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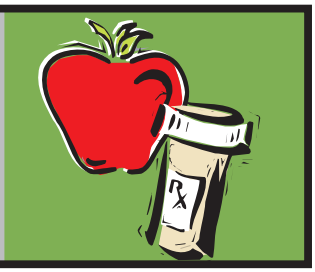
Food and Drug Law A Practice Focus

Dodging *Daubert*

Suits against drug-makers are using bad science to invent causation.



BY JOE G. HOLLINGSWORTH
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"Jurors who voted against Merck said much of the science sailed right over their heads. 'Whenever Merck was up there, it was like wah, wah, wah,' said juror John Ostrom, imitating the sounds Charlie Brown's teacher makes in the television cartoon. 'We didn't know what the heck they were talking about.' "
—*The Wall Street Journal, Aug. 22*

"Expert evidence can be both powerful and quite misleading because of the difficulty evaluating it."
—*Daubert v. Merrell Dow Pharmaceuticals Inc. (1993)*

In the flurry of news reports after the recent $253 million Vioxx verdict, one unfortunately familiar and telling fact stood out: The jurors didn't understand the scientific evidence allegedly linking the drug to the patient's death from an irregular heartbeat.

Had they understood the science, the jurors would have recognized that there are no data demonstrating that Vioxx as it was used by the patient is associated with an irregular heartbeat or, indeed, any cardiac problems.

The Vioxx verdict dramatically highlights a continuing problem in drug and medical-device litigation: A skilled attorney with a sympathetic plaintiff and a convincing expert can hit a huge jackpot in a single case, even if the allegation of causation is based on nothing more than smoke and mirrors.

In its seminal opinion in *Daubert v. Merrell Dow Pharmaceuticals Inc.* (1993), the U.S. Supreme Court sought to protect against this type of runaway-jury confusion by instructing trial judges to serve as gatekeepers against the admission of expert testimony based on irrelevant or unreliable scientific evidence.

Unfortunately, while many trial courts have properly followed *Daubert*'s direction, a number of judges have been as easily misled by expert testimony as the jurors they have been charged with protecting. In these courts the game for plaintiffs counsel and their experts has remained the same: Find a way to package speculative expert testimony to create the illusion of sound scientific evidence for the court, and then rely on sympathy and juror mistrust of pharmaceutical companies to win the prize.

IF IT DOESN'T FIT . . .

The recent Vioxx verdict in *Ernst v. Merck & Co.* in a Texas state court presents a classic example of how plaintiffs counsel can offer scientific evidence that doesn't really fit the facts.

In 2004, notwithstanding years of safe use and successful clinical trials with more than 3,000 patients, Merck voluntarily withdrew Vioxx from the market. The withdrawal was based on a single trial suggesting that patients who used the drug for more than 18 months had an increased incidence of blood clots leading to heart attacks. Using this study, the plaintiff in *Ernst* (the widow of the deceased) claimed that Vioxx had caused a sudden cardiac death.

Yet *Ernst* involved a man who had taken Vioxx for only eight months—less than half the 18 months noted in the study. According to the autopsy, the patient had a sudden cardiac death caused by an irregular heartbeat (or arrhythmia), not a heart attack caused by a blood clot. No scientific evidence exists that eight months of Vioxx use can cause death from cardiac arrhythmia.

Significantly, the patient's autopsy found no evidence of a blood clot. Yet it did find evidence of atherosclerosis (hardened arteries and plaque) that had developed over a period of years. Atherosclerosis is independently associated with numerous cardiac problems, including sudden cardiac death, and there was no scientific basis to exclude this as the sole cause of the patient's death.

In short, the case is a classic "no fit" under *Daubert*.

Plaintiffs counsel Mark Lanier used two arguments to sidestep the gaping scientific hole in his case. First, he papered over the crucial distinction between heart attacks caused by blood clots and sudden cardiac death caused by irregular heartbeats, referring to the patient's injury as "a cardiovascular event." Second, he solicited speculative testimony that the patient might in fact have had a heart attack caused by a blood clot that didn't appear in the autopsy.

These arguments clearly do not satisfy a plaintiff's burden under *Daubert*. As the Supreme Court explained in *General Electric Co. v. Joiner* (1997), "nothing in either *Daubert* or the Federal Rules of

Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert."

The plaintiff's case in *Ernst* was based on a series of speculative leaps, each of which independently should have been excluded under *Daubert*.

First, the plaintiff relied on scientific research associating Vioxx with blood clots, not irregular heartbeats. Courts correctly versed in *Daubert* recognize that study results concerning other types of injuries cannot provide reliable evidence of causation.

Second, the plaintiff failed to establish that the patient had been exposed to Vioxx for a sufficient length of time to support a causal link even with a heart attack. As the Texas Supreme Court held in *Merrell Dow Pharmaceuticals Inc. v. Havner* (1997), a plaintiff cannot satisfy his burden of proffering reliable scientific evidence unless he shows that "his exposure or dose levels were comparable to or greater than those in the studies" upon which he relies.

Third, the plaintiff could not provide any reliable basis for ignoring the evidence that the patient's death was ultimately caused by long-standing atherosclerotic disease, not Vioxx. There was no testable evidence supporting the speculative arguments about a phantom blood clot that caused a heart attack.

The scientific evidence regarding Vioxx clearly did not fit the plaintiff's causation allegations, and the case should never have reached a jury.

Lies, Damn Lies, And Statistics

Similar problems with scientific evidence in lawsuits have arisen with phenylpropanolamine (PPA) products, which include over-the-counter cough and cold medicines used billions of times a year in the United States alone.

In 2003 a federal district judge in a multidistrict litigation proceeding in the Western District of Washington relied on the findings in a single study to admit expert testimony in all federal court cases. This judge permitted testimony that these products can cause both hemorrhagic stroke (when a ruptured blood vessel spills blood into or around the brain) and ischemic stroke (when the brain's blood supply is blocked).

In fact, the single study found a statistically significant association only with hemorrhagic stroke in a single subgroup of patients taking diet drugs that contained PPA. That finding was based on only six cases and a single control.

The study did not find an overall statistically significant association with hemorrhagic stroke. It did not find a statistically significant association between cough or cold remedies (which used a lower dose of PPA than did diet drugs) and hemorrhagic stroke. It did not present any evidence of a link between PPA products and ischemic stroke.

The suggestion of an increased risk of hemorrhagic stroke was also contrary to an earlier published epidemiologic study that found no association and, in fact, reported fewer hemorrhagic strokes in patients who had taken PPA products.

While epidemiological studies generally may be considered the strongest evidence of causation, the existence of an isolated statistically significant result in an epidemiological study does not satisfy *Daubert*. Unfortunately, the District Court accepted mere statistical association as scientific evidence of a causal link.

In so doing, the court disregarded the potential roles of chance, recall bias, and alternative causes as an explanation for the study results. Courts properly educated in *Daubert* have cautioned against relying on statistically significant subgroup analyses, because subgroup analyses too often result in spurious statistical associations through chance alone. Likewise, courts have excluded expert causation testimony based on statistically significant findings where the study failed to address other confounding factors that could have accounted for the apparent association.

Fortunately, the defendants in these PPA suits have succeeded in explaining the scientific evidence at trial. Thus far, they have suffered only a single, small jury verdict in the nine cases that have gone to verdict. Under *Daubert,* however, the PPA litigation should have been stopped at the starting line.

Bedside Manner Is Not Enough

In 2004 a plaintiff in Delaware state court alleged in *Long v. Weider Nutrition Group Inc*. that a dietary supplement containing ephedrine had caused a sudden cardiac death.

The plaintiff (again the decedent's wife) conceded that there was no controlled scientific study showing a link between ephedrine and sudden cardiac death. Nonetheless, the plaintiff argued—and the court agreed, despite Delaware's adoption of *Daubert*—that his experts' causation opinion should be admitted, in large part because the opinion was supported by the experts' differential diagnoses.

A differential diagnosis is a method doctors use to determine which of a list of potential diagnoses best fits a patient's symptoms. In toxic tort litigation, plaintiffs have misused this term to describe a different analysis—more aptly named differential etiology—whereby their experts determine which of a list of potential causes best explains the plaintiff's illness.

Regardless of the name, a differential analysis doesn't reflect any new or improved scientific foundation for the experts' opinions. In opining that a drug or medical device is "more likely than not" the cause of a plaintiff's condition, every causation expert—both pre- and post-*Daubert*—has simply reached a personal opinion that other causes have been excluded.

As properly informed courts have explained, a differential analysis may be a reliable method to rule out established potential causes of a plaintiff's illness (specific causation), but it cannot provide scientific evidence to rule in a drug or medical device as a potential cause of the illness in the first instance (general causation).

Plaintiffs counsel will argue, with some misguided support in case law, that differential diagnosis can support a general causation opinion under *Daubert* because it "is a technique that has widespread acceptance in the medical community, has been subject to peer review, and does not frequently lead to incorrect results" (to quote *Westberry v. Gislaved Gummi AB* (4th Cir. 1999)).

This statement is misleading, at best. A differential diagnosis is nothing more than a case report, with the plaintiff serving as the anecdotal case at issue. While case reports help in making potential causal hypotheses, courts have consistently held they cannot provide the reliable proof of a causal link that *Daubert* demands.

Moreover, the claim that a differential diagnosis does not often lead to an incorrect result is demonstrably false. European regulators in particular have tried in vain to come up with reliable differential diagnosis-like algorithms by which to judge individual case reports as evidence of general causation. Differential diagnosis just does not provide a reliable basis for a general causation opinion. As with the *Ernst* Vioxx case and the PPA stroke cases, the *Long* ephedrine claim should never have been submitted to a jury.

Despite the protections set forth in *Daubert*, too many plaintiffs attorneys in drug and medical-device litigation are still able to masquerade their experts' conjecture as sound scientific evidence. Courts that fail to satisfy their gatekeeping role under *Daubert* to exclude such testimony fail to protect jurors from being bamboozled by junk science, and they thus undermine the integrity of the judicial process.

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