Products Liability Law Daily Wrap Up, EXPERT EVIDENCE—DRUGS—E.D. Pa.: Exclusion of perinatal pharmacoepidemiologist's opinion as unreliable was proper in Zoloft® MDL, (Jan. 27, 2015)

By Susan Lasser, J.D.

In a ruling that is applicable to all cases in the multi-district litigation relating to the prescription antidepressant Zoloft®, a federal district court in Pennsylvania would not reconsider its earlier ruling that a plaintiffs' causation expert's testimony was inadmissible. The court had found that the expert departed from the generally accepted methods and principles of her epidemiological field in multiple ways, and concluded on reconsideration that it did not commit an error of fact or law or abuse its discretion in excluding the expert's testimony as unreliable under the *Daubert* standard. Therefore, it denied the plaintiffs' motion for reconsideration (*In re: Zoloft (Sertraline Hydrocloride) Products Liability Litigation*, January 23, 2015, Rufe, C.).

Background. Zoloft is a prescription antidepressant, part of the class of selective serotonin reuptake inhibitors (SSRIs). The FDA classifies it as a Pregnancy Class C drug, meaning that animal testing has shown adverse effects on fetuses, but there were no adequate and well-controlled studies in humans. The plaintiffs' steering committee (PSC) in the multi-district litigation concerning Zoloft (MDL 2342) proffered an expert report on general causation produced by Dr. Anick Bérard, a perinatal pharmacoepidemiologist. Bérard has conducted epidemiological studies and published peer-reviewed papers on the use of antidepressants by pregnant women, and opined that SSRIs as a class, and Zoloft specifically, may cause various birth defects in the children of mothers who are exposed to the drug. Defendants Pfizer Inc. and Greenstone LLC moved to exclude Bérard's testimony, arguing that her opinions were based upon unreliable methods and principles. The court overseeing the multi-district litigation agreed in an order dated June 27, 2014, finding that her novel methodology was based on principles and methods that were not recognized by the scientific community. The PSC sought reconsideration of the court's ruling.

Prior court opinion on expert testimony. The court commented that its prior opinion "set forth a detailed and multi-faceted rationale" in its finding that the expert's testimony was unreliable. The court had determined that Dr. Bérard did not adhere to the principles of replication and statistical significance; that she used certain principles and methods without demonstrating either that they were recognized by her scientific community or that they otherwise should be considered scientifically valid; that her drawing of conclusions without adequate hypothesis testing was unreliable; that her opinions, which were supported by a "cherry-picked" sub-set of research selected because it was supportive of her opinions (and chosen without adequately addressing non-supportive findings), also were unreliable; and that she failed to reconcile her currently expressed opinions with her prior opinions and her published, peer-reviewed research. The court took all of these factors into account and found that Dr. Bérard departed from well-established epidemiological principles and methods, and that her opinion on human causation should be excluded.

Reconsideration. On reconsideration, the PSC argued that the court erred because the U.S. Supreme Court's reasoning in *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309 (2011), and the U.S. Court of Appeals for the Third Circuit's opinion in *Deluca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941 (3d Cir. 1990), did not permit the current court "to apply a bright-line rule" and exclude their general causation expert for drawing conclusions about causation in the absence of replicated, statistically significant associations.

However, the court took issue with the PSC's assertion that it took a bright-line position on the legal necessity of "replicated statistically significant epidemiological findings in order to establish general causation." It also said that it hadn't relied on any holding by another court. Instead, the court stated that it set forth its factual finding that epidemiologists, such as Dr. Bérard, who in examining potential teratogens—*i.e.*, agents that interfere with normal embryonic development—generally will not draw causal conclusions absent replicated statistically significant epidemiological findings and application of the "Bradford-Hill criteria," which are well-established causation criteria used by epidemiologists. The court said that in its earlier ruling it was describing a scientific methodology and not setting forth a legal standard. Further, it evaluated Dr. Bérard's methods according to *Daubert* principles, and did not apply a "bright-line" exclusionary rule to her causation analysis.

The court reviewed the published literature that Dr. Bérard and other experts relied upon and reviewed both parties' reports and testimony in coming to its factual findings. It said that its citation to similar language in an unpublished Third Circuit case was made only to demonstrate that other courts had made similar findings as to prevailing standards in the field of pharmacoepidemiology.

The court insisted that it did not hold, as a matter of law, that a causation expert must be excluded under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), in the absence of replicated, statistically significant findings, and that it did not exclude Dr. Bérard's testimony based only on her failure to support her opinions with replicated, statistically significant findings. The court said that it considered statistical significance to be one important indicator of reliable methodology, but that it did not hold that factor as "mechanically control[ling] whether an epidemiological analysis is sufficiently reliable to be admissible."

The court found that Dr. Bérard's method of examining trends in odds ratios and confidence intervals without regard to statistical significance and without further statistical analysis was not completely valid. In addition, in examining the expert's methodology with regard to her analysis of the Bradford-Hill criteria, the court found that strength of association (of which statistical significance is a measure) and replication were only two of the Bradford-Hill criteria for inferring causation. Thus, the court considered the reliability of Dr. Bérard's methodology with regard to *all* of the relevant Bradford-Hill criteria. According to the court, Dr. Bérard's failure to point to replicated, statistically significant findings supporting her conclusions about teratogenic effects was one identified methodological flaw, but was not the only reason for the exclusion of the expert's testimony. The court noted that it also had found that "the Rothman approach," as applied by Dr. Bérard, did not meet the *Daubert* standard; and that there were other problems with Dr. Bérard's methods, including her failure to test certain critical hypotheses, her failure to reconcile her previously expressed opinion that Zoloft was a "first line" drug for use during pregnancy (which she expressed in publications and presentations as recently as 2012) with the opinion she expressed in the current MDL that Zoloft was a teratogen which should be avoided by women who were or may become pregnant, her cherry-picking of studies and data within studies which supported her opinion, and her failure to adequately address certain confusing factors before reaching its evidentiary ruling. The court concluded that it did not err in its earlier conclusion and denied the PSC's motion.

The case is MDL No. 2342 (12-md-2342).

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