BNA, INC.

EXPERT EVIDENCE REPORT

BNA Employee-Owned Since 1947

Reproduced with permission from Expert Evidence Report, Vol. 3, No. 16, 8/18/2003. Copyright © 2003 by The Bureau of National Affairs, Inc. (800-372-1033) http://www.bna.com

Courts in toxic tort cases have split on whether case reports are reliable proof of causation. Most courts, according to attorney Bruce J. Berger, have found that ''the mere existence of such case reports has been held insufficient to support causation opinions by a majority of the courts applying *Daubert* principles to determine scientific reliability.''

''Even case reports published in highly-respected journals . . . must be viewed critically and even with suspicion,'' the author counsels. Case reports are unreliable for a number of reasons, Berger says, and lawyers on both sides should ''look very closely at important case reports to make sure that those bordering on scientific misconduct are discarded.''

Case Reports Present Ample Potential for Scientific Fraud in Toxic Tort Cases

BY BRUCE J. BERGER

In the toxic tort context, case reports as a category of scientific evidence frequently receive the close attention of litigants, their experts, and the courts. Many decisions granting or affirming summary judgment to defendants hold that case reports—*i.e.*, published or unpublished reports, typically from a treating physicians about patients exposed to Factor F who later came down with Disease D—are of limited value in reaching decisions concerning general causation and, in fact, cannot support a scientifically reliable opinion that F can cause D. *See, e.g.*, *Castellow v. Chevron USA*, 97 F. Supp. 2d 780 (S.D. Tex. 2000) (excluding testimony that workplace exposure to benzene from gasoline caused plaintiff's acute myelogenous leukemia where his experts relied exclusively on case reports to support opinion that such exposures were sufficient); *Wehling v. Sandoz Pharms. Corp.*, 162 F.3d 1158 (Table), 1998 WL 546097 (4th Cir. 8/20/98) (unpublished opinion) (affirming exclusion of causation opinion based primarily on two anecdotal case reports).

Other decisions, however, continue to admit opinions that F can cause D based in part upon case reports. See, e.g., *Bonner v. ISP Technologies Inc.*, 259 F.3d 924, 931 (8th Cir. 2001) (upholding admission of evidence de-

Bruce J. Berger is a partner with the law firm of Spriggs & Hollingsworth in Washington, D.C. He is extensively involved in jury trial practice relating to defense of toxic tort claims stemming from environmental releases, and use of pharmaceuticals and pesticides. He can be reached at bberger@spriggs.com.

COPYRIGHT © 2003 BY THE BUREAU OF NATIONAL AFFAIRS, INC., WASHINGTON, D.C. 20037 ISSN 1536-1896

spite fact that plaintiffs' expert relied upon case reports because ''district court had considered this shortcoming'').[1]

The opinions that disparage case reports offer good reasons for doing so. For example, courts have properly held that case reports are of little or no value in the general causation arena because: (i) they cannot be used to derive relative risks—*i.e.*, cannot be used to show that the likelihood of contracting D after exposure to F is significantly different than the likelihood of contracting D after no exposure to F; [2] (ii) a satisfactory rate of error cannot be derived from case reports,[3] (iii) they do not adequately consider potential alternate causes;[4] (iv) they often fail to address the individual's prior medical history, risk factors, use of other medications or drugs, family medical history, and other individual factors necessary to assess a cause-and-effect relationship between the use of the drug and the reported adverse effect; [5] and (v) they are not verifiable through meaningful peer review.[6] Thus, whereas the *absence* of case reports when they might be expected may be a sufficient reason for a court to call into question the causation opinions of plaintiffs' experts,[7] the mere existence of such case reports has been held insufficient to support causation opinions by a majority of the courts applying *Daubert* principles to determine scientific reliability.

The mere existence of such case reports has been held insufficient to support causation opinions by a majority of the courts applying *Daubert* principles to determine scientific reliability.

The deficiencies of case reports as a basis for making causal decisions have been presented to the courts through a variety of means, including the admissions of plaintiffs' experts themselves at deposition and in *Daubert* hearings,[8] the testimony of plaintiffs' experts in earlier cases (typically, when they appeared on behalf of defendants),[9] and, of course, the *Daubert* hearing testimony and/or affidavits of defense experts that the court finds credible.[10] These deficiencies apply generally to all case reports, and litigants often leave it to the court to make its judgments concerning case reports on the basis of these general observations alone.

'Bogus Case Reports.' Experience in the Parlodel litigation has taught us, however, that case reports cannot even be taken at face value. That is, we have encountered published case reports that are so misleading one might justifiably wonder whether the authors truly had the advance of scientific knowledge at heart when they submitted them for publication. It thus behooves attorneys in toxic tort litigation to look very closely at important case reports to make sure that those bordering on scientific misconduct are discarded. Plaintiffs' attorneys obviously risk discrediting their entire case if they allow their experts to rely upon case reports that the defense is later able to demonstrate are bogus. Likewise, defense attorneys do their clients no favors by taking for granted the accuracy of case reports offered by plaintiffs' experts and failing to uncover instances of scientific misconduct.

[1] *Cf. Lauzon v. Senco Prods. Inc.*, 270 F.3d 681, 689 (8th Cir. 2001) (reversing district court for having excluded testimony of expert concerning deficiencies of pneumatic nailer and noting that expert's involvement in ''numerous other cases'' involving same product ''weighed heavily'' in support of admitting his testimony).

[2] See, e.g., *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 463 (W.D. Pa. 2003) (Findings of Fact 226, 234) (case reports rejected as basis for experts' conclusion that lactation-inhibiting drug Parlodel® caused intracerebral hemorrhage).

[3] See, e.g., *Awad v. Merck & Co.*, 213 F.3d 627 (Table), 2000 WL 528649 (2d Cir. May 1, 2000) (affirming 99 F. Supp. 2d 301, 306 (S.D.N.Y. 1999)) (opinion based largely on case reports that rubella vaccine caused chronic pain syndrome was properly excluded, the district court observing that ''the rate of error . . . is likely to be quite high'');

[4] See, e.g., *Soldo*, 244 F. Supp. 2d at 463 (Finding of Fact 225).

[5] *See, e.g., id.* (Finding of Fact 227).

[6] *See, e.g., id.* (Finding of Fact 226).

[7] *See Medalen v. Tiger Drylac U.S.A. Inc.*, ___ F. Supp. 2d ___, 2003 WL 21524542, at *13 (D. Minn. 3/31/03) (excluding opinion that exposure to cadmium- and nickel-containing product caused basal cell carcinoma and observing that plaintiff's expert ''offered no case reports'').

[8] *See, e.g., Soldo*, 244 F. Supp. 2d at 459 (Finding of Fact 177) (discussing *Daubert* hearing testimony of Dr. Kulig as to Parlodel®):

''In the following dialogue, which occurred between Dr. Kulig and Chief Judge McDade in an evidentiary *Daubert hearing, Dr. Kulig conceded that epidemiologic studies are the best evidence of causation:*

THE COURT: If you had a choice between that type of study [epidemiologic study] and adverse event reporting sheet, which would you choose?

THE WITNESS: Well, if it was the only choice?

THE COURT: Yes, if that was the only choice.

THE WITNESS: And the epidemiologic study was a good one. I would obviously choose that.

THE COURT: You would choose it in every case when it's matched against something else, wouldn't you?

THE WITNESS: If it was well performed.

THE COURT: Yes.

THE WITNESS: Yes.

Kulig/*Nussel* Hearing Transcript, Apr. 6, 1999, Vol. II at 170 (Att.2C).''

[9] *See, e.g., id.* (Finding of Fact 178) (discussing testimony of Dr. Kulig on behalf of breast implant defendant):

''Dr. Kulig testified that he uses 'exactly the same' scientific methodology in assessing whether a substance causes a potential adverse event in both his Parlodel® litigation work on behalf of plaintiffs and his breast implant litigation work on behalf of defendants. 11/8 Tr. at 36-37 (Kulig). He testified to his scientific methodology in the breast implant litigation as follows:

Q. Doctor, on a more general level, *can a cause and effect relationship be established* with a disease as common as breast cancer in humans *without first showing an association through a controlled study?*

A. *No.*

Q. Can it be shown with case reports?

A. No.

Q. Can it be shown with case series, multiple case reports?

A. No.''

(Emphasis added.)

[10] *See, e.g., id.* (Finding of Fact 792) (citing testimony of defense expert, Dr. David Buchholz).

 COPYRIGHT © 2003 BY THE BUREAU OF NATIONAL AFFAIRS, INC., WASHINGTON, D.C. EXER ISSN 1536-1896

Attorneys on both sides in toxic tort litigation should look very closely at important case reports to make sure that those bordering on scientific misconduct are discarded.

What kinds of misconduct have we encountered? The Parlodel® litigation has provided a bonanza of bogus case reports. In one instance, an expert for the plaintiffs—who collected from plaintiffs' lawyers cases of women allegedly harmed by Parlodel®—published reports about the same woman and the same incident in two different medical journals, ostensibly as different cases. Obviously, the multiplication of reports about the same case distorts the scientific literature and lends unwarranted support for the advocates of general causation. Because case reports often include minimal identifying facts, and the author decides at his discretion exactly which facts are to be included, such misconduct can go unnoticed for years and may never be brought to light. In the instance to which we refer the author, when confronted at deposition, maintained that the simultaneous submission of the same case to two different journals was a ''mistake.'' No retraction has ever been published to our knowledge.

The same expert witness proved to be extremely selective as to the underlying facts included in his case reports. To convey the impression that Parlodel® was a dangerous drug, incidentally increasing his usefulness as an expert witness, his published case reports involving Parlodel® commonly left out important information, which, if included, would easily have led readers to recognize the existence of plausible alternative causes of the adverse events at issue. In one case involving an ischemic stroke allegedly caused by Parlodel®, this author *cum* expert witness failed to reveal that the patient's treating physicians diagnosed her with vasculitis, an obvious alternative explanation for her stroke. In another, the author failed to mention that the patient had been diagnosed with fibromuscular dysplasia—again a likely alternative explanation for her stroke.[11] In both case reports, the omitted information was inconsistent with the causal theory of plaintiffs' experts.

Thorough discovery—including, for example, seeking court intervention to compel the disclosure of back-up documentation for case reports authored by and relied upon by the expert—will often uncover such alternative likely causes and, if so, the misleading published case report may not adversely affect the litigation. However, in any later claims involving the same drug, where the defendant is different or represented by different counsel, the author's significant omission in the case report may well not be discovered and the case report will therefore continue to bear weight that it does not deserve.

The most egregious misconduct unearthed in the Parlodel® litigation involves a case report entitled *Possible Bromocriptine-induced Myocardial Infarction*, written by Larrazet, et al., and published in Annals of Int. Med. 118:199-200 (1993). The Larrazet report described a French woman who had taken Parlodel® for the prevention of physiological lactation and, during treatment, had a myocardial infarction (''MI''). Her doctors performed an angiogram on her and determined that the MI was caused by coronary vasospasm. Among other things, they placed the patient—a smoker—on antispasm drugs.

Because of prior case reports, her treaters were suspicious that Parlodel® may have contributed to the MI and decided to conduct an experiment on their patient. They told her to stop taking her antispasm medication and pay a return visit to their offices. There, they ''rechallenged'' her with another Parlodel® pill and, two hours later, conducted a second angiogram. Their published report states that her right coronary artery was then found to be in spasm.

It is undisputed that spasms of coronary arteries can arise simply because the catheter that is used to inject the dye into the aorta *near* the opening of the artery in fact is erroneously entered *into* the artery in question and the resultant irritation of the artery wall itself causes spasm.[12] Thus, Larrazet, et al., took pains in their published case report to assure readers that catheter-induced spasm had been ruled out as a possible explanation for the spasm seen during the ''rechallenge'' angiogram. They stated that ''the operator was careful not to intubate deeply the right coronary artery,'' and published a photograph of what was purportedly the beginning of the angiogram that did, indeed, seem to demonstrate the catheter tip far removed from the spasm. The photograph thus appeared to prove the authors' claims that the spasm they observed was not due to the catheter itself but, instead, was the result of something else, most likely (they claimed) the drug they gave to their patient two hours earlier.

Plaintiffs' litigation experts relied heavily upon this publication as support for their theory that Parlodel® could cause, not only MI but a variety of different types of stroke. As early as 1993 (the year of publication) plaintiffs' experts were writing expert witness reports referring to the Larrazet article as ''angiographically demonstrated Parlodel-induced coronary spasm,'' and concluding from this article that ''*There can be no doubt* that Parlodel® administration increases the risk of causing an undesirable cardiac problem in normal healthy women.'' (Emphasis added.)

A Dr. Kulig, who has appeared for plaintiffs in almost every Parlodel® case, testified in 1995 that Parlodel® can cause MI, basing his opinion on ''case reports, including rechallenges done by Larrazet, for example, where *we know* that the drug causes vasospasm of coronary arteries.'' (Emphasis added.) Dr. Kulig later relied upon the Larrazet case report, with no qualifications, to tell juries that Parlodel® was supposedly ca-

[11] The author also did not mention that the patient (a) was obese, (b) had episodes of elevated blood pressure both before and during a prior pregnancy, (c) had previously used Parlodel® with no adverse effects, (d) had a family history of hypertension, (e) had used other medications at the time of her stroke, and (f) had an arteriogram showing no evidence of vasospasm, *i.e.*, no evidence to support the causal theory advanced in the case report.

[12] *The Heart*, J. Willis Hurst, M.D., ed., (McGraw Hill: 7th ed. 1990) at 1124 (angiographic evidence for spasm must be ''differentiated from catheter-related spasm'').

pable of causing stroke.[13] With specific regard to the location of the catheter tip being far removed from the point of spasm, plaintiffs' experts who had never looked at the actual angiogram testified that it was ''plain as the nose on my face [that] [the spasm] was beyond the catheter tip.''[14] And, based in part upon testimony highlighting the supposed importance of the Larrazet report, some courts denied Sandoz's *Daubert* challenges to plaintiffs' experts. *See*, *e.g.*, *Globetti v. Sandoz Pharms. Corp.*, 111 F. Supp. 2d 1174, 1178-79 (N.D. Ala. 2000) (devoting paragraph to Larrazet report).[15]

In fact, the photograph published in the Larrazet case report supposedly reflecting the position of the catheter far removed from the locus of spasm was taken seconds after the catheter had, in fact, been placed at the exact location of the spasm, deep in the artery, pressing against the arterial wall. Thus the catheter tip itself was the obvious cause of the spasm, and the case report cannot be used to implicate any effects of the drug Parlodel®.

That the published report falsely stated where the catheter had been came to light fortuitously. A plaintiff's attorney in a Parlodel® case decided to call upon a senior author of the Larrazet report (not Dr. Larrazet) to be an expert witness. This physician—who had placed his name on the report but may not have ever seen the actual angiogram itself—came to the United States from France with a copy of the angiogram and provided it to plaintiffs' counsel, who then made a copy available to defense counsel. Only after defense counsel asked their own cardiologist to look at the angiogram did the truth became known: The catheter that supposedly had never been near the location of the spasm was, in fact, *exactly* there at the outset of the procedure.

Even Sandoz's uncovering this blatant misrepresentation in the medical literature did not prevent plaintiffs from continuing to use the Larrazet report to foster the idea that Parlodel® can cause MI and stroke. In one MI trial, Sandoz's cardiologist was prevented on procedural grounds from telling the jury about her discovery of the misrepresentation.[16] In another trial involving an MI allegedly caused by Parlodel®, the court denied Sandoz's motion *in limine* to exclude testimony concerning Larrazet, even after being *presented* with a copy of the angiogram on a CD and complete instructions concerning how to view it and the significance of what he would be observing. It is not clear whether the judge did or did not view the angiogram.[17]

Finally, in *Colangelo v. Sandoz Pharms. Corp.*, No. 95 L 5635, Cook County, Ill., a stroke case, defense counsel convinced the trial judge of the importance of scheduling extensive oral arguments on motions *in limine*. On the first day of these arguments, the trial judge actually stepped down from the bench and reviewed a frame-by-frame playback of the angiogram on defense counsel's laptop computer. *Colangelo v. Sandoz Pharms. Corp.*, No. 95 L 5635, Cook County, Ill., Hearing Transcript, 10/24/02, at 104-10. After viewing the hard evidence, the trial judge granted Sandoz's motion *in limine*, and ruled that the Larrazet case report could not be relied upon in any way by plaintiffs' experts and certainly not shown to the jury.[18] *Id.* at 128 (''I find that reference to the Larrazet case is likely to cause confusion to the jury, will waste time, and therefore is prejudicial.'') Whether other courts before whom Parlodel® cases are still pending follow the ruling in *Colangelo* remains to be seen.

View Reports Critically. Our experience makes clear that even case reports published in highly-respected journals such as the Annals of Internal Medicine must be viewed critically and even with suspicion. Judicial decisions disparaging experts' reliance on case reports in support of general causation are correct in their observations. These decisions might well go further than they have, however, because case reports can be fraudulent just like other work published by scientists or medical doctors. Litigants must be diligent not to accept case reports at face value.

---

[13] *See*, *e.g.*, *Warren v. Sandoz Pharms. Corp.*, No. 95-107, Rankin County, MS (7/18/97), Trial Transcript at 64-66 (Larrazet case report was ''important'' evidence of causation). The trial resulted in a defense verdict that was affirmed on appeal. *Warren v. Sandoz Pharms. Corp.*, 783 So. 2d 785 (2000), *cert. denied*, (5/3/01).

[14] Deposition of Denis Petro, M.D., in *Kittleson v. Sandoz Pharms. Corp.*, 0:98-CV-2277, D. Minn. 2/9/00, p. 351.

[15] The denial of defendant's *Daubert* motion could not be appealed because the trial court refused to certify the question for interlocutory appeal and the trial that followed resulted in a hung jury. *Compare, e.g.*, *Siharath v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347 (N.D. Ga. 2001), *aff'd*, 295 F.3d 1194,1196 (11th Cir. 2002) (granting defendant's *Daubert* motion and summary judgment); *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp/ 2d 1015 (E.D. Mo. 2000), *aff'd*, 252 F.3d 986 (8th Cir. 2001) (same); *Hollander v. Sandoz Pharms. Corp.*, 95 F. Supp. 2d 1230 (W.D. Okla. 2000), *aff'd*, 289 F.3d 1193 (10th Cir. 2002) (same).

[16] The trial ended in a hung jury. *Kittleson v. Sandoz Pharms. Corp.*, FILE NO. 98-CV-2277, D Minn.

[17] As stated above, this trial too ended in a hung jury. *Globetti v. Sandoz Pharms. Corp. CV-98-TMP-2649-SVS.*

[18] Trial in this case is now set for January 2004.

 COPYRIGHT © 2003 BY THE BUREAU OF NATIONAL AFFAIRS, INC., WASHINGTON, D.C. EXER ISSN 1536-1896