A Prescription for Injustice

Litigation Leading Science

By Whitt Steineker and Riley Griffin

Unreliable speculation cannot provide a foundation for truth. To ascertain truth, courts must fulfill their obligations to act as gatekeepers, but defense attorneys must help them.

Parties and courts in complex product liability cases often wrestle with whether the current state of science with respect to the particular product at issue in the case permits the judicial process to perform its essential role of yielding a reliable result based in fact. The justice system is grounded in a search for truth, curating the scientific evidence that the litigants are allowed to present to juries, filtering out the unsubstantiated "junk science," and ensuring that experts opining on essential questions of causation rely on reliable scientific principles, methods, and results. Otherwise, jurors—who are almost never trained scientists—are put in the position of making scientific determinations without the benefit of knowing which evidence is supported by reliable science.

More than 20 years ago, Seventh Circuit Judge Richard Posner wrote that "[t]he 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). Other courts around the country have followed Judge Posner's lead. *Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 671 (6th Cir. 2010); *In re Mirena IUD Prods. Liab. Litig.*, 169 F. Supp. 3d 396, 430 (S.D.N.Y. 2016); *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1177–78 (E.D. Wash. 2009); *Grp. Health Plan, Inc. v. Philip Morris, Inc.*, 188 F. Supp. 2d 1122, 1131 (D. Minn. 2002). Unfortunately, however, not all courts heed this admonition; instead, some courts allow trials to move forward and juries to render verdicts based on unsubstantiated conjecture.

This article examines what happens when law leads science, illustrating the pitfalls by analyzing two multidistrict litigations—the ones involving Chantix and silicone breast implants—and then it identifies techniques for avoiding those pitfalls. And although the two illustrations below were large, multidistrict litigations, the same challenges from law leading science (and the same techniques for counter-

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ing those challenges) apply with equal force to a single-plaintiff case in which the product or issue is the subject of actively evolving scientific research and questions, the answer to which could bear on the ultimate issues in the case.

No Smoking Gun: The Chantix Litigation

In 2006, Chantix was approved by the U.S. Food and Drug Administration (FDA) and entered the market as the first new smoking-cessation medication in years, with a novel mechanism of action, which separated it from other smoking-cessation therapies. The initial reaction to the product from the scientific community was positive, and the product proved successful in the marketplace. In September 2007, however, musician Carter Albrecht was shot and killed by a neighbor who mistook Mr. Albrecht for an intruder. At the time of the incident, Mr. Albrecht was reported to be extremely intoxicated and in a dispute with his girlfriend, during which his behavior was reported to be out of the ordinary. Mr. Albrecht's girlfriend blamed Chantix for his behavior and resulting death because she believed that Albrecht's use of Chantix caused him to experience the neuropsychiatric symptoms that ultimately, if indirectly, led to his death. The incident drew widespread media attention, leading to a surge of anecdotal reports of patients experiencing neuropsychiatric events while taking Chantix.

Amid this spike in anecdotal reporting, the FDA instructed Pfizer to include warnings about possible neuropsychiatric effects in the Chantix label. In July 2009, the FDA ordered Pfizer to add a Boxed Warning—the strongest type of prescription drug warning, which is prominently displayed within a black box near the top of the label and often referred to as a "black box warning"—to the Chantix label. The Boxed Warning advised that patients being treated with Chantix should be monitored for neuropsychiatric symptoms "including changes in behavior, hostility, agitation, depressed mood, and suicide-related events, including ideation, behavior, and attempted suicide." Pfizer Labs, Chantix Label (rev. Nov. 2011), https://www.fda.gov/. The label noted, however, that scientists had not "establish[ed] a causal relationship to drug exposure." *Id.* The FDA also asked Pfizer to conduct a clinical trial—known as the EAGLES study—to analyze whether Chantix actually caused neuropsychiatric events in patients.

Unsurprisingly, several lawsuits followed the national coverage of the Albrecht incident and the addition of the Boxed Warning. In 2009, a multidistrict litigation (MDL) was established in the Northern District of Alabama. *See In re Chantix (Varenicline) Prods. Liab. Litig.*, 655 F. Supp. 2d 1346, 1347–48 (J.P.M.L. 2009). The claims and allegations in the *In re: Chantix* litigation involved the adequacy of the warnings in the label and the timing of label changes.

About three years into the litigation, the MDL court granted summary judgment for Pfizer on all failure-to-warn claims based on neuropsychiatric injury arising after the July 2009 label change that added the Boxed Warning, finding that the Boxed Warning was adequate as a matter of law. *See In re Chantix (Varenicline) Prods. Liab. Litig.*, 881 F. Supp. 2d 1333, 1343 (N.D. Ala. 2012). The court's order left some combination of negligence, strict liability, breach of warranty, fraudulent misrepresentation, and state consumer fraud claims for the remaining plaintiffs to pursue.

The first bellwether case involved a 67-year-old man who was prescribed Chantix on November 21, 2007, and committed suicide on November 29, 2007. The plaintiff argued that Chantix caused the decedent to commit suicide. The then-existing science on the question of general causation did not fully support the plaintiff's claims. For example, the plaintiff designated as an expert, among many others, Dr. Joseph Glenmullen, a psychiatrist who opined that (1) Chantix can cause neuropsychiatric injuries, and (2) "Chantix was a substantial contributing factor in causing" the decedent's death. Mem. Op. and Order at 51–52, *In Re: Chantix (Varenicline) Prods. Liab. Litig.*, No: 2:10-cv-1463-IPJ (N.D. Ala. Sept. 18, 2010). Dr. Glenmullen based his opinion regarding the decedent on a differential diagnosis and asserted that the decedent was part of a "small vulnerable subpopulation of patients" susceptible to "Chantix psychiatric side effects." *Id.* Dr. Glenmullen, however, could not define, describe, or characterize this "subpopulation" in any way, and there was no scientific literature that identified any "subpopulation" or described any "vulnerability" in any type of patient who might use Chantix. *Id.* Pfizer argued that Dr. Glenmullen failed to articulate or to apply any scientific methodology and that there was no concrete science that supported Dr. Glenmullen's opinion that Chantix caused the decedent to commit suicide. *Id.* at 52, 54.

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In large part because of the gaps in the existing scientific literature and shortcomings such as those in Dr. Glenmullen's (and other experts') opinions, Pfizer asked the court to stay the proceedings until pending clinical trials were completed to determine the science relevant to the plaintiff's allegations. In particular, Pfizer wanted the opportunity to present to the jury the outcome of clinical trials bearing on the issue of general causation—*i.e.*, whether Chantix actually can cause serious neuropsychiatric events, including suicide and depression, as alleged in the lawsuits. On the eve of the first bellwether trial, Pfizer informed the court that one such clinical trial—which Pfizer had been instructed to conduct by the European Medicines Agency—was being published that day and asked the court to continue the trial while the parties and their experts had an opportunity to examine the results of the clinical trial. Def.'s Mot. for Contin. and/or Stay, *In Re: Chantix (Varenicline) Prods. Liab. Litig.*, No:2:10-cv-1463-IPJ (N.D. Ala. Oct. 16, 2012).

Despite the fact that this clinical trial and others already in the pipeline could have helped establish or rule out general causation, and confirm or refute precisely the type of expert opinion offered by Dr. Glenmullen and others, the court ruled that the litigation would go forward as scheduled. Order Den, Def.'s Mot. to Continue, *In Re: Chantix (Varenicline) Prods. Liab. Litig.*, No: 2:10-cv-1463-IPJ (N.D. Ala. Oct. 16, 2012). The court reasoned that (1) Pfizer did not give the court any idea what the results of the study were, (2) Pfizer alone controlled the release date of the study results in question, (3) Pfizer waited to release the results until the proverbial "eve of trial," (4) Pfizer had requested a continuance right before trial when the trial had been set for over a year and Pfizer had known about the study, and (5) the court would be greatly inconvenienced. *Id.* Shortly after the court's ruling on this issue, the first bellwether trial settled, other cases followed suit, and the MDL was terminated in 2014.

The Chantix neuropsychiatric MDL exemplifies how patience would have been helpful and informative, and it serves as an example to cite in future courts when the litigation appears to be leading the science.

In late 2016, the results of the EAGLES study were made public. EAGLES was the largest clinical trial of approved smoking-cessation medicines—including 8,144 adult smokers—and was designed to compare the neuropsychiatric safety of Chantix with placebo and nicotine patch. Press Release, Pfizer, Chantix/Champix (Varenicline) Results from the Largest Global Clinical Trial of Smoking Cessation Medicines Published in The Lancet (Apr. 22, 2016), available at http://www.pfizer.com. No statistically significant increase in the incidence of serious neuropsychiatric adverse events was found with Chantix compared to placebo and nicotine patch. *Id.* Patients taking Chantix had significantly higher continuous abstinence rates than patients treated with other smoking-cessation therapies. *Id.*

Shortly after the publication of the EAGLES study, the FDA determined that the risk of serious side effects due to Chantix use on mood, behavior, or thinking was "lower than previously suspected" and removed the Boxed Warning for serious mental health side effects from the Chantix drug label. FDA Drug Safety Communication: FDA Revises Description of Mental Health Side Effects of the Stop-Smoking Medicines Chantix (Varenicline) and Zyban (Bupropion) to Reflect Clinical Trial Findings, U.S. Food & Drug Admin. (Dec. 16, 2016), available at https://www.fda.gov.

The results of the EAGLES study, and the FDA action that followed, cast doubt on the merit of all of the plaintiffs' claims in the Chantix MDL. Had the Chantix MDL court not allowed the litigation to get ahead of the science, Chantix cases that were settled in 2013 and 2014 likely would have been disposed of in a far different manner based on the scientific evidence that general causation could not be established, and plaintiffs' experts in the MDL would have had to overcome an observational study of more than 8,000 participants that contradicted their theories. The litigation cost untold millions of dollars to all parties, and it had real-world implications. To start, "the public perception of Chantix was adversely affected, and it is likely that use of a highly effective smoking cessation medication declined as a result." Michelle Yeary, *Chantix: A Lesson in Why Litigation Should Not Be Allowed to Get Ahead of Science*, Drug & Device L. Blog (Sept. 8, 2016), available at https://www.druganddevicelawblog.com.

Ultimately, the Chantix neuropsychiatric MDL exemplifies how patience would have been helpful and informative, and it serves as an example to cite in future courts when the litigation appears to be leading the science.

Breast Implant Litigation: A Precursor

Multidistrict litigation nearly two decades earlier in the same federal district court offers another example—with even more significant consequences—of the pitfalls of litigation leading science. In the 1980s and 1990s, thousands of women across the country filed lawsuits after anecdotal reports suggested a link between silicone breast implants and certain autoimmune diseases. When the lawsuits were filed, there was a lack of research on the alleged link, and plaintiffs' experts had various theories for general causation. The media played an important role in disseminating information—often inaccurate information—about implants, and the stories were often sensationalized and hyper-focused on unproven medical risks. Peter J. Goss *et al.*, *Clearing Away the Junk: Court-Appointed Experts, Scientifically Marginal Evidence, and the Silicone Gel Breast Implant Litigation*, 56 Food & Drug L.J. 227, 235 (2001). The lack of conclusive clinical data allowed the press, citizen advocacy groups, and the public to assume the worst. *Id.*

While studies to determine any link between silicone breast implants and autoimmune disease were ongoing, cases went to trial, and plaintiffs received large jury awards. One of the manufacturers, Dow Corning, ultimately filed for bankruptcy, citing the burden of its breast implant litigation, after agreeing to pay more than $3 billion to settle claims. Gina Kolata, *Panel Confirms No Major Illness Tied to Implants*, N.Y. Times, June 21, 1999), available at http://www.nytimes.com. Other breast implant manufacturers agreed to pay nearly $4 billion more. *Id.*

While the manufacturers were settling and paying billions of dollars, the controlled studies were completed and provided clear evidence that the product did not, in fact, cause injuries. The MDL court had also appointed a National Science Panel, as Fed. R. Evid. 706 permits, to review the science independently, and Congress directed the Institute of Medicine to investigate whether silicone breast implants caused major diseases. When the results were in, the scientific community concluded that there was no scientific basis for the plaintiffs' autoimmune claims. It is difficult to fathom how many billions of dollars were spent on claims that may not

have been paid at all if the courts hearing breast implant cases had allowed the science to catch up before permitting juries to award crippling verdicts based on ultimately debunked conjecture.

Strategies for Avoiding the Pitfalls

In practice, attorneys can attempt to avoid the pitfalls of litigation leading science using a variety of techniques.

Anecdotal Reports Are Not Reliable Science

Often, as was the case in the Chantix and breast implant litigations, a wave of pharmaceutical and mass tort cases can result from a series of anecdotal reports. These reports deal with only one or a few patients or consumers, and they are not reliable evidence of causation. Yet they often capture the attention of news outlets and the plaintiffs' bar, leading to a rash of case filings.

Anecdotal reports and case studies show correlation, not causation. And because they lack controls, such reports universally are regarded as unreliable, insufficient evidence of causation. *See McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1250 (11th Cir. 2005) ("Uncontrolled anecdotal information offers one of the least reliable sources to justify opinions about both general and individual causation."). Anecdotal studies are "for raising questions and comparing clinicians' findings," but not for proving causation. *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1316 (11th Cir. 1999). In the face of "controlled, population-based epidemiological studies," anecdotal studies "pale in comparison." *Id.*

One individual's, or even one physician's, opinion of causation is guesswork without science or data to support it. *See Rosen*, 78 F.3d at 319. In the scientific arena, anecdotal reports, without other scientific data to back them up, are considered useful but untested hypotheses. *See Tamraz*, 620 F.3d at 677. In the courtroom, anecdotal reporting should generally be treated as inadmissible speculation. *Id.*

The unreliability of anecdotal reports should be brought to a court's attention as early as possible. Such reports do not meet the standard for causation, and this argument can be used as an early tool—for example, as part of a *Daubert* motion addressing reliability, as a summary judgment argument, or as a basis for a motion in limine—to keep unreliable evidence out of the courtroom and help thwart a wave of further litigation.

Understand the Current Scientific Landscape

To understand whether litigation is leading the science in a particular case, an attorney must fully understand the current state of the science and whether study-based scientific developments are anticipated soon or in the future. Products, and medications specifically, made the subject of mass tort litigation typically are the subject of a number of studies examining the products' efficacy and safety. Often the results of such a study could play a critical, even dispositive, role in litigation involving such a product or medication.

The nature of clinical trials and observational studies means that an attorney will know that the trial or study is underway months, if not years, in advance of the publication of the results. Attorneys should speak with their clients and experts in the field to understand the future landscape of scientific development fully.

Educate a Court Early

Armed with the knowledge about the current state of the science and anticipated upcoming developments, the next step is to educate a court early and often. As soon as an attorney learns about upcoming clinical trials or observational studies, he or she should consider notifying the court so that the parties and the court can begin to make scheduling decisions with that information in mind. As was the case in the Chantix MDL, plaintiffs are likely to want to hurry the process, so it is the defense attorney's job to make sure that a court understands why a study is important, how it may affect the litigation, and why the court should delay the litigation until the results of the study are known. It can be very difficult to convince a court to delay the process the closer you get to trial, so the earlier the better.

Part of educating a court is encouraging the court to take seriously its role as a gatekeeper to ensure that expert evidence is reliable. *See Daubert v. Merrell Dow Pharm.*, 509 U.S. 579, 597 (1993). *Daubert* instructs federal trial courts to serve as gatekeepers, ensuring that the subject of the expert testimony is scientific "knowledge" grounded "in the methods and procedures of science." *Id.* at 589–90. Results of an ongoing study involving a product at issue can be crucial to the reliability of an expert's opinion, particularly when the study either will confirm or refute the proffered expert opinions. When a study is underway that could answer a question at issue in a case, without the study results, expert testimony is insufficiently reliable. A court should recognize as gatekeeper that a study that would improve expert opinion reliability calls for a continuance of the case until that information is available.

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Articulate a Clear Timeline and Basis for Allowing the Science to Develop

An attorney must determine what exactly a study will prove or disprove and when a conclusion from the study will be published. Critical to the likelihood of convincing a court to delay the trial of a case is the ability to articulate clearly to the court (1) why the science is not yet where it needs to be to present to the jury reliable scientific evidence upon which the jury can render a fair and just verdict, and (2) why the ongoing clinical trial or trials will assist

the parties, their experts, and the court in bringing the science where it needs to be.

The most opportune time to seek a delay is when the science around a product is both unsettled and actively evolving. Some products have been studied and researched for decades in ways that leave few questions unanswered regarding the products' overall safety and efficacy. Others, however, as was the case with Chantix in the years immediately after it entered the market, have been studied enough to earn regulatory approval but not to answer questions of general causation in the variety of potential cases that a product manufacturer may encounter.

Courts can educate themselves and jurors by appointing independent experts to testify and consult on complex scientific matters.

An attorney should provide this information to a court with as much specificity as possible because this information will be crucial to convincing the court that the litigation should be placed on hold until a study is completed. The Chantix and breast implant litigation mentioned above can be used to explain why a court should wait for studies to be completed before plowing ahead with litigation.

Consider Asking for Court-appointed Expert

Courts can educate themselves and jurors by appointing independent experts to testify and consult on complex scientific matters. A judge's power to appoint experts derives from both Fed. R. Evid. 706 and the court's inherent authority under Fed. R. Evid. 104 to address "[p]reliminary questions concerning… the admissibility of evidence." Under Rule 104, an expert reports to the court but does not testify or otherwise interact with the jury. Under Rule 706, a court-appointed expert typically testifies to the jury and is subject to cross-examination.

Any party may ask the court to appoint an independent expert under Rule 706, and the decision whether to do it is left to the discretion of the trial court. Seeking the appointment of an independent expert may be useful when plaintiffs disclose a particularly effective expert or one known for being a professional plaintiffs' expert. If a court decides to appoint an independent expert under Rule 706, counsel can be involved in the expert-selection process by suggesting experts to be considered. The court, however, ultimately controls the expert-selection process. *See Daubert*, 509 U.S. at 595.

Whether through Rule 104 or Rule 706, parties should consider taking advantage of the court's power to appoint experts as technical advisors, testifying witnesses, and members of consulting panels, particularly when faced with plaintiffs' experts armed with little more than anecdotal reports, unsubstantiated conjecture, and "junk science."

Likely Challenges and Possible Responses

Plaintiffs' attorneys and plaintiffs generally will make certain arguments to thwart defense attorneys' requests to delay litigation until clinical trials conclude, to let the science catch up to the litigation.

Plaintiffs Drive Innovation and Keep Public Safe

A common argument by plaintiffs and plaintiffs' attorneys is that it is their role to drive innovation and to keep the public safe from big businesses that value profits over customer safety. They often view the FDA as, at best, turning a blind eye to industry misconduct and often being in the pockets of pharmaceutical companies. They view themselves as the guardians of consumer safety. The Chantix MDL court seemed to adopt this view, stating that "[s]ometimes litigation has forced science to keep up." Order Den. Def.'s Mot. to Continue 2, n.1, *In Re: Chantix (Varenicline) Prods. Liab. Litig.*, No: 2:10-cv-1463-IPJ (N.D. Ala. Oct. 16, 2012).

Plaintiffs' attorneys will say that if they do not keep companies accountable for their products, the companies will never do the work to make safer products. They will argue that delaying litigation until the conclusion of clinical trials is just a tactic to allow pharmaceutical companies to continue making and selling dangerous products, while consumers are injured and plaintiffs are denied their day in court. The response to such arguments is that the courtroom is a place for truth and valid science, not conjecture and speculation. Courtrooms are not laboratories, and judges, attorneys, and juries are not scientists. They cannot make the necessary scientific determinations that are required in complex litigation without the scientific data from studies. Since judges and juries generally lack scientific training, they often are incapable of distinguishing between sound science and pseudo-science. Coordinating a trial schedule to incorporate the conclusion of relevant clinical trials and studies will increase the likelihood that jury verdicts will be based on truth rather than speculation and emotion.

Specific Causation Is Sufficient

Plaintiffs' attorneys may argue that specific causation is sufficient, absent scientific data that a product generally causes harm. Plaintiffs' attorneys often would like to use the testimony of a doctor and his or her diagnosis as their only evidence of causation. But the law is clear that a plaintiff must prove both general causation and specific causation. A plaintiff must prove that a product can produce a particular disorder or disease, and then that the product did, in fact, produce that disorder or disease in him or her. A doctor's opinion is not reliable if science does not support a finding of general causation.

A diagnosis by a doctor is not a sufficient causal finding by itself. *See Tamraz*, 620 F.3d at 674; *Gass v. Marriott Hotel Servs., Inc.*, 501 F. Supp. 2d 1011, 1019 (W.D. Mich. 2007), *rev'd on other grounds*, 558 F.3d 419 (6th Cir. 2009); *Glaser v. Thompson Med. Co.*, 32 F.3d 969, 977 (6th Cir. 1994).

To satisfy *Daubert*, the following questions must be answered in the affirmative: "(1) Did the expert make an accurate diagnosis of the nature of the disease? (2) Did the expert reliably rule in the possible causes of it? (3) Did the expert reliably rule out the rejected causes?" *Tamraz*, 620 F.3d at 674. These questions cannot be answered

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satisfactorily unless there is science showing the general causation data on which the expert relied.

Unfair Delay for Plaintiffs

Plaintiffs' attorneys will argue that postponing a trial to allow clinical trials to be concluded constitutes unfair delay. There is, however, no virtue in pressing forward in litigation if there is not sufficient science to support causation. Even though the litigation would move faster and a plaintiff would have a resolution earlier, that resolution would be based on evidence that could be proved wrong once a study has completed. The breast implant litigation and the bankruptcy of Dow Corning provide stark examples of precisely how this can play out.

To be sure, in certain types of cases, litigation should not be delayed due to a plaintiff's right to have his or her day in court. In a consumer fraud case, for example, the central question is whether the consumer was misled, and there may be no future event that could affect the answer to that question. Product cases, and pharmaceutical cases in particular, are different because very often a future event (such as the publication of the results of a clinical trial) bears directly on the central questions of a case—namely, whether a product was defective and unreasonably dangerous, and whether the warnings associated with the product were adequate.

Conclusion

As mentioned at the beginning of this article, the justice system is grounded in a search for truth. Allowing the science to lead litigation is the only sensible approach to ascertaining truth in complex products cases. Any other approach necessarily relies on inherently unreliable principles and methods that are antithetical to the scientific method and the search for truth. As the Supreme Court made clear in *Daubert*, the goal of "reaching a quick, final, and binding legal judgment" on matters that are "often of great consequence" is not advanced by accepting hypotheses and conjectures in the place of reliable scientific evidence. Defense counsel must be attuned to these issues and work early in the litigation to make sure that the science leads litigation, not the other way around. FD