UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF VERMONT

COLLEEN AND STEVE LYMAN Plaintiffs, v. PFIZER, INC., WYETH, INC., SCHWARZ PHARMA, INC., PLIVA USA, INC., ACTAVIS-ELIZABETH, L.L.C. Individually and as a subsidiary of ACTAVIS, INC. and as successor to PUREPAC PHARMACEUTICAL, INC, Defendants.	:	Case no. 2:09-cv-262

Memorandum Opinion and Order Re: *Daubert* Motions[1]

In this action seeking to hold certain pharmaceutical companies responsible for Plaintiff Colleen Lyman having developed tardive dyskinesia as a result of her long-term ingestion of the prescription drug metoclopramide, Defendant PLIVA USA, Inc. ("PLIVA") has moved to exclude the testimony of Plaintiffs' experts Dr. Philip Seeman, Dr. Daniel Tarsy and Dr. Suzanne Parisian. Plaintiffs Colleen and Steve Lyman have moved to exclude the testimony of PLIVA's expert James Morrison. All motions argue that *Daubert v. Merrell Dow Pharmaceuticals, Inc.*,

[1] In its Opinion and Order issued today, the Court has dismissed Defendants Pfizer, Inc., Wyeth, Inc., Schwarz Pharma, Inc. and Actavis-Elizabeth, L.L.C. from this case. Their *Daubert* motions, and *Daubert* motions directed against their witnesses, ECF Nos. 215, 217, 220, 221, 223, 225, 226, 227, 230, 232, 234 and 235, are therefore **denied as moot**.

509 U.S. 579 (1993), requires the exclusion or limitation of these witnesses' testimony. The motions regarding the testimony of Dr. Seeman, Dr. Tarsy and James Morrison, ECF Nos. 213, 214 and 224, are **denied**. The motion regarding the testimony of Dr. Parisian, ECF No. 212, is **granted in part and denied in part.**

The party proffering expert testimony has the burden of establishing its admissibility "by a preponderance of proof." *Daubert*, 509 U.S. at 592 n. 10. Rule 702 of the Federal Rules of Evidence provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
> (b) the testimony is based on sufficient facts or data;
> (c) the testimony is the product of reliable principles and methods; and
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. The rule requires a district court to ensure that scientific or technical evidence is both relevant and reliable. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 147 (1999); *Daubert*, 509 U.S. at 589.

In assessing reliability, in addition to the factors set forth in Rule 702, a district court may consider

> (1) whether a theory or technique has been or can be tested; (2) "whether the theory or technique has been subjected to peer review and publication;" (3) the technique's "known or potential rate of error" and "the

> existence and maintenance of standards controlling the technique's operation;" and (4) whether a particular technique or theory has gained general acceptance in the relevant scientific community.

United States v. Williams, 506 F.3d 151, 160 (2d Cir. 2007) (quoting *Daubert*, 509 U.S. at 593-94). *Daubert*'s factors do not apply to all experts or in every case, however; the reliability inquiry is a flexible one. *Id*. (quoting *Kumho Tire*, 526 U.S. at 141; *Daubert*, 509 U.S. at 594).

The inquiry focuses "solely on principles and methodology, not on the conclusions that they generate." *Daubert*, 509 U.S. at 595. In keeping with the "liberal thrust" of the Federal Rules of Evidence, *id*. at 588, "[v]igorous cross-examination, presentation of contrary evidence and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Id.* at 596; *see also Olin Corp. v. Certain Underwriters at Lloyd's London*, 468 F.3d 120, 134 (2d Cir. 2006) (approving the techniques of cross-examination and presentation of opposing expert testimony to expose weaknesses in an expert's testimony).

Nevertheless, "proffered 'expert testimony should be excluded if it is speculative or conjectural.'" *Major League Baseball Props., Inc. v. Salvino, Inc.*, 542 F.3d 290, 311 (2d Cir. 2008) (quoting *Boucher v. U.S. Suzuki Motor Corp.*, 73 F.3d 18, 21 (2d Cir. 1996)). "An expert's conclusory opinions are similarly inappropriate." *Id.*

Motion to Exclude Testimony of Philip Seeman, M.D.

PLIVA contends that Dr. Seeman's testimony must be excluded in its entirety on relevancy grounds; because he is not qualified to offer epidemiology opinions; his epidemiology opinions are not based on sufficient facts or data and lack a scientifically valid basis; and his "mechanism" opinion is an irrelevant hypothesis that lacks a scientifically valid basis.

Dr. Seeman, a renowned neuropsychopharmacologist, provided two reports in connection with this case. In both reports he describes the mechanism by which daily metoclopramide use causes tardive dyskinesia: "the long-term partial blockade of dopamine D2 receptors by metoclopramide (in the basal ganglia) and the long-term accumulation of metoclopramide in the neuromelanin (of the [substantia] nigra) which causes nerve-cell-membrane damage, combine to lead to dopamine supersensitivity of dopamine receptors in the motor-controlling regions of the brain, resulting in clinical tardive dyskinesia." Seeman Report 1, ECF Nos. 214-2, 3. He opines that metoclopramide shares similar chemical properties with antipsychotic drugs, and can have a similar toxic effect on the nervous system. Seeman Report 10, ECF No. 214-3. He also concludes that the occurrence of extrapyramidal symptoms ("EPS") in metoclopramide-treated patients is "common[;] . . . it occurs much more frequently than one in 500 patients and is comparable to that found for the

phenothiazines and other dopamine antagonists. In actuality, it occurs in at least 15% of patients being treated with metoclopramide at doses of 30 to 40 mg per day . . . ." *Id.* at 20.

PLIVA argues that Dr. Seeman's opinion as to the relative rate at which metoclopramide produces tardive dyskinesia is irrelevant because Plaintiffs' claim that it should have strengthened the warnings on its label for metoclopramide has been dismissed as preempted. *See* Op. & Order 9, ECF No. 192 (citing *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2581 (2011)). Although it is true that the Lymans are precluded from pursuing their claim that a generic drug manufacturer such as PLIVA had a duty to provide stronger warnings than the FDA-approved labeling, PLIVA takes too narrow a view of relevance. Evidence is relevant, of course, if "it has any tendency to make a fact more or less probable than it would be without the evidence; and []the fact is of consequence in determining the action." Fed. R. Evid. 401. As PLIVA itself has argued, in order to prove their remaining claim against PLIVA, Plaintiffs will have to produce evidence that long-term metoclopramide use can cause tardive dyskinesia, and that Colleen Lyman's use of metoclopramide caused her tardive dyskinesia. An opinion that the occurrence of EPS in metoclopramide-treated patients is common is highly relevant. Moreover, Rule 702 permits testimony that will help the trier of

fact understand the evidence, as well as determine a fact in issue. Dr. Seeman's testimony is relevant on both grounds.

As to Dr. Seeman's qualifications, PLIVA merely argues that they do not qualify him to testify as an expert on epidemiology. Plaintiffs do not offer Dr. Seeman as an expert on epidemiology, and they contend that Dr. Seeman does not offer any epidemiological opinions in this case. A medical doctor does not have to be an epidemiologist in order to testify about epidemiological studies. *See, e.g.*, *United States v. Thorn*, 317 F.3d 107, 114-15 (2d Cir. 2003) (in which a medical doctor specializing in asbestos-related disease was permitted to testify about various epidemiological studies of asbestos exposure); *DeLuca v. Merrell Dow Pharm.*, 911 F.2d 941, 953 (3d Cir. 1990) (noting that a pharmacologist was qualified to testify about his interpretation of epidemiological evidence), *abrogated on other grounds*, *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 748 (3d Cir. 1994).

What PLIVA characterizes as an epidemiological opinion is Dr. Seeman's numerical comparison of an annual "incidence" of tardive dyskinesia associated with metoclopramide compared with tardive dyskinesia associated with certain antipsychotic drugs. PLIVA contends that this calculation violates fundamental epidemiology principles, being an attempt to calculate an incidence rate using prevalence data. Dr. Seeman defines his use

of the term "incidence rate" in his report as patients revealing tardive dyskinesia per year expressed as a percentage of patients being treated with metoclopramide. Seeman Report 5.

PLIVA accurately observes that "incidence rate" and "incidence study" have specialized meanings in epidemiology. *See* Fed. Judicial Ctr., Reference Manual on Scientific Evidence 389, 392 (2d ed. 2000). "Incidence rate" refers to the number of people in a specified population who develop a particular disease during a given period. *Id.* at 392. "Incidence study" or "cohort study" is a study in which groups of individuals are identified who have been differentially exposed to a drug that is hypothesized to cause a disease, and observed in order to determine if the exposed group is more likely to develop the disease. *Id.* at 389. Dr. Seeman's use of the term "incidence rate" as he defines it to describe his calculations does not connote that his examination of various studies constituted an epidemiological incidence study. Indeed, because the notion that long-term metoclopramide use can cause tardive dyskinesia is not particularly controversial at this point, *see Mensing*, 131 S. Ct. at 2572, 2573 ("Evidence has accumulated that long-term metoclopramide use can cause tardive dyskinesia . . ."), conducting a classic incidence study to determine if metoclopramide users were at increased risk for tardive dyskinesia would not appear to be essential to the Plaintiffs'

proof of general causation.

The import of Dr. Seeman's testimony will be that metoclopramide use produces tardive dyskinesia at a higher rate than that of certain other drugs, and an explanation of why that may be so. Dr. Seeman has explained his methodology, and his methods and opinions have been published in peer-reviewed journals. PLIVA takes issue with this proposed testimony; however its attacks on the sufficiency and validity of Dr. Seeman's opinions go to the weight, not the admissibility of the testimony. *See*, e.g.*, Ruiz-Troche v. Pepsi Cola of Puerto Rico Bottling Co.*, 161 F.3d 77, 85 (1st Cir. 1998) (reversing for abuse of discretion a district court's ruling that an expert's technique for calculating drug dosage was insufficiently reliable); *In re Baycol Prods. Litig.*, 532 F. Supp. 2d 1029, 1066 (D. Minn. 2007) (holding that the fact that the exact mechanism of a drug-related injury is not yet known does not preclude a well-reasoned and scientifically based opinion on the matter); *In re: Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 289 F. Supp. 2d 1230, 12247 (W.D. Wash. 2003) ("The fact that the mechanism remains unclear does not call the reliability of the opinion into question; "'[c]ausation can be proved even when we don't know precisely *how* the damage occurred, if there is sufficiently compelling proof that the agent must have caused the damage *somehow*.'") (quoting *Daubert v. Merrell Dow Pharm., Inc.*,

43 F.3d 1311, 1314 (9th Cir. 1995)).

The motion to exclude the testimony of Dr. Seeman, ECF No. 214, is **denied.**

Motion to Exclude the Testimony of Daniel Tarsy, M.D.

PLIVA moves to exclude the testimony of Dr. Tarsy on the grounds that his opinions do not fit the facts of this case, that his report does not comply with Rule 26 of the Federal Rules of Civil Procedure and that he should not be permitted to testify about topics concerning which he has not made the required Rule 26 disclosures.

Dr. Daniel Tarsy, a board-certified neurologist who specializes in movement disorders, a professor of neurology at Harvard Medical School, and director of the Parkinson's Disease & Movement Disorders Center at Beth Israel Deaconess Medical Center, routinely treats individuals who have been diagnosed with movement disorders. Plaintiffs disclosed Dr. Tarsy as an expert who would testify about the cause of Colleen Lyman's tardive dyskinesia and torticollis, including the relationship of metoclopramide to her injury and the potential impact of other medications that may be related to her injury.

Dr. Tarsy testified at his deposition that the development of tardive dyskinesia usually requires continuous exposure for several months. In PLIVA's view Mrs. Lyman did not take metoclopramide continuously for a period of several months, and

therefore Dr. Tarsy's opinion does not "fit" the facts of this case. *See Daubert*, 509 U.S. at 591. As this Court has indicated in its decision on Defendants' dispositive motions, whether Mrs. Lyman took metoclopramide on a daily basis for several months is a jury question. *See* Op. & Order dated July 20, 2012, at III.A., ECF No. 311. If the jury finds that Mrs. Lyman took metoclopramide continuously for a period of several months, then Dr. Tarsy's opinion will "fit" the facts of the case. If it fails to so find, then Plaintiffs will have failed to prove that metoclopramide caused her injuries, and PLIVA will be entitled to judgment.

Rule 26 of the Federal Rules of Civil Procedure requires that a witness who will be testifying as an expert must provide a written report that must contain:

> (I) a complete statement of all opinions the witness will express and the basis and reasons for them;
> (ii) the facts or data considered by the witness in forming them;
> (iii) any exhibits that will be used to summarize or support them;
> (iv) the witness's qualifications, including a list of all publications authored in the previous 10 years;
> (v) a list of all other cases in which, during the previous 4 years, the witness testified as an expert at trial or by deposition; and
> (vi) a statement of the compensation to be paid for the study and testimony in the case.

Fed. R. Civ. P. 26 (a)(2)(B).

Dr. Tarsy's report states that he agrees with the diagnosis

that Mrs. Lyman has tardive "dystonia,"[2] caused by metoclopramide. His opinion is based on his review of medical records and a video of Colleen Lyman. Dr. Tarsy's report also states that he is prepared to offer testimony on the properties of neuroleptic medications such as metoclopramide and other topics involving neuroleptic medications and tardive dyskinesia if requested. Dr. Tarsy's report is accompanied by an extensive curriculum vitae, listing his qualifications and publications and the cases in which he has provided testimony. Although his report does not list his compensation in this case, Plaintiffs submitted the information as part of their disclosure.

A party faced with a failure to disclose information required by Rule 26(a) may move to compel disclosure and for appropriate sanctions. Fed. R. Civ. P. 37(a)(3)(A). Dr. Tarsy was disclosed as a witness on August 11, 2010. He was deposed on October 25, 2011. Apparently PLIVA did not find the disclosure and report so deficient as to hamper its ability to explore through deposition the bases for Dr. Tarsy's opinion on the cause of Mrs. Lyman's condition, nor has it argued that it has suffered prejudice as a result of the alleged deficiencies. Instead, nearly seven months after the disclosure, it chooses to move to

[2] Dr. Tarsy defines tardive dystonia as "a variant of tardive dyskinesia which is well established to be caused by chronic treatment with antipsychotic drugs and metoclopramide." Tarsy Report 2, ECF No. 213-5.

exclude Dr. Tarsy's testimony in its entirety. Under the circumstances, with ample time to move for fuller disclosure and a more detailed report, and with ample time to depose the expert, any failure to disclose is harmless. *See* Fed. R. Civ. P. 37(c)(1); *see also, e.g.*, *In re Methyl Tertiary Butyl Ether (MBTE) Prods. Liab. Litig.*, 643 F. Supp. 2d 471, 482 (S.D.N.Y. 2009) (holding that deficiencies in expert report were harmless where there was no evidence of unfair surprise).

PLIVA also argues that Dr. Tarsy may not testify about "other topics," such as "the biochemical/medicinal effects and properties of neuroleptic medications, including Reglan, [and] their ability or relative propensity to cause TD . . . .," PLIVA Mem. 7-8, ECF No. 213-1, because his report did not discuss his opinions on these topics. Dr. Tarsy was deposed extensively concerning among other things, his opinions on dystonias in general, tardive dystonia, their causes, the propensities of other drugs to cause tardive dystonia, his familiarity and agreement or disagreement with the literature, and the theories about the mechanism in the brain that produces tardive dyskinesia. If Dr. Tarsy seeks to testify about additional topics that were not disclosed or about which he was not deposed, PLIVA may renew its objection to the proposed testimony at trial.

The motion to exclude the testimony of Dr. Daniel Tarsy, ECF No. 213, is therefore **denied.**

Motion to Exclude the Testimony of Suzanne Parisian, M.D.

PLIVA moves to exclude the testimony of Dr. Parisian on the grounds that her methodology is unreliable; her opinions are contrary to law; and she is not qualified or permitted to testify about a generic pharmaceutical company's legal obligations. Plaintiffs' disclosure identified Dr. Parisian as an expert in Federal Drug Administration ("FDA") rules and regulations that relate to drug companies. Dr. Parisian's 189-page report included summaries of six opinions, five of which have been rendered moot by the dismissal of the other defendants in this case. With respect to PLIVA, Dr. Parisian offers the opinion that it

> was required by the Food, Drug and Cosmetic Act to conduct pharmacovigilance, monitor the medical literature about [metoclopramide], report changes in the [metoclopramide] safety profile to FDA and voluntarily update its label to adequately warn about the increased and permanent risks of chronic [metoclopramide]. Yet, [PLIVA] continued to fail to behave as a responsible United States Pharmaceutical Manufacturer. It failed to conduct adequate pharmacovigilance and it failed to voluntarily take steps to update its [metoclopramide] label to adequately warn physicians and patients like Ms. Lyman of the unacceptable risks of chronic [metoclopramide] including tardive dyskinesia.

Parisian Report 21, ECF No. 212-4.

In *PLIVA v. Mensing*, the United States Supreme Court held that state tort claims against generic drug manufacturers for failure to provide adequate warning labels were preempted. 131 S. Ct. 2567, 2581 (2011). As a consequence, this Court dismissed

claims against PLIVA for failure to unilaterally change its label. Applying the *Mensing* holding required dismissal of negligent design and manufacturing claims as well. Op. & Order 9, ECF No. 192. Additional claims relating to a duty to monitor and report safety information were inadequately pled and also dismissed. *Id.* at 11. In its ruling on Defendants' dispositive motions, the claims against PLIVA for breach of warranties, fraud and fraudulent and negligent concealment have now also been dismissed.

One claim remains in the case against PLIVA: a product liability failure-to-warn claim based on its failure to update its label to include FDA-approved warnings against the risk of developing tardive dyskinesia with use of the drug beyond twelve weeks. Testimony about whether a generic drug manufacturer has a legal duty to conduct pharmacovigilance, monitor medical literature, report safety changes and unilaterally update its label is irrelevant, because it cannot form the basis for a state-law personal injury suit after *Mensing*. The testimony is therefore excluded under Federal Rule of Evidence 401.

Dr. Parisian is also expected to testify about the role of the FDA, the Food, Drug and Cosmetic Act, the process by which a new drug obtains FDA approval, FDA's oversight of generic drug manufacturers, "label" and "labeling" as it is used in FDA regulations, and the history of Reglan® and metoclopramide

regulation. She is qualified to give the testimony.

Dr. Parisian, a pathologist by training, is a former Chief Medical Officer at the FDA, and clinical instructor for the FDA's staff college for FDA reviewers for drug devices. She worked at the FDA for four years in a variety of capacities, and dealt with pre-market and post-market compliance issues for medical devices, on health risk assessments, product recalls, labeling, and product safety alerts. After she left the FDA in 1995 she founded a regulatory and medical consulting firm specializing in FDA regulations concerning drugs and drug devices. She has considerable experience with the FDA, its regulatory requirements and procedures, and has been permitted to testify in numerous cases involving not only medical devices but pharmaceutical products. *See, e.g.*, *Lemons v. Novartis Pharm. Corp.*, No. 3:08-CV-00361, __ F. Supp. 2d ___, 2012 WL 965977 at *5-6 (W.D.N.C. Mar. 21, 2012); *Kammerer v. Wyeth*, No. 8:04CV196, 2011 WL 5237757 at *4 (D. Neb. Nov. 1, 2011); *Forman v. Novartis Pharm. Corp.*, 794 F. Supp. 2d 382, 383 (E.D.N.Y. 2011); *In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 192 (S.D.N.Y. 2009).

The Court finds that Dr. Parisian's knowledge of the FDA's regulatory requirements will assist the jury to understand the evidence pertaining to drug approval and drug labeling requirements. Fed. R. Evid. 702(a); *see also id.* advisory committee's note (noting that it may "be important in some cases

for an expert to educate the factfinder about general principles . . . ."). Any proffered testimony from Dr. Parisian that expresses a legal conclusion or communicates a legal standard is excluded, however. *See Hygh v. Jacobs*, 961 F.2d 359, 363-64 (2d Cir. 1992) ("Whereas an expert may be uniquely qualified by experience to assist the trier of fact, [s]he is not qualified to compete with the judge in the function of instructing the jury."); *In re Rezulin Prods. Liab. Litig.*, 309 F. Supp. 2d 531, 541 (S.D.N.Y. 2004) ("[T]estimony that states a legal conclusion [will be excluded], although factual conclusions on an ultimate issue to be decided by the jury are permissible."); *see also In re Fosamax*, 645 F. Supp. 2d at 192 ("Dr. Parisian's commentary on any documents and exhibits in evidence will be limited to explaining the regulatory context in which they were created, defining any complex or specialized terminology, or drawing inferences that would not be apparent without the benefit of experience or specialized knowledge.").

The motion to exclude the testimony of Dr. Parisian, ECF No. 212, is therefore **granted in part and denied in part.**

Motion to Exclude the Testimony of James Morrison

The Plaintiffs have moved to exclude the expert testimony of James Morrison on the grounds that his opinions lack foundation, misstate the law and are based on an incorrect assumption. James Morrison, a consultant and expert in drug regulatory matters,

worked for the FDA for thirty-seven years. He chaired the committee that drafted the FDA's regulations implementing the Hatch-Waxman Amendments of 1984, which set forth the process for generic drug approval. He opines that PLIVA conformed to FDA practices, policies and procedures and with industry standards with respect to the labeling of metoclopramide. He is prepared to describe PLIVA's adverse event reporting and complaint handling obligations, and to opine that PLIVA is not obligated to monitor the literature on metoclopramide, or to send out "Dear Doctor" letters.

Plaintiffs' objections to Morrison's testimony go to its weight, not its admissibility. They do not challenge his qualifications as a regulatory expert. Contrary to their assertion, Morrison does not offer legal standards or conclusions. The Court finds that Morrison's testimony will assist the trier of fact. Plaintiffs' disagreement with his opinion that PLIVA complied with FDA requirements will undoubtedly be subject to rigorous cross-examination, but it is not grounds for exclusion of his testimony. *See Daubert*, 509 U.S. at 595 ("The focus, of course, must be solely on principle and methodology, not on the conclusions that they generate."); *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 285 (E.D.N.Y. 2007) ("The mere fact that an expert's testimony conflicts with the testimony of another expert or scientific

study does not control admissibility."); *In re Omeprazole Patent Litig.*, 490 F. Supp. 2d 381, 412 (S.D.N.Y. 2007) (quoting *McCullock v. H.B. Fuller Co.*, 61 F.3d 1038, 1044 (2d Cir. 1995)); *see also* Fed. R. Evid. 702, advisory committee's note ("[E]xperts sometimes reach different conclusions based on competing versions of the facts. The emphasis in the [rule] on 'sufficient facts or data' is not intended to authorize a trial court to exclude an expert's testimony on the ground that the court believes one version of the facts and not the other.").

The motion to exclude the testimony of James Morrison, ECF No. 224, is **denied.**

Conclusion

For the foregoing reasons, PLIVA's motions, ECF Nos. 213 and 214 are **denied**; PLIVA's motion, ECF NO. 212, is **granted in part and denied in part**. The Lymans' motion, ECF No. 224, is **denied**.

Dated at Burlington, in the District of Vermont, this 20th day of July, 2012.

/s/William K. Sessions III
William K. Sessions III
U.S. District Court Judge