Legal Backgrounder

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Law Leading Science:
The Ninth Circuit Makes a *Messick* of Differential Diagnosis

by Matthew A. Reed

In 1996, Judge Richard Posner of the U.S. Court of Appeals for the Seventh Circuit burnished his reputation for pithy legalisms by observing that "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). Alas, the truth of that statement appears to be in doubt in the Ninth Circuit.

In *Messick v. Novartis Pharmaceuticals Corp.*, --- F.3d ---, 2014 WL 1328182 (9th Cir. Apr. 4, 2014), the Ninth Circuit considered the district court's grant of a *Daubert* motion against plaintiff's specific causation expert, a medical doctor employing a "differential diagnosis." The district court excluded the expert because he never explained the scientific basis for his conclusion, and thus was unreliable. The Ninth Circuit reversed, holding that the expert's clinical experience and reference to a medical association's diagnostic criteria were sufficiently scientific to support his specific causation opinion. This holding improvidently blesses a physician's diagnosis of disease and approximation of its cause in the clinical setting—a pragmatic process necessarily born of little time, incomplete information, empathy with the patent, and risk aversion—as a product of the scientific method, and thus raises the potential for the law to impose liability for which there is insufficient scientific support.

DISTRICT COURT OPINION

Factual Background. Linda Messick was diagnosed with breast cancer, and subsequently underwent a regimen of radiation therapy and several medications. Thereafter, she was diagnosed with osteoporosis, which was treated with Zometa and Aredia therapies. Those drugs, manufactured and sold by Novartis, are bisphosphonates prescribed for the management of metastatic disease to the bone and other bone diseases and conditions.

During and after her use of Zometa and Aredia, Messick developed a series of dental maladies culminating in exposed bone in her mouth that did not heal completely for three years, and which she characterized as osteonecrosis of the jaw ("ONJ"). She subsequently filed suit against Novartis, alleging that Aredia and Zometa caused her ONJ, and that Novartis knew or should have known that its drugs were capable of causing ONJ, but failed to warn her prior to her use of them. Novartis filed *Daubert* motions challenging several of Messick's experts, as well as a motion for summary judgment. This Legal Backgrounder, however, will focus solely on Novartis' *Daubert* motion challenging Messick's retained medical causation expert.

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Daubert Analysis. After acknowledging its gatekeeping responsibility under Federal Rule of Evidence 702 to ensure that all expert testimony was relevant and reliable, the district court began its analysis by noting the expert had not conducted any prelitigation research into bisphosphonates or ONJ. His opinion was instead predicated on his "extensive experience" with ONJ and his review of 6 medical articles. The court held that his opinion that bisphosphonates were generally capable of causing ONJ was supported scientifically by his reliance articles. It was the differential diagnosis underlying his specific causation opinion—that Aredia and Zometa caused Messick's ONJ—that was unscientific.

"Differential diagnosis" is a standard technique employed by medical clinicians where a patient's disease is diagnosed by "ruling-in" all potential diseases that might cause his symptoms, then "ruling-out" all diseases whose symptoms do not match his presentation. In the end, a physician is left with the disease that most likely accounts for the patient's condition. Diagnosis of disease, however, is much different from a scientific determination of its cause. Thus, several federal appellate courts have noted that when a physician uses the "rule-in, rule-out" methodology to determine the *cause* of a plaintiff's disease, this is properly a "differential etiology," not "differential diagnosis." *See*, *e.g.*, *Myers v. Illinois Central R.R. Co.*, 629 F.3d 639, 644-45 (7th Cir. 2010); *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1252 (11th Cir. 2005); *Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 669-73 (6th Cir. 2010).

Thus, while the expert characterized his analysis as a "differential diagnosis," the resulting specific causation opinion demonstrates he was actually performing a differential etiology. His analysis, however, identified not only 6 potential risk factors for ONJ *causation*, but also three criteria for bisphosphonate-related ONJ ("BRONJ") *diagnosis* set forth by the American Association of Oral Maxillofacial Surgeons ("AAOMS"). He thus opined that bisphosphonates caused Messick's ONJ because the criteria for BRONJ *diagnosis* were met, but did not "rule out" the five risk factors for ONJ *causation* he identified other than bisphosphonate use. It was the absence of a scientific explanation for his disregard of the remaining five risk factors that caused the district court to rule his specific causation opinion unreliable. Indeed, the court noted, "when asked if there is 'any scientifically reliable way for him to determine in a patient who has multiple risk factors at one time which of those particular risk factors is causing the underlying necrotic bone in the jaw,' he answered 'no.'"

As a result of its *Daubert* rulings on the medical causation expert and other of Messick's experts, the district court found she had insufficient evidence to prove causation. The district court therefore granted summary judgment, from which Messick appealed.

NINTH CIRCUIT OPINION AND ANALYSIS

The Ninth Circuit reversed the district court's exclusion of the expert's specific causation opinion for failure to explain its scientific basis. It was enough, the court said, that the expert relied on "his own extensive clinical experience" and "his examination of Messick's records, treatment, and history." "Medicine partakes of art as well as science," the court held, "and there is nothing wrong with a doctor relying on extensive clinical experience when making a differential diagnosis." The Ninth Circuit therefore held that a physician's clinical experience in determining the etiology of disease is a scientifically rigorous process sufficient to meet *Daubert*'s reliability standard. However, as numerous courts have noted, this is simply not the case.

Doctors are driven by "the rigors and necessities of their clinical practices to conclude that temporal association equals causation, or at least that it provides an adequate proxy in the chaotic and sometimes inconclusive world of medicine. This shortcut aids doctors in their clinical practices because their most important objective day-to-day is to help their patients and 'first, do no harm,' as their Hippocratic oath

requires." *Siharath v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347, 1372 (N.D. Ga. 2001), *aff'd sub. nom.*, *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194 (11th Cir. 2002), *reh'g and reh'g en banc denied*, 48 Fed. Appx. 330 (11th Cir. 2002).

As a result,

> [w]hen physicians think about etiology in a clinical setting, … they may think about it in a different way from the way judges and juries think about it in a courtroom. Getting the diagnosis right matters greatly to a treating physician, as a bungled diagnosis can lead to unnecessary procedures at best and death at worse. But with etiology, the same physician may often follow a precautionary principle: If a particular factor might cause a disease, and the factor is readily avoidable, why not advise the patient to avoid it? Such advice – telling a welder, say, to use a respirator – can do little harm, and might do a lot of good. This low threshold for making a decision serves well in the clinic but not in the courtroom, where a decision requires not just an educated hunch but at least a preponderance of the evidence.

Tamraz v. Lincoln Elec. Co., 620 F.3d 665, 673 (6th Cir. 2010) (emphasis in original) (overturning district court's admission of expert as an abuse of discretion).

There is therefore an enormous gap "between clinical process, in which conclusions must be extrapolated from incomplete data" immediately in order to avoid patient injury, "and the scientific method, in which conclusions must be drawn from an accepted process." *Rider*, 295 F.3d at 1196. That is why most federal appellate courts, including the Ninth Circuit, require that an expert using differential etiology not only demonstrate the potential causes he "rules-in" are actually capable of causing the disease, but that he "systematically and scientifically rul[e] out specific causes until a final, suspected cause remains." *Kilpatrick v. Breg Inc.*, 613 F.3d 1329, 1342 (11th Cir. 2010); *see also Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 885 (10th Cir. 2005); *Clausen v. M/V NEW CARISSA*, 339 F.3d 1049, 1057-58 (9th Cir. 2003); *Myers*, 629 F.3d at 644-45; *Tamraz*, 620 F.3d at 674. Remarkably, the *Messick* court specifically acknowledged that "[w]hen an expert rules out a potential cause in the course of a differential diagnosis, the expert must provide reasons for rejecting alternative hypotheses using scientific methods and procedures." Yet it allowed the expert's specific causation testimony despite his failure to rule out five risk factors for ONJ other than bisphosphonates, and despite his inability to provide a scientific basis for his conclusion that bisphosphonates caused Messick's ONJ.

The *Messick* Court added that the expert also relied on the AAOMS definition of BRONJ. But that definition is for the purposes of disease *diagnosis*, not causation, and thus does nothing to aid his differential etiology. More importantly, the court was unconcerned by the fact that "the current level of evidence does not fully support a cause-and-effect relationship between bisphosphonate exposure and necrosis of the jaws." The resulting willingness to allow the plaintiff's claims to proceed, despite a fundamental deficit of supporting scientific evidence, has already been warned against by numerous federal appellate courts—and, arguably, the Supreme Court. *See*, *e.g.*, *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 596-97 (1993); *Tamraz*, 620 F.3d at 677-78; *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996); *Rider*, 295 F.3d at 1202.

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CONCLUSION

Instead of accepting the current limitations of science, the *Messick* court deemed the medical clinician's truncated etiological determination—which is properly focused on avoiding harm to the patient, rather than ascertaining a disease's true cause—as sufficiently "scientific" to satisfy *Daubert*. As a result, specific medical causation may now be testified to by a treating physician in the Ninth Circuit despite a deficit of support in the scientific literature, and despite the physician's inability to identify which among a multitude of risk factors actually caused a disease.

In short, the Ninth Circuit has signaled its willingness to allow the law to lead science. This will affect more than the truth of Judge Posner's observation: Entire industries whose members are unfortunate enough to face suit in the Ninth Circuit now face the unnecessary destruction of jobs and stifling of innovation that comes from the imposition of liability with inadequate scientific support. *See*, *e.g.*, *Tamraz*, 620 F.3d at 677-78 (citing *New York Times* article "describing how scientists concluded, years after litigation, billions in settlements, and the bankruptcy of a major manufacturer, that no evidence tied breast implants to health problems.").

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