Products Liability Law Daily Wrap Up, EXPERT EVIDENCE—DRUGS—E.D. Pa.: Causation expert in Zoloft® MDL failed to apply methodology consistently to data, (Dec. 4, 2015)

By Susan Lasser, J.D.

Pfizer, Inc., the manufacturer of the prescription antidepressant, Zoloft®, successfully challenged the admissibility of testimony by the causation expert offered by the plaintiffs in the multi-district litigation concerning the drug. The federal district court in Pennsylvania overseeing the MDL held that the expert failed to apply his methodology faithfully to the relevant data, and, therefore, excluded his testimony from trial (*In re: Zoloft (Sertraline Hydrocloride) Products Liability Litigation*, December 2, 2015, Rufe, C.).

Background. The plaintiffs in the Zoloft MDL offered Nicholas Jewell, Ph.D., a professor of biostatistics at the University of California, Berkeley, as a general causation expert. His opinion was that Zoloft use during a woman's early pregnancy (first trimester) was capable of causing, or contributing to causing, cardiovascular birth defects in newborns. Pfizer challenged the admissibility of the evidence, asserting that Dr. Jewell had used unreliable methods to form his opinion.

Teratology is the scientific field which deals with the cause and prevention of birth defects. Although the "gold standard" for epidemiological studies is the double-blind, randomized control trial, such studies are not ethically conducted on pregnant women. Therefore, the research on teratogens relies on less rigorous observational studies. Inferences about causation still can be made, but greater scrutiny as to the role of chance and possible sources of bias must be made to determine whether a study is a weak indicator of causation. The court explained that epidemiological studies examining the effects of medication taken during pregnancy on birth defects calculate a relative risk or odds ratio. The authors of the studies Dr. Jewell reviewed relied upon adjusted odds ratios, where available, when drawing conclusions. An odds ratio calculation is only an estimate. Thus, researchers also use statistical formulas to calculate confidence intervals. The court noted that a statistically significant result can indicate that the increased risk (here, of a birth defect) found is unlikely to result from chance alone. Dr. Jewell was asked to opine as to whether Zoloft *causes* the birth defects at issue, which required analysis beyond the identification of statistical correlations reported in published epidemiological studies. To infer a causal relationship from an association, scientists look at well-established criteria (the Bradford-Hill criteria), which include the strength of the association between the exposure and the outcome; the temporal relationship between the exposure and the outcome; the dose-response relationship; replication of findings; the biological plausibility of such an association; alternative explanations for the association; the specificity of the association; and the consistency with other scientific knowledge.

Pfizer's challenge to Dr. Jewell's testimony focused on the methods he used to determine whether there was a true association between maternal Zoloft use and cardiac birth defects, his assessment of the replicability and consistency of study results, and his efforts to address alternative explanations (chance, bias, confounding) for detected associations and the specificity of the association.

Reliability concerns. The court found that because of certain methodological weaknesses, the expert could not testify in the MDL. The court concluded that Dr. Jewell failed to apply consistently the scientific methods he articulated, deviated from or downplayed certain well-established principles of his field, and inconsistently applied methods and standards to the data so as to support his *a priori* opinion. The court expressed concern that he placed importance upon statistical principles when they supported his opinion, and ignored them when they did not. Moreover, the court concluded that no reliable inferences or conclusions could be drawn from the meta-analysis conducted by Dr. Jewell for purposes of the litigation. According to the court, the expert would not be able to adequately explain to the jury why he believed that the positive associations between maternal Zoloft use and cardiac birth defects, reported in some papers, were true associations, and not the result of a study flaw, confounding, bias, or other factor; nor reconcile those studies which reported no increased risk of cardiac birth defects with his opinion. Because it found that the expert's opinion was based on his failure to faithfully apply reliable scientific and statistical methods and because his testimony was likely to confuse or mislead the jury, the court excluded Dr. Jewell's testimony at trial under the Federal Rules of Evidence 403 and 702, and the

principles outlined in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

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

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Companies: Pfizer, Inc.

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