the "general acceptance" test had been supplanted by the reliability test articulated in Rule 702. The question was resolved in three cases decided by the Supreme Court. *Daubert v. Merrell Dow Pharm.,* 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993); *Gen. Elec. Co. v. Joiner,* 522 U.S. 136, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997); *Kumho Tire Co., Ltd. v. Carmichael,* 526 U.S. 137, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999). These cases are commonly referred to as the *Daubert* trilogy.

Since *Daubert,* courts are charged with determining whether scientific evidence is sufficiently reliable to be presented to a jury. The *Daubert* court made it clear that the requirement of reliability found in Rule 702 was the centerpiece of any determination of admissibility. 509 U.S. at 589, 113 S.Ct. 2786. The Supreme Court identified four factors used to determine the reliability of scientific evidence: 1) whether the 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. *Id* at 593–94, 113 S.Ct. 2786.

In *Joiner,* the Supreme Court established the standard for reviewing trial court rulings of admissibility, and held that such rulings would be made under an abuse of discretion standard. 522 U.S. at 141, 118 S.Ct. 512. The *Joiner* court also established the important test of analytical "fit" between the methodology used and the conclusions drawn. *Id* at 146, 118 S.Ct. 512. The court reasoned that just because a methodology is acceptable for some purposes, it may not be acceptable for others, and a court may not admit evidence when there is "simply too great an analytical gap between the data and the opinion proffered." *Id.*

In *Kumho Tire,* the Supreme Court made it clear that testimony based solely on the experience of an expert would not be admissible. 526 U.S. at 157, 119 S.Ct. 1167. The expert's conclusions must be based on sound scientific principles and the discipline itself must be a reliable one. *Id* at 156, 119 S.Ct. 1167. The key consideration is whether the expert "employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Id.* The court emphasized that judges have considerable leeway in both how to test the reliability of evidence and determining whether such evidence is reliable. *Id* at 151–53, 119 S.Ct. 1167.

The *Daubert* trilogy, in shifting the focus to the kind of empirically supported, rationally explained reasoning required in science, has greatly improved the quality of the evidence upon which juries base their verdicts. Although making determinations of reliability may present a court with the difficult task of ruling on matters that are outside of its field of expertise, this is "less objectionable than dumping a barrage of scientific evidence on a jury, who would likely be less equipped than the judge to make reliability and relevance determinations." *Allison v. McGhan Med. Corp.,* 184 F.3d 1300, 1310 (11th Cir.1999). The district court did not abuse its discretion in holding that the evidence presented by plaintiffs' experts does not meet the standard of reliability.

III. The Plaintiffs' Theory of Causation

Plaintiffs sought to introduce the testimony of five experts. All five possessed impressive credentials and were found to be well qualified by the district court, three over the defendants' objection. For a summary of the experts' credentials and qualifications, see the district court opinion, *Siharath*, 131 F.Supp.2d at 1352–54. Two of the experts, Doctors Kulig and Dukes, testified at the *Daubert* hearing. The experts presented a detailed argument for the cause of the plaintiffs' hemorrhagic strokes that may be summarized as follows:

1) The active ingredient in Parlodel is bromocriptine, a member of the class of drugs known as ergot alkaloids.

2) Other ergot alkaloids can cause vasoconstriction, which suggests that bromocriptine causes vasoconstriction.

3) Animal studies also suggest that bromocriptine causes vasoconstriction.

4) Vasoconstriction can cause high blood pressure and ischemic stroke (stroke caused by decreased blood flow to the brain).

5) If vasoconstriction and high blood pressure can cause ischemic stroke, it can also cause hemorrhagic stroke (stroke caused by a rupturing of a blood vessel).

6) Thus, Parlodel caused the plaintiffs' hemorrhagic strokes.

IV. The Evidence Presented

The scientific evidence presented by plaintiffs in support of their theory of causation may be grouped into six categories: 1) epidemiological studies that, on the whole, may point weakly toward causation; 2) case reports in which injuries were reported subsequent to the ingestion of Parlodel; 3) dechallenge/rechallenge tests that implied a relationship between Parlodel and stroke; 4) evidence that ergot alkaloids (a class of drug that includes bromocriptine) may cause ischemic stroke; 5) animal studies indicating that under some circumstances, bromocriptine may cause vasoconstriction in dogs and other animals; and, 6) the FDA statement withdrawing approval of Parlodel's indication for the prevention of lactation.

A. Epidemiology

Epidemiology, a field that concerns itself with finding the causal nexus between external factors and disease, is generally considered to be the best evidence of causation in toxic tort actions. Plaintiffs presented four epidemiological studies. Three of the four appear to have found no relationship or a negative relationship between Parlodel and stroke. Another may suggest a positive relationship. Nonetheless, both parties agree that none of the studies present statistically significant results and that the epidemiological evidence in this case is inconclusive.

Plaintiffs argue that the district court erred by requiring epidemiological studies, effectively ruling against them because they could not produce sufficient epidemiological evidence linking Parlodel to stroke. Having carefully reviewed the record, we conclude that the district court did not require epidemiological studies.

[1] It is well-settled that while epidemiological studies may be powerful evidence of causation, the lack thereof is not fatal to a plaintiff's case. In *Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986 (8th Cir.2001) and *Hollander v. Sandoz Pharm. Corp.*, 289 F.3d 1193 (10th Cir.2002), cases with facts nearly identical to those presented here, the Eighth and Tenth Circuits affirmed the respective district courts' exclusion of evidence that Parlodel had caused a hemorrhagic stroke, concluding that the plaintiffs' evidence was not

sufficiently reliable to be presented to a jury. Those appellants argued, as the appellants do here, that epidemiological evidence is not required to prove causation. Both courts properly ruled that it was not required. This Court has long held that epidemiology is not required to prove causation in a toxic tort case. *See Wells v. Ortho Pharm. Corp.*, 788 F.2d 741, 745 (11th Cir.1986) (holding that "a cause-effect relationship need not be clearly established by animal or epidemiological studies."). Accordingly, this case presents the difficult question of whether the evidence submitted to prove causation, in the absence of epidemiology, was sufficient to meet the requirements of *Daubert*.

B. Case reports.

Much of the plaintiffs' expert testimony relied on case reports in which patients suffered injuries subsequent to the ingestion of Parlodel. Although a court may rely on anecdotal evidence such as case reports, *Allison*, 184 F.3d at 1312, courts must consider that case reports are merely accounts of medical events. They reflect only reported data, not scientific methodology. Some case reports are a very basic form report of symptoms with little or no patient history, description of course of treatment, or reasoning to exclude other possible causes. The contents of these case reports were inadequate, even under the plaintiffs' expert's standards, to demonstrate a relationship between a drug and a potential side effect.

[2] Some case reports do contain details of the treatment and differential diagnosis. Even these more detailed case reports, however, are not reliable enough, by themselves, to demonstrate the causal link the plaintiffs assert that they do because they report symptoms observed in a single patient in an uncontrolled context. They may rule out other potential causes of the effect, but they do not rule out the possibility that the effect manifested in the reported patient's case is simply idiosyncratic or the result of unknown confounding factors. As such, while they may support other proof of causation, case reports alone ordinarily cannot prove causation. *See, e.g., Haggerty v. Upjohn Co.*, 950 F.Supp. 1160, 1165 (S.D.Fla.1996) (stating that "while case reports may provide anecdotal support, they are no substitute for a scientifically designed and conducted inquiry." (citation omitted)), *aff'd without op.*, 158 F.3d 588 (11th Cir.1998). The record demonstrates that the district court carefully considered the case reports and properly concluded that the case reports did not by themselves provide reliable proof of causation.

C. Dechallenge/rechallenge Data

[3] Plaintiffs' experts provided dechallenge/rechallenge data that they argue suggests a link between Parlodel and stroke. A test is a "dechallenge" test when a drug that is suspected of causing a certain reaction is withheld to see if the reaction dissipates. The drug may then be reintroduced in a "rechallenge" to see if the reaction reoccurs. These reports, which may be analogized to controlled studies with one subject, can be particularly useful in determining whether a causal relationship exists. Nonetheless, because none of the studies involved a patient with the particular injury suffered by the plaintiffs, they do not provide data useful in determining whether Parlodel caused the plaintiffs' injuries.

On appeal, plaintiffs presented two dechallenge/rechallenge reports that they assert are particularly convincing evidence of causation. In one, a woman developed severe headaches and hallucinations while taking bromocriptine. All symptoms disappeared when the drug was withheld.

When bromocriptine was readministered, she complained of chest pain and tests revealed total occlusion of a coronary artery. One month later, she was given the drug again and tests revealed a seventy percent arterial constriction. This report indicates at best a relationship between Parlodel and localized arterial spasm. Plaintiffs have presented insufficient evidence on which the district court could have concluded that this report is evidence that Parlodel causes systemic vasoconstriction, high blood pressure, or hemorrhagic stroke.

The other report presented by the plaintiffs involves a woman who reported partial paralysis in her left arm and left leg after taking her first dose of Parlodel. Her symptoms disappeared shortly thereafter, and she did not take Parlodel again until her physician was present. Upon taking the drug again, she experienced essentially the same symptoms. Plaintiffs imply that this report is relevant because the woman's symptoms were a result of stroke. A careful review of this report, however, reveals that it does not provide any evidence that the patient suffered a stroke, let alone evidence that Parlodel caused a stroke. Both neurologists who examined the patient questioned whether her symptoms were real and reported that the most likely cause of her symptoms was psychosomatic. One neurologist opined that if the symptoms were real, it was possible that her symptoms were a result of *hypo* tension, or decreased blood pressure. Because the plaintiffs' causation argument relies on a conclusion that Parlodel causes high blood pressure, this report does not provide reliable evidence in support of their theory.

Thus, these dechallenge/rechallenge reports suggest at most a possibility that Parlodel may cause localized vasoconstriction, and may suggest that it causes hypotension. They cannot be considered reliable evidence of a relationship between Parlodel and stroke because neither of them involve stroke. Moreover, dechallenge/rechallenge tests are still case reports and do not purport to offer definitive conclusions as to causation.

Plaintiffs argue that the district court completely ignored the dechallenge/rechallenge reports before it. This overstates the case. The district court discussed several of the case reports by way of example, and concluded that they were unreliable as evidence that Parlodel causes hemorrhagic stroke. The case reports that discussed dechallenge and rechallenge evidence were not sufficiently related to the case at hand to merit further discussion. Of the seven such reports emphasized by the plaintiffs, three did not arise postpartum—a significant fact since risk of stroke is greatly increased in the postpartum period. Of the four arising postpartum, three did not discuss dechallenge/rechallenge evidence related to stroke or seizure, but only as to other suspected effects of Parlodel—hypertension, coronary (not cerebral) vasospasm and occlusion, hallucinations, and headache. This Court's discussion of the dechallenge/rechallenge reports relied upon by the plaintiffs demonstrates that the district court did not abuse its discretion in holding that they are not reliable evidence of a link between Parlodel and hemorrhagic stroke.

D. Chemical Analogies

Bromocriptine is one of many drugs in a class known as ergot alkaloids. Plaintiffs sought to introduce evidence that because other ergot alkaloids cause vasoconstriction, then it is proper to conclude bromocriptine must do so as well. There is an insufficient basis in the record for this Court to hold that the district court abused its discretion by not drawing such a con-

clusion. Ergot alkaloids encompass a broad class of drugs with great chemical diversity, and "[e]ven minor deviations in chemical structure can radically change a particular substance's properties and propensities." *Glastetter,* 252 F.3d at 990 (citation omitted). The district court, after a detailed review of the properties of ergot alkaloids, concluded that plaintiffs failed to come forward with even a theory as to why the mechanism that causes some ergot alkaloids to act as vasoconstrictors would more probably than not be the same mechanism by which bromocriptine acts to cause vasoconstriction. The district court did not abuse its discretion in doing so.

E. Animal Studies

Plaintiffs offered evidence of animal studies in which bromocriptine demonstrated vasoconstrictive properties in dogs and certain other animals. Plaintiffs did not offer any animal studies that suggest that bromocriptine causes stroke, or even high blood pressure. The district court discussed each of these studies and was within its discretion in concluding that plaintiffs offered insufficient evidence on which that court could base a conclusion that the effect of bromocriptine would be the same on humans as it is on animals.

F. FDA Findings

Plaintiffs presented evidence that the FDA issued a statement withdrawing approval of Parlodel's indication for the prevention of lactation. The district court concluded that the language in the FDA statement itself undermined its reliability as proof of causation. In the statement, the FDA did not purport to have drawn a conclusion about causation. Instead, the statement merely states that possible risks outweigh the limited benefits of the drug. This risk-utility analysis involves a much lower standard than that which is demanded by a court of law. A regulatory agency such as the FDA may choose to err on the side of caution. Courts, however, are required by the *Daubert* trilogy to engage in objective review of evidence to determine whether it has sufficient scientific basis to be considered reliable. The district court did not abuse its discretion in concluding that the FDA actions do not, in this case, provide scientific proof of causation.

V. Applying the Evidence to the Plaintiffs' Theory of Causation

[4] The deficiencies in the evidence reveal three gaps in the causal argument advanced by the plaintiffs. First, plaintiffs suggest that because bromocriptine is an ergot alkaloid, it causes vasoconstriction. Although some other ergot alkaloids do cause vasoconstriction, plaintiffs offered insufficient evidence for the district court to find that bromocriptine does so as well. This is not a case where the Court finds the evidence offered to be unreliable. In this case the record contains no evidence at all of this hypothesis. Instead, it contains principally speculation and conjecture.

Because the ergot alkaloid class of drugs has a wide range of effects, it is not obvious that bromocriptine should have the same effects as other drugs in that class. Indeed, two widely-reported symptoms associated with bromocriptine are vasodilation and hypotension, precisely the opposite of what the plaintiffs allege. Plaintiffs did offer a theory as to why the drug might cause either vasodilation or vasoconstriction, depending on the vascular characteristics of the patient, a theory that the defendants concede the district court did not correctly explain in its opinion. This minor error does not affect the correctness of the district court's conclusion however, because the plaintiffs did not offer suffi-

ciently reliable evidence to support their theory.

Second, the plaintiffs urge the Court to extrapolate the results of animal studies to humans. As with the plaintiffs' evidence of chemical properties, the district court did not err in finding no basis for doing so. Plaintiffs' experts admitted that with respect to animal studies generally, what happens in an animal would not necessarily happen in a human being. Accordingly, it is necessary for plaintiffs to offer some rationale for the suggestion that the vascular structures of humans and animals are sufficiently similar in this context to conclude that bromocriptine's effects on animals may be extrapolated to humans. Plaintiffs have not done so.

As the Supreme Court held in *Joiner,* scientific evidence must "fit" the plaintiff's theory of causation. In this case, neither the chemical compound evidence nor the animal study evidence "fits" as evidence relevant to the cause of plaintiffs' injuries.

Third, plaintiffs argue that because there is some evidence that bromocriptine causes ischemic stroke, it also causes hemorrhagic stroke. This is the most untenable link in the causal chain. Strokes are broadly classified into two categories: ischemic and hemorrhagic. Ischemic strokes occur as a result of lack of blood flow to the brain. Hemorrhagic strokes occur as a result of bleeding within the brain. Thus, although the two conditions share a name, they involve a wholly different biological mechanism. The evidence that suggests that Parlodel may cause ischemic stroke does not apply to situations involving hemorrhagic stroke. This is a "leap of faith" supported by little more than the fact that both conditions are commonly called strokes. Plaintiffs argue that as a result of the vasoconstriction caused by Parlodel, blood pressure may increase to the point that blood vessels in the brain rupture. Plaintiffs have offered no reliable evidence that Parlodel increases blood pressure to such dangerous levels. Even if they had, they failed to offer proof of how such an increase in blood pressure can precipitate a hemorrhagic stroke.

Since the shortcomings in the evidence render the theory unreliable, the district court did not abuse its discretion in excluding the plaintiffs' evidence of causation.

VI. Conclusion

In the absence of epidemiology, plaintiffs may still prove medical causation by other evidence. In the instant case, however, plaintiffs simply have not provided reliable evidence to support their conclusions. To admit the plaintiffs' evidence, the Court would have to make several scientifically unsupported "leaps of faith" in the causal chain. The *Daubert* rule requires more. Given time, information, and resources, courts may only admit the state of science as it is. Courts are cautioned not to admit speculation, conjecture, or inference that cannot be supported by sound scientific principles. "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).

Plaintiffs argue that the district court erred in requiring a checklist of types of evidence to prove causation. This argument misinterprets the district court's opinion. The district court, after finding that the plaintiffs' evidence was unreliable, noted that certain types of other evidence may have been considered reliable, including peer-reviewed epidemiological literature, a predictable chemical mechanism, general acceptance in learned treatises, or a very large number of case reports. In so doing, the district court was not compiling a list of required types of evidence.

Rather, it was highlighting the plaintiffs' failure to present evidence in any of several categories that would have been persuasive.

Plaintiffs also argue that the district court ignored important evidence. As a preliminary matter, this Court has considered the evidence the plaintiffs allege was ignored and has found nothing upon which to base a conclusion that Parlodel causes hemorrhagic stroke. The Court also notes that it has no reason to believe that the district court did not examine the entire record in this case. On the contrary, there is every indication that the district court correctly stated in its opinion that it had carefully "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." 131 F.Supp.2d at 1350. The district court held a three-day hearing in which two of the plaintiffs' experts were allowed to testify and were subjected to cross-examination. The district court's twenty-five page published opinion meticulously discusses the evidence and considers whether it was reliable, concluding after a thorough analysis that it was not.

The district court's conclusion is in conformity with numerous other decisions. Two circuit court opinions have addressed the issue of Parlodel and hemorrhagic stroke. *See Glastetter v. Novartis Pharm. Corp.,* 252 F.3d 986 (8th Cir.2001); *Hollander v. Sandoz Pharm. Corp.,* 289 F.3d 1193 (10th Cir.2002). Both courts, presented with facts and evidence nearly identical to what is presented here, affirmed the district courts' exclusion of the plaintiffs' scientific evidence as unreliable. There are at least four district court opinions involving Parlodel that, despite slight differences in facts or evidence, reach the same ultimate result. *See Caraker v. Sandoz Pharm. Corp.,* 188 F.Supp.2d 1026 (S.D.Ill.2001); *Douglas v. Sandoz Pharm. Corp.,* 2000 WL 33342286 (M.D.N.C.2000); *Brumbaugh v. Sandoz Pharm. Corp.,* 77 F.Supp.2d 1153 (D.Mont.1999). Two Parlodel cases in which the evidence of causation of injury was admitted involved injuries different from the hemorrhagic strokes alleged in the instant case. *Brasher v. Sandoz Pharm. Corp.,* 160 F.Supp.2d 1291 (N.D.Ala.2001) (admitting evidence that Parlodel caused *ischemic* stroke); *Globetti v. Sandoz Pharm. Corp.,* 111 F.Supp.2d 1174 (N.D.Ala.2000) (admitting evidence that Parlodel caused acute myocardial infarction).

We hold that the district court did not abuse its discretion in concluding that the Plaintiffs' scientific proof of causation is legally unreliable and inadmissible under the standards set by the *Daubert* trilogy.

AFFIRMED.

AMERICAN TOWER LP, a Delaware limited partnership, Tritel Communications Inc., a Delaware corporation, et al., Plaintiffs–Appellees,

v.

CITY OF HUNTSVILLE, David Williams, individually and in his capacity as a Member of the Board of Zoning Adjustment of the City of Huntsville, et al., Plaintiffs–Appellants,