Products Liability Law Daily Wrap Up, EXPERT EVIDENCE—DRUGS—N.J. Super.: Testimony by plaintiffs' experts in New Jersey Accutane litigation excluded as unreliable, (Feb. 25, 2015)

Products Liability Law Daily Wrap Up

By John W. Scanlan, J.D.

The testimony of two experts for plaintiffs in multi-county litigation in New Jersey against Hoffman-LaRoche, Inc., the maker of Accutane, was excluded by a New Jersey Superior Court. Although the court found the experts to be highly qualified personally, it determined that their methodologies were unreliable because they were more in the nature of advocacy than objective science (*In re: Accutane Litigation*, February 20, 2015, Johnson, N.).

Background. A number of plaintiffs began bringing suit in New Jersey against Hoffman-LaRoche, Inc., the manufacturer of Accutane (Isotretinoin), a drug approved by the FDA to treat recalcitrant nodular acne, alleging that Accutane had caused them to develop Crohn's Disease. These suits have been consolidated since 2005 in Multi-County Litigation No. 271. In this proceeding, Hoffman-LaRoche and its related corporate entities moved to exclude the testimony of two experts for the plaintiffs: Dr. Arthur A. Kornbluth, whose testimony was proffered on the issue of general causation, and Dr. David Madigan, who was to assess existing studies examining the association between Isotretinoin and Crohn's Disease. Hoffman-LaRoche proffered its own experts: Dr. Maria Oliva-Hempker, to opine on general causation and to assess Dr. Kornbluth's methodology, and Dr. Steven N. Goodman, to opine on whether the methodologies of Dr. Kornbluth and Dr. Madigan were reliable and whether there was a scientific basis for the plaintiffs' claim that Isotretinoin was a cause of Crohn's Disease.

Studies. After examining nine risk assessment epidemiological studies submitted by the parties on the relationship between Isotretinoin and Inflammatory Bowel Disease/Crohn's Disease, the court concluded that there was no epidemiologic evidence to justify a reasonable inference that there was a link between Isotretinoin and Crohn's Disease. The plaintiffs relied upon only one of the studies—the "Sivaraman Study"—which examined only 509 subjects, while ignoring other larger studies. This study—a one page abstract published without footnotes—had concluded that Isotretinoin exposure did not appear to confer risk for Crohn's disease in the absence of antibiotic exposure, which clearly did not offer support for a causative risk association between Isotretinoin and Crohn's Disease. The quality of this study was not of a kind upon which experts normally rely, according to the court.

Furthermore, the court also examined ten studies regarding the prodrome (the length of time between the first symptoms and a conclusive diagnosis) of IBD; it concluded that the results of the single study that had been relied upon by the plaintiffs—the "Pimentel Study"—was not reliable enough to submit to the jury because it had only 76 subjects, of whom 26 were diagnosed with Crohn's Disease and had been referred by other gastroenterologists because they had been difficult to manage or diagnose. The plaintiffs' experts had ignored much larger, population-based studies in favor of a single, much smaller study whose subjects essentially had been cherry-picked.

The court said that the plaintiffs' reliance upon these two studies was fatal and revealed the lengths to which their legal counsel and experts were willing to "contort the facts and torture the logic" in support of their hypothesis. The studies were insignificant and the scientific literature did not support reliance upon them.

FDA reports, case reports, and animal studies. Throughout their testimony, the plaintiffs' experts had referenced FDA Adverse Event Reporting System (FAERS) reports. The FDA itself had identified limitations with this data, and plaintiffs' expert Dr. Madigan had previously written about these limitations. The court noted that there were concerns about the potential for abuse of the FDA reporting system, in that a treatise published in

2014 said that 3.6 percent of the more than 3.3 million cases overall were reported by attorneys, whereas 87.8 percent of the cases involving IBD and Isotretinoin were reported by attorneys.

The court stated that the plaintiffs had characterized case reports as inherently valuable evidence, but that *The Reference Manual on Scientific Evidence* (3rd edition) issued by the Federal Judicial Center and the National Research Council of the National Academies, which it said provided excellent guidance indicating what the scientific community thinks to be reasonable, ranked case reports "at the bottom of the medical evidence hierarchy."

The plaintiffs' experts also proffered the results of animal studies. However, again citing the *Reference Manual*, the court found that these tests provided no meaningful support for Dr. Kornbluth's causation hypothesis. It could not be known whether any harm caused by Isotretinoin to the dogs' intestines was permanent because the dogs had been euthanized at the conclusion of the testing and because dogs cannot develop IBD.

Testimony of Dr. Madigan and Dr. Kornbluth. The opinions of Dr. Madigan were conclusion-driven, rather than methodology-based, according to the court. Instead of pooling the quantitative results of the studies to attempt a more precise estimate of the risk, he disregarded eight of them, which had studied about 2.1 million people, in favor of a single-page non-peer reviewed study of 26 subjects that fell very short of reliable evidence and opined that this study provided a reliable basis for arriving at an informed risk assessment. His role, the court said, was to provide an expert opinion using "plausible-sounding statistical challenges" to explain away the results of the large population-based observational studies in order to clear the way for Dr. Kornbluth's hypothesis, regardless of whether his efforts led the discussion closer to scientific truth.

The court further criticized the reasoning of Dr. Kornbluth as wanting the court to reject the best evidence available while accepting inferior evidence because it was all he could find to support his causation hypothesis. His written report showed his hypothesis was a muddle of ambiguities and pure speculation, and courts may not allow juries to consider medical causation testimony that consists of conjecture. He was highly selective regarding the scientific opinions that he found reliable, and relied on selected portions of the Sivaraman Study while he was at odds with its authors' methods and conclusions. The court found his discussion of his hypothesis for the biological mechanism of the development of Crohn's Disease as caused by Isotretinoin was far short of compelling, and his testimony was replete with convenient assumptions to bridge analytical gaps in his methodology.

The case is No. 271(MCL) .

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Companies: Hoffman-LaRoche, Inc.

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