IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

IN RE: LIPITOR (ATORVASTATIN CALCIUM) MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	**MDL No. 2:14-mn-02502-RMG** **CASE MANAGEMENT ORDER NO. 68** **This Order relates to all cases.**

This matter is before the Court on Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on the Issue of General Causation. (Dkt. No. 972). For the reasons stated below, the motion is GRANTED IN PART AND DENIED IN PART.

I. Background

In this MDL, Plaintiffs allege that Lipitor caused their Type 2 diabetes. "[I]n order to carry the burden of proving a plaintiff's injury was caused by exposure to a specified substance," a plaintiff must demonstrate general and specific causation. *Zellers v. NexTech Ne., LLC*, 533 F. App'x 192, 196 (4th Cir. 2013) *cert. denied*, 134 S. Ct. 911 (2014); *accord Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 263 (4th Cir. 1999). "General causation is whether a substance is capable of causing a particular injury or condition in the general population and specific causation is whether a substance caused a particular individual's injury." *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 881 (10th Cir. 2005). "Plaintiff[s] must first demonstrate general causation because without general causation, there can be no specific causation." *Id.* Here, if Lipitor is not capable of causing diabetes, it follows that it is not the cause of diabetes in particular plaintiffs.

A. Epidemiological Method for Establishing General Causation

Epidemiology provides "the primary generally accepted methodology for demonstrating a causal relation between a chemical compound and a set of symptoms or disease."[1] *In re Meridia Products Liab. Litig.*, 328 F. Supp. 2d 791, 800 (N.D. Ohio 2004), *aff'd*, 447 F.3d 861 (6th Cir. 2006); *Siharath v. Sandoz Pharm. Corp*., 131 F. Supp. 2d 1347, 1356 (N.D. Ga. 2001), *aff'd sub nom. Rider v. Sandoz Pharm. Corp*., 295 F.3d 1194 (11th Cir. 2002); *Conde v. Velsicol Chem. Corp*., 804 F. Supp. 972, 1025-26 (S.D. Ohio 1992), *aff'd*, 24 F.3d 809, 814 (6th Cir.1994).

It is well established in case law and undisputed by the parties that epidemiologists use a two-part process for determining causation. (Dkt. No. 972 at 27-28; Dkt. No. 1053 at 13); *e.g.*, *Ambrosini v. Labarraque*, 101 F.3d 129, 136 (D.C. Cir. 1996); *In re Fosamax Products Liab. Litig.*, 645 F. Supp. 2d 164, 187 (S.D.N.Y. 2009); *Giles v. Wyeth, Inc.*, 500 F. Supp. 2d 1048, 1053 (S.D. Ill. 2007). First, epidemiological studies must establish an association between exposure to a drug and a disease. (Dkt. No. 1053 at 12; Dkt. No. 972 at 27); *e.g., Ambrosini*, 101 F.3d at 136; *McMunn v. Babcock & Wilcox Power Generation Grp., Inc*., No. CIV.A. 10-143, 2013 WL 3487560, at *15 (W.D. Pa. July 12, 2013); *In re Fosamax*, 645 F. Supp. 2d at 187; *Beckwith v. Matrixx Initiatives, Inc*., 467 F. Supp. 2d 1316, 1327 (M.D. Ala.2006); *Soldo v. Sandoz Pharm. Corp.*, 244 F. Supp. 2d 434, 461 (W.D. Pa.2003); s*ee also* Reference Manual on Scientific Evidence (RMSE) 566 (3d ed. 2011) ("[T]he first question an epidemiologist

[1] In initial briefing, Plaintiffs describe the epidemiological method for proving causation as "The Scientific Method for Establishing Causation." (Dkt. No. 1053 at 13). However, they now argue that some of their experts use other reliable methods. "Epidemiological studies are not necessarily required to prove causation, as long as the methodology employed by the expert in reaching his or her conclusion is sound." *Benedi v. McNeil–P.P.C., Inc*., 66 F.3d 1378, 1384 (4th Cir.1995). To the extent that Plaintiffs' experts use other methods, they are addressed further below. However, it is useful to review the primary method for establishing general causation.

addresses is whether an association exists between exposure to the agent and disease."). An association exists between exposure to a drug and a disease when the two "occur together more frequently than one would expect by chance." RMSE at 566; *accord In re Fosamax*, 645 F. Supp. 2d at 187; (*accord* Dkt. No. 1053 at 13). In other words, an association exists when people exposed to the drug have a higher incidence of the disease and the difference is not simply due to chance. Two common ways for evaluating whether a difference between those exposed to a drug and those not exposed could have occurred simply by chance is to calculate a p-value and to calculate the confidence interval for the relative risk ratio. RSME at 576, 580.

A p-value "represents the probability that an observed positive association could result from random error even if no association were in fact present." *Id*. at 576. "To minimize false positives, epidemiologists use a convention that the p-value must fall below some selected level . . . for the results of the study to be statistically significant" and, thus, establish an association. *Id*. The most common significance level in science is .05. *Id*. at 577. Thus, generally, a study's authors will only find that an association exists between a drug and a disease if the p-value is less than .05.

A second common way to evaluate whether an observed difference is due to chance is to calculate the confidence interval for the relative risk ratio. RSME at 580. The relative risk ratio is the risk of disease among people exposed to the drug divided by the risk of the disease among those not exposed to the drug. RMSE at 627. For instance, if the risk of developing diabetes while on Lipitor is 6% and the risk of developing diabetes not on Lipitor (i.e., in a placebo group) is 4%, then the relative risk of developing diabetes for Lipitor is 6/4 or 1.5. A relative risk of 1.0 indicates no difference between the two groups; the risk in the two groups is the same (e.g., 5% divided by 5% or 20% divided by 20%). A relative risk ratio above 1 indicates an

increased risk in the exposed group, and a relative risk ratio less than one indicates a decreased risk in the exposed group.

A confidence interval is essentially a "margin of error" for the estimated relative risk ratio. *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1174 (N.D. Cal. 2007). It is the "range of possible values" for the actual relative risk ratio, given the data and pre-selected level of confidence. RMSE at 580. "So, for example, if a given study showed a relative risk of 1.40 (a 40 percent increased risk of adverse events), but the 95 percent confidence interval is .8 to 1.9, we would say that we are 95 percent confident that the true value, that is, the actual relative risk, is between .8 and 1.9." *In re Bextra & Celebrex*, 524 F. Supp. 2d at 1174. "Because the confidence interval includes results which do not show any increased risk, and indeed, show a decreased risk, that is, it includes values less than 1.0, we would say the study does not demonstrate a 'statistically significant' increased risk of an adverse outcome." *Id.*

Randomized, double-blind, clinical trials are the "gold standard" for determining whether an association exists. *Id.* at 555; (*see also* Singh Rep., Dkt. No. 972-6 at 6-7.) However, the Reference Manual on Scientific Evidence recognizes that observational studies can be sufficient to establish an association.[2] *See id.* at 217-18 ("Observational studies can establish that one factor is associated with another, but work is needed to bridge the gap between association and causation."); (*see also* Singh Rep., Dkt. No. 972-6 at 7 ("Absent such placebo-controlled trials to

[2] Observational studies "provide good evidence" where (1) "[t]he association is seen in studies with different designs, on different kinds of subjects, and done by different research groups," (2) "[t]he association holds when effects of confounding variables are taken into account by appropriate methods," and (3) "[t]here is a plausible explanation for the effect of the independent variable." RMSE at 221.

For definitions and descriptions of randomized control trials and various types of observational studies, see RMSE at 220-222, 555-565.

address this question, we rely on meta-analysis of randomized controlled trials to determine causation. Observational studies are often used in this setting.")).

"Once an association has been found between exposure to an agent and development of a disease, researchers consider whether the association reflects a true cause-effect relationship." RMSE at 597; (Dkt. No. 1053 at 14); (Dkt. No. 972 at 28); *accord Ambrosini*, 101 F.3d at 136 *McMunn*, 2013 WL 3487560, at *15. In assessing causation, epidemiologists "first look for alternative explanations for the associations, such as bias or confounding factors," and then apply the Bradford Hill factors to determine whether an association reflects a truly causal relationship. RMSE at 598-600; *see also, e.g., In re Zoloft (Sertraline Hydrochloride) Products Liab. Litig.*, 26 F. Supp. 3d 449, 454-55 (E.D. Pa. 2014), *recon. denied*, 2015 WL 314149 (E.D. Pa. Jan. 23, 2015); *McMunn*, 2013 WL 3487560, at *15; *Soldo*, 244 F. Supp. 2d at 461; *In re Neurontin Mktg., Sales Practices, & Products Liab. Litig.*, 612 F. Supp. 2d 116, 132 (D. Mass. 2009); *In re Fosamax*, 645 F. Supp. 2d at 187. These factors are (1) strength of the association, (2) replication of the findings, (3) specificity of the association, (4) temporal relationship, (5) dose-response relationship (aka biological gradient), (6) biological plausibility, (7) consistency with other knowledge (aka coherence), (8) consideration of alternative explanations, and (9) cessation of exposure.[3] RMSE at 600; *In re Zoloft*, 26 F. Supp. 3d at 454-55.

Whether an established association is causal is a matter of scientific judgment, and scientists appropriately employing this method "may come to different judgments" about whether a causal inference is appropriate. *Milward v. Acuity Specialty Products Grp., Inc.*, 639 F.3d 11, 18 (1st Cir. 2011); RMSE at 222, 598; *see also* RMSE at 552 ("Assessing whether an

[3] The Reference Manual lists slightly different "guideline" factors than Sir Bradford Hill's original factors. *Compare* RSME at 600 *with* Sir Austin Bradford Hill, The Environment and Disease: Association or Causation?, 58 Proc. Royal Soc'y Med. 295, 295-300 (1965)), *available at* Dkt. No. 972-32. However, the factors are largely the same.

association is causal requires an understanding of the strengths and weaknesses of the study's design and implementation, as well as a judgment about how the study findings fit with other scientific knowledge."). However, the authors of the Reference Manual on Scientific Evidence "emphasize that [the Bradford Hill factors] are employed only *after* a study finds an association to determine whether that association reflects a true causal relationship." RSME at 598-99 (emphasis in original); *see also, e.g., Mathews v. Novartis Pharm. Corp.*, No. 3:12-CV-314, 2013 WL 5780415, at *27 (S.D. Ohio Oct. 25, 2013) ("Unless there is a statistically significant association between the drug and the disease, the Bradford-Hill analysis to determine causation is inapplicable."); *Wagoner v. Exxon Mobil Corp.*, 813 F. Supp. 2d 771, 803 (E.D. La. 2011) ("[T]he set of criteria known as the Bradford Hill criteria has been widely acknowledged as providing an appropriate framework for assessing whether a causal relationship underlies a statistically significant association between an agent and a disease.").

B. The Court's Ruling Regarding Dosage

Lipitor is prescribed in four different doses: 10 mg, 20 mg, 40 mg, and 80 mg.[4] Plaintiffs' general causation experts initially "opine[d] that Lipitor can cause diabetes, without specifying the precise dose at which this effect begins." (Dkt. No. 1159 at 26). If a study suggested an increased risk of diabetes, the experts "ascribe[d] the risk to all doses." (*E.g.*, Dkt. No. 972 at 269.) The Court, however, was concerned as to whether Plaintiffs' experts had sufficient facts and data to support their causation opinions at all doses of Lipitor, and even whether the experts would be willing to offer an opinion at low doses, given the available data. *See In re Seroquel Products Liab. Litig.*, No. 6:06-MD-1769-ORL-22D, 2009 WL 3806434, at *18 (M.D. Fla. June 18, 2009) (Expert offering a causation opinion "declined to even speculate"

[4] At times, Plaintiffs have referred to these doses as "therapeutic" doses of Lipitor.

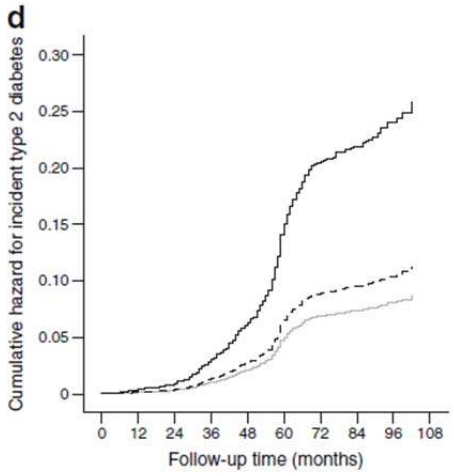
about doses of 12.5 and 25 milligrams "because she had not seen any studies evaluating doses that low."); *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1175-76 (N.D. Cal. 2007) ("It is unsurprising that most of plaintiffs' experts agree that the available evidence at 200 mg/d is inadequate to prove causation," where there were no randomized controlled trials, meta-analyses, or observational studies that found an association between Celebrex 200 mg/d and a risk of heart attack or stroke.). The Plaintiffs' experts agreed, and some even emphatically argued, that there was a dose-response relationship, meaning that any risk of diabetes is higher at higher doses of Lipitor. (*See* Pls. Br., Dkt. No. 1159 at 26 (arguing their "experts *did* find a dose-response relationship" (emphasis in original)). And the data with regard to 80 mg of Lipitor was starkly different from the data with regard to 10 mg of Lipitor.

Starting with randomized controlled trials, a post hoc analysis of data from the randomized clinical trial SPARCL found a statistically significant increase in the risk of diabetes for patients randomized to 80 mg of Lipitor versus those on placebo, (Dkt. No. 972-29 at 2), and a post hoc analysis of the randomized clinical trial TNT that found a statistically significant increased risk of diabetes for patients randomized to 80 mg of Lipitor versus those on 10 mg of Lipitor, (Dkt. No. 1449-2 at 7; Dkt. No. 1159-10).[5] In contrast ASCOT, the only randomized

[5] Another post hoc analysis of TNT found that the risk difference between 80 mg and 10 mg was not statistically significant. (Dkt. No. 972-29 at 2.) The difference between the two studies was the definition of diabetes used. The definition used by the Waters study, which did not find a statistically significant difference, was "more restrictive . . . than standard criteria" for diagnosing diabetes. (Dkt. No. 1449-2 at 6-7). The Court makes no value judgments with regard to relative benefits or limitations of the Preiss and Waters studies, but only notes that at least one of them had a statistically significant finding. *See In re Avandia Mktg., Sales Practices & Products Liab. Litig.*, No. 2007-MD-1871, 2011 WL 13576, at *9 (E.D. Pa. Jan. 4, 2011) ("Although [the expert] did cite to studies in which the results were not statistically significant, his conclusions did not rest on those studies alone; rather, they were used to bolster the conclusions he drew from studies in which the findings were statistically significant.").

controlled clinical trial with diabetes as a pre-specified endpoint compared 10 mg of Lipitor to placebo and found ***no*** statistically significant difference between the two groups with regard to the incidence of new-onset diabetes. (Dkt. No. 972-26 at 6). In ASCOT, 2.4% of the placebo group developed diabetes, compared to 3.0% of the Lipitor group. (Dkt. No. 972-26 at 6). The study authors stated that "the difference[] [was] based on a small number[] of events and are probably the result of chance variation." (*Id*. at 7-8).

Turning to observational studies, Cederberg (2015) found a statistically significant increased risk of diabetes in patients taking 20 mg or 40 mg of Lipitor versus placebo, but found no such association at 10 mg of Lipitor. (Dkt. No. 1159-1 at 4, 6). The difference in the incidence of new-onset diabetes at 10 mg of Lipitor versus the mid-doses (20 mg & 40 mg) of Lipitor in Cederberg is quite telling:



In this graph, labelled "Risk by dose of atorvastatin," the grey line is the incidence of new-onset diabetes in the no-statin treatment group, the dotted line is the incidence of new-onset diabetes in the 10 mg/day group, and the black line is the incidence of diabetes in the mid-dose group of 20 mg & 40 mg/day. (Dkt. No. 1159-1 at 6). This graph shows why the Reference Manual on Scientific Evidence warns that "a risk estimate from a study that involved a greater exposure is not applicable to an individual exposed to a lower dose." RMSE at 613 n.196.

The Carter (2013) observational study found a statistically significant association between diabetes and moderate and high dose statins, a group that included 20 mg, 40 mg, and 80 mg of Lipitor, compared to low dose statins, which included 10 mg of Lipitor. (Dkt. No.

1159-15 at 5). This study may support a causation opinion at higher doses of Lipitor but not at 10 mg; the study specifically finds that the risk, if any, from lower dose statins, including Lipitor 10 mg, is meaningfully different from the risk at higher dose statins.

Another observational study, Culver (2012), found a statistically significant increase in diabetes risk for those on Lipitor versus placebo, but did not break down data by dose or disclose the doses taken by participants. (Dkt. No. 1159-16 at 6). Given Plaintiffs experts' testimony that the effect of Lipitor is dose-dependent, this study may support a causation opinion at the highest dose of Lipitor but not at lower ones. Any observed effect might be the result of high doses of Lipitor in the study. *See* RMSE at 613 n.196 ("[A] risk estimate from a study that involved a greater exposure is not applicable to an individual exposed to a lower dose."). The only meta-analysis in the record that looks at the effect of Lipitor by dose, Navarese (2013), did not find a statistically significant association at 80 mg or 10 mg of Lipitor.[6] (Dkt. No. 972-48 at 6, 7).

Finally, a study conducted by Dr. Quon and his colleagues regarding the metabolic effects of Lipitor found statistically significant increases in insulin sensitivity and HbA1C at 20 mg, 40 mg, and 80 mg of Lipitor, but not at 10 mg.[7] (Dkt. No. 1159-17 at 6, Figures 2, 3). Plaintiffs' experts readily admit that these endpoints are not equivalent with new-onset diabetes. (*See, e.g.*, Dkt. No. 1440-6 at 40 (insulin resistance not a valid surrogate for Type II diabetes); *id.* at 40-41 (a person can have high levels of insulin resistance without having Type II diabetes); *id.* at 42 ("Insulin resistance doesn't tell you anything about glycaemia."); *id.* at 184 (a patient can display hyperglycemia "without frank diabetes")). And the Court agrees that these metabolic

[6] This meta-analysis looked at a number of clinical trials involving statins, but only two of these trials involved data for 10 mg of Lipitor: ASCOT and TNT. (Dkt. No. 972-48 at 4).

[7] The study found no increases in blood glucose levels at any dosage. (Dkt. No. 1159-17 at 4). As explained below, other studies do not find any association between these metabolic effects and Lipitor.

studies cannot substitute for studies showing an association between the drug and the disease Plaintiffs allege was caused by the drug—diabetes. However, they are still relevant to the second step of an epidemiological causation opinion; for example, Dr. Singh considers this information with regard to the biological plausibility Bradford Hill factor. The Cederberg observational study also found a statistically significant increase in insulin sensitivity and insulin secretion for patients on 20 mg or 40 mg of Lipitor. (Dkt. No. 1159-1 at 8). For 10 mg of Lipitor, the study found a statistically significant difference in insulin sensitivity versus placebo but not in insulin secretion. (*Id.*).

In sum, several studies show a statistically significant association between exposure to higher doses of Lipitor (20 mg, 40 mg, or 80 mg daily) and new-onset diabetes. But Plaintiffs cannot point to a single study that shows an association between 10 mg of Lipitor and new-onset diabetes. (Dkt. No 1460 at 27). All three studies to specifically consider 10 mg—a clinical trial (ASCOT), an observational study (Cederberg), and a meta-analysis (Navarese)—all find no statistically significant difference in the incidence of new-onset diabetes between 10 mg of Lipitor and placebo. (Dkt. No. 1460 at 11). The Koh (2010) study on metabolic effects similarly found some effects at higher doses but not low doses of Lipitor.

After a review of this data and a detailed review and discussion of the relevant case law, the Court held that "at least where the experts agree that there is a dose-response relationship and where there is evidence that an association no longer holds at low doses, dose certainly matters, and Plaintiffs must have expert testimony that Lipitor causes, or is capable of causing, diabetes at particular dosages." (CMO 49, Dkt. No. 1197 at 11). None of Plaintiffs' experts had provided such opinions. However, over Defendant's strenuous objection, the Court reopened discovery and allowed Plaintiffs' experts to submit supplemental reports addressing whether Lipitor causes

diabetes at particular dosages. (*Id.*). Those supplemental reports have been issued, the experts' depositions have been taken again, the parties have submitted supplemental briefing to the Court on whether these opinions should be excluded under Rule 702, additional oral argument has been held, and Pfizer's motion to exclude Plaintiffs' expert testimony on general causation is ripe for this Court's review.

II. Legal Standard

Under Rule 104(a) and 702, "the trial judge must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable." *Daubert v. Merrell Dow Pharm., Inc*., 509 U.S. 579, 589 (1993). Thus, the trial court must ensure that (1) "the testimony is the product of reliable principles and methods," that (2) "the expert has reliably applied the principles and methods to the facts of the case," and (3) that the "testimony is based on sufficient facts or data." Fed. R. Evid. 702(b), (c), (d). "This entails a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid," *Daubert*, 509 U.S. at 592-93, and whether the expert has "faithfully appl[ied] the methodology to facts." *Roche v. Lincoln Prop. Co.*, 175 F. App'x 597, 602 (4th Cir. 2006).

Factors to be considered include "whether a theory or technique . . . can be (and has been) tested," "whether the theory or technique has been subjected to peer review and publication," the "known or potential rate of error," the "existence and maintenance of standards controlling the technique's operation," and whether the theory or technique has garnered "general acceptance." *Daubert*, 509 U.S. at 593-94; *accord United States v. Hassan*, 742 F.3d 104, 130 (4th Cir. 2014). However, these factors are neither definitive nor exhaustive, *United States v. Fultz*, 591 F. App'x 226, 227 (4th Cir. 2015), *cert. denied*, 135 S. Ct. 2370 (2015), and "merely illustrate[] the types of factors that will bear on the inquiry." *Hassan*, 742 F.3d at 130. Courts have also considered

whether the "expert developed his opinions expressly for the purposes of testifying," *Wehling v. Sandoz Pharm. Corp.*, 162 F.3d 1158 (4th Cir. 1998), or through "research they have conducted independent of the litigation," *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995) (on remand), and whether experts have "failed to meaningfully account for . . . literature at odds with their testimony." *McEwen v. Baltimore Washington Med. Ctr. Inc.*, 404 F. App'x 789, 791-92 (4th Cir. 2010).

Rule 702 also requires courts "to verify that expert testimony is 'based on sufficient facts or data.'" *E.E.O.C. v. Freeman*, 778 F.3d 463, 472 (4th Cir. 2015) (quoting Fed. R. Evid. 702(b)). Thus, "trial judges may evaluate the data offered to support an expert's bottom-line opinions to determine if that data provides adequate support to mark the expert's testimony as reliable." *Id.* The court may exclude an opinion if "there is simply too great an analytical gap between the data and the opinion offered." *Id.* "The proponent of the [expert] testimony must establish its admissibility by a preponderance of proof." *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 199 (4th Cir. 2001).

The Court is mindful that the *Daubert* inquiry involves "two guiding, and sometimes competing, principles." *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 261 (4th Cir. 1999). "On the one hand . . . Rule 702 was intended to liberalize the introduction of relevant expert evidence," *id.*, and "the trial court's role as a gatekeeper is not intended to serve as a replacement for the adversary system." *United States v. Stanley*, 533 F. App'x 325, 327 (4th Cir. 2013), *cert. denied*, 134 S. Ct. 1002 (2014). On the other, "[b]ecause expert witnesses have the potential to be both powerful and quite misleading, it is crucial that the district court conduct a careful analysis into the reliability of the expert's proposed opinion." *United States v. Fultz*, 591 F.

App'x 226, 227 (4th Cir. 2015), *cert. denied*, 135 S. Ct. 2370 (2015); *accord Westberry*, 178 F.3d at 261.

III. Dr. Singh

Dr. Singh is an epidemiologist and an Assistant Professor of Medicine at Johns Hopkins University.[8] (Dkt. No. 972-6 at 3-4, 43). He used the standard epidemiological method described above to reach his conclusions in his initial report. (*See* Dkt. No. 972-6). Dr. Singh performed a systematic literature search, where he (1) determined, *a priori*, characteristics of studies that he would include for consideration; (2) searched the databases PUBMED and CLINICAL TRIALS for a specified time frame using the search terms "statins" and "diabetes"; and (3) reviewed each study that met his pre-specified criteria. (Dkt. No. 972-6 at 8-9, 10). Dr. Singh discussed the resulting studies, conducted his own meta-analysis, and noted that multiple studies found a statistically significant association between statins and incident diabetes. (*Id*. at 10-26, 28-30). After finding that "statins are associated with diabetes disease development," Dr. Singh then turned to the question of causation. (*Id*. at 34). He applied the Bradford Hill factors, considered alternative hypotheses and limitations, and concluded that, "within a reasonable degree of medical and scientific certainty that statins as a class, including atorvastatin, are causally linked with type 2 diabetes." (*Id*. at 34-42, 42).

Pfizer attacks Dr. Singh's methodology, alleging he did not properly consider the progression of the diabetes disease process, improperly ignored the small size of the alleged risk, did not appropriately address biological plausibility, and did not appropriately adjust for confounding factors. (Dkt. No. 972 at 13, 17, 30-31, 31-32, 34, 49). The Court denies Pfizer's motion based on these grounds. The application of Bradford Hill is a well-recognized method

[8] Defendant does not object to Dr. Singh's qualifications as an epidemiologist.

for determining causation, *Knight v. Kirby Inland Marine, Inc*., 363 F. Supp. 2d 859, 863 (N.D. Miss. 2005), and Dr. Singh did consider and weigh biological plausibility and the size of the association at issue. (Dkt. No. 972-6 at 36, 39). That Pfizer's experts may disagree about the biological plausibility piece or weigh the small size of the association differently than Dr. Singh is a matter of scientific judgment and a matter for cross-examination, not exclusion of Dr. Singh's testimony.

Pfizer also argues that Dr. Singh lacks sufficient facts and data to support his causation opinion at doses less than 80 mg. (Dkt. No. 972 at 49-52). Dr. Singh testified that "there's a dose responsiveness," and that "it's clearly possible that [a] drug has an effect at higher dose, but no effect at lower dose." (Singh Depo. at 70; Dkt. No. 972-3 at 162). However, he did not look at the effect of different dosages of Lipitor, and if a study showed an increased risk of diabetes, he simply "ascribe[d] the risk to all doses." (Dkt. No. 972-3 at 269). Ascribing the risk of high doses of a drug to low doses is improper, particularly where there is dose responsiveness. *See* RMSE at 613 n.196 ("[A] risk estimate from a study that involved a greater exposure is not applicable to an individual exposed to a lower dose."). As explained above, the Court held that in the context of this case, experts had to provide opinions with regard to specific doses and allowed Dr. Singh to serve a supplemental report that addressed whether Lipitor could cause diabetes at various dosages. (CMO 49, Dkt. No. 1197). The Court now turns to whether Dr. Singh has sufficient facts and data to support his opinions at various dosages and to Dr. Singh's methodology in his supplemental report.

A. 80 mg

Dr. Singh's 80 mg opinion is supported by SPARCL/Waters (statistically significant increase in new-onset diabetes in Lipitor 80 mg group vs. placebo), TNT (statistically significant

increase in new-onset diabetes in Lipitor 80 mg group versus Lipitor 10 mg group according to Preiss study but not statistically significant increase according to Waters study), Waters (2013) (pooled post hoc analysis of TNT and IDEAL, finding a statistically significant increase in diabetes in Lipitor 80 mg group vs. comparator (either 10 mg or simvastatin)), Carter observational study (statistically significant increased risk of new-onset diabetes in high and moderate dose statin users compared to low dose statin users), Cederberg observational study (which, according to Dr. Singh, provides evidence of biological plausibility), Koh (2010) article (which, according to Dr. Singh, "suggest[s] that insulin resistance may be one possible biological mechanism for atorvastatin to cause diabetes"), and the NDA data and safety updates (which, according to Dr. Singh, "suggest clinically significant increase in blood glucose elevation" and "establishes coherence between this data and the epidemiologic studies"). (Dkt. No. 1449-2 at 26-27, 31-32).

The Court finds that Dr. Singh's opinion that Lipitor at 80mg/day can cause diabetes supported by sufficient facts and data and admissible under Rule 702. First, studies have found a statistically significant increase in the risk of diabetes in patients taking 80 mg of Lipitor, satisfying the first step of the epidemiological method for determining causation. Second, Dr. Singh applied the Bradford Hill factors and, based on his scientific judgment, determined that 80 mg of Lipitor is causally related to Type 2 diabetes. That Pfizer disagrees with the opinion is no reason to exclude it. It is not the Court's role to determine whether Dr. Singh is correct, only whether his opinion is based on sufficient facts and data and reliable.

B. 10 mg

Dr. Singh states that his opinion that 10 mg of Lipitor is capable of causing diabetes is based on (1) ASCOT, (2) data from SPARCL and TNT, (3) the Clinical Safety Updates from

1999 and 2001, (4) Koh (2010), and (5) the fact that "[r]egulatory labels do not distinguish between various does of atorvastatin and diabetes." (Dkt. No. 1449-2 at 28-31, 32-33). None of this evidence establishes an association between 10 mg of Lipitor and diabetes.

Dr. Singh states that based on ASCOT alone, "one can neither confirm nor deny that atorvastatin 10 mg is associated with a significantly increased risk of type 2 diabetes." (Dkt. No. 1449-2 at 32). He testifies that there are two possible reasons that ASCOT did not find a statistically significant association: "One is obviously low power. The other is no risk exists. I mean, you know, let's not forget that. I mean, that is also possible." (Dkt. No. 1440-5 at 190). When asked how he knew the finding in ASCOT was due to low power, rather than the due to the fact that no association exists, Dr. Singh testified, "I don't know that . . . I am not saying that, you know, I know that is true. I mean, both possibilities, that's why my report states that, you know, only there is a direction of effect."[9] (*Id*.)

With regard to SPARCL and TNT, Dr. Singh conducted an indirect treatment comparison of Lipitor 10 mg, Lipitor 80 mg, and placebo to determine an adjusted indirect estimate of a hazard ratio for Lipitor 10 mg versus placebo. (Dkt. No. 1449-2 at 28-29). He found an estimated hazard ratio of 1.25 that was not statistically significant (confidence interval of 0.93-1.66). (*Id*. at 29). Thus, this finding, like that of ASCOT, Cederberg, and Navarese[10] suggests

[9] Dr. Singh testifies that because we simply do not know whether there is a risk at 10 mg or not according to ASCOT, the study does not "exonerate" Lipitor 10 mg and prove that it is "safe." (Dkt. No. 1440-5 at 190). While true, "[i]t is important to recall . . . that the burden is on Plaintiffs to show that well-conducted epidemiological studies do show a statistically significant relationship . . . . It is not Defendant's burden to show the lack of such relationship." *Siharath v. Sandoz Pharm. Corp*., 131 F. Supp. 2d 1347, 1358 (N.D. Ga. 2001), *aff'd sub nom. Rider v. Sandoz Pharm. Corp*., 295 F.3d 1194 (11th Cir. 2002).

[10] Dr. Singh did not mention Cederberg or Navarese, both of which found no statistically significant association at 10 mg, in the 10 mg section of his report. In his report, he states that "[t]here are no observational studies that directly report on the risk of diabetes associated with

that either these studies are not sufficiently powered to detect a difference in the 10 mg group, or that "no risk exists." (Dkt. No. 1440-5 at 190).

Dr. Singh relies on the Clinical Safety Updates and the Koh study only for his analysis as to biological plausibility, one of the Bradford Hill factors; he does not rely on them to establish an association between 10 mg of Lipitor and diabetes. (Dkt. No. 1440-5 at 328-329).

With regard to the FDA label, the decision by the FDA to require warnings on a drug label, standing alone, does not suffice to establish causation.[11] *In re Neurontin Mktg., Sales Practices, & Products Liab. Litig.*, 612 F. Supp. 2d 116, 137 (D. Mass. 2009). As the Neurontin court explained,

> It is widely recognized that, when evaluating pharmaceutical drugs, the FDA often uses a different standard than a court does to evaluate evidence of causation in a products liability action. Entrusted with the responsibility of protecting the public from dangerous drugs, the FDA regularly relies on a risk-utility analysis, balancing the possible harm against the beneficial uses of a drug. Understandably, the agency may choose to "err on the side of caution," *Rider*, 295 F.3d at 1201, and take regulatory action such as revising a product label or removing a drug from the marketplace "upon a lesser showing of harm to the public than the preponderance-of-the-evidence or more-like-than-not standard used to assess tort liability." *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1250 (11th Cir. 2005) (quoting *Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 991 (8th Cir. 2001)). In fact, FDA regulations provide that the agency can issue an Alert or warning label even before causation is established, (Hr'g Tr. 128–9, June 19, 2008 (Blume)), and the agency has, in a recent guidance document, stated that it has "begun taking a more comprehensive approach to making information on

---

atorvastatin 10 mg." (Dkt. No. 1449-2 at 29). However, in deposition, he admits this is "erroneous" because Cederberg, an observational study, did directly report on the risk of diabetes associated with Lipitor 10 mg and found no statistically significant association. (Dkt. No. 1440-5 at 245).

[11] The Court also notes that the FDA did not require a warning that Lipitor or statins caused diabetes but that "[i]ncreases in HbA1c and fasting serum glucose levels have been reported with HMG-Co-A reductase inhibitors, including Lipitor." (Dkt. No. 970-28 at 7.). While increased blood glucose levels are related to diabetes, experiencing an increase in glucose levels is not synonymous with developing diabetes. (*See, e.g.*, Dkt. No. 1440-6 at 184 (a patient can display hyperglycemia "without frank diabetes")).

> potential drug risks available to the public earlier." (FDA Amicus Br. 2) (quoting Guidance: Drug Safety Information–FDA's Communication to the Public (March 2007)). This earlier disclosure allows "healthcare professionals and patients [to] ... consider the information when making decisions about medical treatment" even when there may be "uncertainties in the data." *Id.* at 3. As such, the decision by the FDA to require warnings on a drug label, without more, does not suffice to establish causation.

In re Neurontin, 612 F. Supp. 2d at 136-37.

Plaintiffs argue that while none of this evidence alone might be sufficient for a causation opinion, that taken together, there is "smoke," and that behind the smoke, "there is, after all a fire." (Dkt. No. 1395 at 4). To be sure, it is possible for the entirety of the evidence to support an opinion even when individual pieces of evidence are not sufficient in isolation, but it is also possible that multiple pieces of insufficient evidence add up to insufficient evidence. For example, the Supreme Court upheld the exclusion of expert testimony in *General Electric Co. v. Joiner,* where the experts relied on, among other things, four epidemiological studies. 522 U.S. 136, 145 (1997). In one of these studies, the authors of the study were unwilling to state that exposure had caused the disease. In another, the results were not statistically significant, and in the other two, clear confounding factors were present. *Id.* at 145-46. The Supreme Court held that the district court concluded "that there [was] simply too great an analytical gap between the data and the opinion proffered," and that the district court "did not abuse its discretion in so doing." *Id.* at 146. Despite having four studies that arguably provided "smoke" for the plaintiff's theory, the Supreme Court found that the experts' opinions were "connected to existing data only by the *ipse dixit* of the expert." *Id.*

The critical guide for the Court in determining whether the evidence, taken as a whole, is sufficient to support an opinion under Rule 702 is whether it would be sufficient in the relevant field or is sufficient under the applied methodology. After all, the object of *Daubert* is to ensure

that an expert "employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999).

Thus, the question before this Court is whether this evidence is sufficient for a causation opinion under the epidemiological/Bradford Hill method. In other words, has Dr. Singh "reliably applied" the Bradford Hill method to reach a causation opinion at 10 mg. The Court finds that he has not. It is undisputed by the parties that Step 1 of this methodology is to look at whether an association exists, whether two variables "occur together more frequently than one would expect by chance." RMSE at 566. While a causation opinion need not be based on epidemiological studies, *Benedi v. McNeil-P.P.C., Inc.*, 66 F.3d 1378, 1384 (4th Cir.1995), it is well established that the Bradford Hill method used by epidemiologists ***does*** require that an association be established through studies with statistically significant results.[12] *See, e.g.*, *Mathews v. Novartis Pharm. Corp.*, No. 3:12-CV-314, 2013 WL 5780415, at *27 (S.D. Ohio Oct. 25, 2013) ("Unless there is a statistically significant association between the drug and the disease, the Bradford-Hill analysis to determine causation is inapplicable."); *McMunn*, 2013 WL 3487560, at *15 ("Step one looks to whether there is a statistically significant association between a substance and a specific disease. . . . If no association between the exposure and the disease is supported by the scientific literature, there is no basis to find a causal relationship exists and the analysis should end there."); *Frischhertz v. SmithKline Beecham Corp.*, No. CIV.A. 10-2125, 2012 WL 6697124, at *3 (E.D. La. Dec. 21, 2012) ("The Bradford-Hill criteria can only be applied after a statistically significant association has been identified."); *Wagoner*,

[12] *Milward v. Acuity Specialty Products Grp., Inc.*, 639 F.3d 11 (1st Cir. 2011), on which Plaintiffs rely, is no exception. There, the expert "noted that ***epidemiological studies have found a statistically significant increased incidence of AML in benzene-exposed workers*** and have identified a dose-response relationship." *Id.* at 19 (emphasis added).

813 F. Supp. 2d at 803 ("[T]he set of criteria known as the Bradford Hill criteria has been widely acknowledged as providing an appropriate framework for assessing whether a causal relationship underlies a statistically significant association between an agent and a disease."); *In re Fosamax*., 645 F. Supp. 2d at 188 ("Several courts that have considered the question have held that it is not proper methodology for an epidemiologist to apply the Bradford Hill factors without data from controlled studies showing an association."); *Soldo*, 244 F. Supp. 2d at 461 ("[A]pplication of the Bradford Hill criteria depends first upon an association by epidemiology between a disease and an exposure to an agent. The association must rule out chance.").

Courts exclude expert testimony that attempts to start at step two, applying the Bradford Hill criteria without adequate evidence of an association. For example, in *Dunn v. Sandoz Pharm. Corp*., 275 F. Supp. 2d 672 (M.D.N.C. 2003), there was no epidemiological study demonstrating an association between the drug Parlodel and stroke, but Plaintiff argued that her expert could apply the Bradford Hill criteria without such a study and survive *Daubert*. The court excluded the expert's Bradford Hill testimony finding that according to scientific literature, the Reference Manual, and case law, Bradford Hill is used to evaluate "whether an association shown by a study establishes causation." *Id*. at 679. Thus, without a study establishing an association, the court found Plaintiff's expert had "not demonstrated the utilization of a reliable scientific methodology." *Id*.; *see also In re Bausch & Lomb, Inc. Contact Lens Sol. Products Liab. Litig*., No. CIV A 2:06MN77777DCN, 2009 WL 2750462, at *12 (D.S.C. Aug. 26, 2009) (holding tests that suggest biological plausibility were "insufficient to demonstrate causation, and unreliable under *Daubert*, absent evidence establishing an association between MoistureLoc and non-Fusarium infections"); *Perry v. Novartis Pharm. Corp*,564 F. Supp. 2d 452, 468 (E.D. Pa. 2008) ("[N]on-existence of good data does not allow expert witnesses to speculate or base their

conclusions on inadequate supporting science. In cases where no adequate study shows the link between a substance and a disease, expert testimony will generally be inadmissible, even if there are hints in the data that some link might exist.").

Other courts have reached the same conclusion:

> [T]he Court concludes that the Bradford-Hill criteria were developed for the purposes of determining whether, when an association between an exposure and a disease has already been demonstrated, that association is causal or not. Review of the criteria themselves, as set forth in the seminal remarks of Dr. Bradford-Hill, shows that an epidemiologic foundation is a prerequisite for application of his criteria. "The Bradford-Hill criteria start with an association demonstrated by epidemiology and then apply such criteria as the temporal sequence of events, the strength of the association, the consistency of the observed association, the dose-response relationship, and the biologic plausibility of the observed association." *In re Breast Implant Litig.*, 11 F. Supp. 2d at 1233 n. 5. Accordingly, because plaintiff's experts have not demonstrated any statistically-significant epidemiologic study showing an increased risk of postpartum stroke in women using Parlodel, application of the Bradford-Hill criteria is unwarranted.

Soldo v. Sandoz Pharm. Corp., 244 F. Supp. 2d 434, 569 (W.D. Pa. 2003); *see also Frischhertz v. SmithKline Beecham Corp.*, No. CIV.A. 10-2125, 2012 WL 6697124, at *3 (E.D. La. Dec. 21, 2012) ("Because there is no data showing an association between Paxil and limb defects, no association existed for Dr. Goldstein to apply the Bradford-Hill criteria. Hence, Dr. Goldstein's general causation opinion is not reliable.").

In the *Zoloft* MDL, Plaintiffs' general causation expert relied on multiple studies that showed a positive association but were not statistically significant. The court noted that "in the field of epidemiology, the generally accepted method for determining whether a substance is a potential teratogen is to look for statistically significant associations between medication exposure and a pattern of birth defects, which are consistent and replicated across epidemiological studies, and to then apply the Bradford Hill criteria." *In re Zoloft (Sertraline Hydrochloride) Products Liab. Litig.*, 26 F. Supp. 3d 449, 455 (E.D. Pa. 2014). The court stated

that while epidemiology is not a novel form of scientific expertise, the expert's "reliance on trends in non-statistically significant data to draw conclusions about teratogenicity, rather than on replicated statistically significant findings, *is* a novel methodology." *Id*. at 456 (emphasis in original). The court concluded that "Dr. Berard has failed to demonstrate that her reliance on non-statistically significant findings is accepted within her scientific community," and the court excluded her opinion. *Id*. at 457; *see also Rosen v. Ciba–Geigy Corp*., 78 F.3d 316, 319 (7th Cir. 1996) ("The courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it.").

Similarly here, Plaintiffs have failed to demonstrate that Dr. Singh's reliance on non-statistically significant "trends" is accepted in his field, that non-statistically significant findings have served as the basis for any epidemiologist's causation opinion in peer-reviewed literature, or that standards exist for controlling the technique's operation (e.g., are "trend" opinions only allowed for certain p-values or for small confidence intervals?). These *Daubert* factors all suggest a lack of reliability. Even more to the point, Dr. Singh, himself, testifies that a lack of statistical significance means that either a study has "low power" or "no risk exists," and that he "does not know" which of these possibilities is the case. (Dkt. No. 1440-5 at 190). Thus, his own testimony demonstrates that studies without statistical significance are insufficient to support a causation opinion.

Under these circumstances, the Court finds that Dr. Singh's 10 mg opinion is not based on sufficient facts and data and that he did not reliably apply the epidemiological/Bradford Hill

method, which requires at the outset a statistically significant association before applying the Bradford Hill factors to make a judgment about whether the observed association is causal.[13]

C. 20 mg and 40 mg

Given the data described above, the Court thought that it might be possible for an epidemiologist to determine that Lipitor 20 mg and Lipitor 40 mg were capable of causing diabetes, even if there was not sufficient evidence for an opinion about Lipitor 10 mg. Unlike Lipitor 10 mg, at least one study, Cederberg, has found a statistically significant association between Lipitor 20 mg and 40 mg and diabetes. Also unlike 10 mg, the Koh study found statistically significant increases in insulin sensitivity and HbA1C at 20 mg, 40 mg, and 80 mg. (Dkt. No. 1159-17 at 6, Figures 2, 3). However, Dr. Singh testifies that he cannot reach an opinion about whether 20 mg and 40 mg of Lipitor causes diabetes without the conclusion that 10 mg of Lipitor causes diabetes. (Dkt. No. 1440-5 at 71). His opinion that Lipitor 20 mg and Lipitor 40 mg causes diabetes is an inference based on the fact that Lipitor 10 mg and Lipitor 80mg causes diabetes: "[i]t is difficult to imagine how atorvastatin 10 mg and 80 mg can increase the risk of diabetes without similar risk seen with atorvastatin 20 mg and 40 mg." (Dkt. No. 1449-2 at 34).

The Court initially thought Dr. Singh's opinion might be based on a mistake of fact. When asked what studies produce a statistically significant finding that Lipitor 20 mg or Lipitor 40 mg increases the risk of Type 2 diabetes, Dr. Singh responded, "None," despite the fact that

[13] Even if Dr. Singh's Lipitor 10 mg causation opinion were not excluded under Rule 702, it may not be sufficient evidence for 10 mg Plaintiffs to survive summary judgment. *See Wheelahan v. G D Searle & Co.*, 814 F.2d 655 (table), 1987 WL 267679 at *3 (4th Cir. 1987) ("The court cannot properly draw any conclusions about the increased risk when that increase is not statistically significant. Dr. Daling's epidemiological evidence therefore was insufficient to support a verdict in favor of the plaintiffs.").

Cederberg made such a finding. (Dkt. No. 1440-5 at 70; *see also id*. at 110 (incorrectly testifying that Lipitor 10 mg was the reference group)[14]; *id*. at 245 (same); Dkt. No. 1449-2 at 27 (incorrectly reporting that "low dose atorvastatin" was the reference group)). However, at oral argument, Plaintiffs' counsel repeatedly assured the Court that Dr. Singh's statement in his deposition was referring to the fact that no ***clinical*** trials reported a statistically significant finding with regard to 20 mg and 40 mg of Lipitor. (Dkt. No. 1460 at 21-23). Plaintiffs' counsel stated that Dr. Singh understood that Cederberg, an observational study, found a statistically significant association at Lipitor 20 mg and Lipitor 40 mg. (*Id*. at 22). However, counsel insisted that, notwithstanding this knowledge, Dr. Singh did not have sufficient data concerning Lipitor 20 mg or Lipitor 40 mg to form an opinion regarding whether those doses are capable of causing diabetes unless he could rely on his opinion that Lipitor 10 mg caused diabetes. (Dkt. No. 1384 at 6; Dkt. No. 1460 at 23). Because the Court has disallowed Dr. Singh's causation opinion for Lipitor 10 mg, for the reasons set forth above, Dr. Singh, by his own testimony, is unable to offer a causation opinion regarding Lipitor 20 mg or Lipitor 40 mg.

IV. Dr. Quon

Dr. Quon is an endocrinologist and diabetes expert. He has a Ph.D. in Biomedical Engineering and an M.D. (Dkt. No. 972-42 at 2). He has previously worked at the NIH and as a professor at the University of Maryland School of Medicine. (*Id*. at 2, 3; Dkt. No. 1440-6 at 88-89). The "overarching goal" of Dr. Quon's research "is to understand molecular mechanisms of insulin action, insulin resistance, and endothelial dysfunction as they related to diabetes, obesity and their cardiovascular complications." (Dkt. No. 972-42 at 4).

[14] The reference group in Cederberg was the non-statin group. (Dkt. No. 1159-1 at 5). The high dose and low dose groups were not directly compared. (*See generally*, Dkt. No. 1159-1).

A. Dr. Quon's Qualifications in Epidemiology

Dr. Quon, however, is not an expert in epidemiology, (Dkt. No. 1440-6 at 17), and his deposition highlights the fact that he is unfamiliar with basic principles of the field. For example, Dr. Quon testifies that Cederberg is a clinical trial and interventional study, not an observational study. (*Id*. at 163-64). Dr. Singh testifies that Dr. Quon is incorrect on this point, that Cederberg is an observational study, and that he "would be out of this business" if he thought otherwise.[15] (Dkt. No. 1440-5 at 48-49). As another example, Dr. Quon has never heard of the phrase "confounding by indication." (Dkt. No. 1440-6 at 258). Dr. Singh testifies that confounding by indication "is a well-recognized issue that epidemiologists . . . take into account when evaluating observational data," that the phrase is "very common" in the field, and that epidemiologists always address confounding by indication "to the extent possible," though most observational studies "cannot eliminate it." (Dkt. No. 1440-5 at 61).

Dr. Quon also testifies that in clinical trials, the patient's own baseline is a "more important and better control" than a placebo group. (Dkt. No. 1440-6 at 214; *see also id.* at 209-10 ("[T]he patient's own baseline, and the patient actually is, in some sense, his own control, which is a better control that placebo."); *id*. at 225 ("[T]he most relevant comparison is not to placebo, but to the patient's own baseline.")). He testifies that with regard to clinical trials, "I agree that the lack of a placebo is not as strong as having a placebo plus the baseline, but having the baseline alone without the placebo is already quite strong." (*Id*. at 210). Thus, even though he acknowledges that the risk of diabetes goes up with age, (*Id*. at 216-17), Dr. Quon seems to

[15] Dr. Quon also appears to believe Cederberg compared Lipitor users to their baseline as well as to a non-Lipitor group, which is incorrect. (Dkt. No. 1440-6 at 251-52).

interpret any increase in diabetes among the Lipitor group as an increase that must be *caused* by Lipitor.

For example, one of the tables in the safety trial data showed the percentage of patients that had elevated glucose (> 1.25 normal) in the placebo group and in the group taking 40 mg of Lipitor.[16] (*Id*. at 224). Despite the fact that the 40 mg Lipitor group had a ***lower*** percentage of patients with elevated glucose than the placebo group, Dr. Quon still testified that one could conclude from this table that 40 mg of Lipitor had an adverse effect on blood glucose because "[t]here are two patients, 1.5 percent who had hyperglycemia as a result of taking Atorvastatin. That's when compared to themselves." (*Id*. at 225). In his attempt to interpret this data, he clearly misses the concept that some people in the Lipitor group will develop diabetes regardless of whether they take Lipitor or not.

Dr. Singh testifies that while Dr. Quon is "very strong on his . . . science in terms of insulin resistance," he has "obvious weaknesses in design, like when you compare baselines to . . . end of study outcomes." (Dkt. No. 1440-5 at 23). Dr. Singh testifies that when a researcher compares outcomes to a group's baseline (rather than a control group), he is not accounting for the fact that "baseline values are correlated with terminal values" or for "secular change over time" (i.e., that some changes, like the development of diabetes, will occur over time even in the absence of an intervention). (*Id*. at 294; *see also id*. at 23-24). Dr. Singh testifies that comparing outcomes to baseline "is done a lot" in the mechanistic studies like that performed by Dr. Koh and Dr. Quon but "it is a real problem" in epidemiology. (*Id*. at 294-95). Dr. Singh testifies that Dr. Quon has good studies on diabetes and insulin resistance, "[b]ut I'm not sure he is the strongest person I would go to if I wanted to get an epidemiology perspective." (*Id*. at 23).

[16] The table presumably also included other doses, but this deposition testimony is focused on Lipitor 40 mg versus placebo.

B. Dr. Quon's Methodology

Given that Dr. Quon is not an epidemiologist, it is unsurprising that he does not use the epidemiological/Bradford Hill method to determine whether Lipitor causes diabetes. However, neither of his reports states what methodology he is using or attempting to use to reach his conclusions, and the method is not obvious from the face of the reports. (*See* Dkt. No. 972-42; Dkt. No. 1449-1). Plaintiffs assert that Dr. Quon is using the method of a literature review. (Dkt. No. 1460 at 38-39). Assuming conducting a literature review, without more, is a valid methodology,[17] it "must still be performed appropriately." *Doe v. Ortho-Clinical Diagnostics, Inc.*, 440 F. Supp. 2d 465, 472 (M.D.N.C. 2006).

A reliable literature review "uses formal search methods to allow a researcher to obtain a neutral 'snapshot' of the existing research on a particular question." *In re Zimmer Nexgen Knee Implant Products Liab. Litig.*, No. 11 C 5468, 2015 WL 5050214, at *3 (N.D. Ill. Aug. 25, 2015). Thus, as in Dr. Singh's report, such a review "begins with a formal, transparent, and reproducible search for studies that address a proposed research question." *Id*. (internal quotes omitted). Plaintiffs provided examples of peer-reviewed articles that employed the literature review methodology, and, in these examples, authors conducted such a formal search to allow the authors to obtain a complete view of the literature, rather than cherry-picking articles based on the authors' biases. (*See, e.g.*, Dkt. No. 1441-2 at 20 ("A systematic literature search of MEDLINE, EMBASE and Cochrane CENTRAL was conducted . . ."); *id*. at 30 ("[W]e reviewed articles published in the Scielo and Pubmed databases, which assessed or described the

[17] *See Konrick v. Exxon Mobil Corp.*, No. CV 14-524, 2016 WL 439361, at *13 (E.D. La. Feb. 4, 2016) ("Dr. Waters' report provides no indication that Dr. Waters applied the Bradford Hill criteria or any other accepted methodology to the applicable literature. Without any explanation of Dr. Waters' methodology or application of her analytical methods to the literature, the report does not provide a reliable basis for Dr. Waters' opinion.").

association between the use of statins and the risk of diabetes up to June 2015."); *id*. at 37 ("Medline and Embase were systematically searched to identify relevant literature . . ."); *id*. at 47 ("Medline, Embase, and the Cochrane Central Register of Controlled Trials were searched for randomized controlled endpoint trials of statins conducted from 1966 to 2012 . . . "); Dkt. No. 1441-3 at 28 ("[L]iterature was retrieved from searches of computerized databases, hand searches, and authoritative texts employing the key words . . ."); *id*. at 35 ("A search of pertinent RCTs conducted from November 1994 to October 2012 was performed by 2 independent investigators covering the MEDLINE, Cochrane, Google Scholar, and Embase databases as well as abstracts and presentations from major cardiovascular meetings using the search string. . . ."); *id*. at 51 ("A literature search was performed using MEDLINE from 2000 to October 2013 . . .")). Dr. Quon also acknowledged that this is the proper methodology for a literature review. (*See* Dkt. No. 1440-6 at 156 ("[W]e review the totality of the literature. That's the point of the review article.")).

However, Dr. Quon's reports did not review the "totality of the literature," and Plaintiffs have made no showing whatsoever that he performed any search to obtain relevant literature, rather than cherry-picking studies that supported his conclusion. In his initial report, Dr. Quon discussed observational studies Culver, Corrao, Macedo, and Carter, the NDA trials, SPARCL, TNT/Waters, IDEAL, and his own studies on the metabolic effects of statins. (Dkt. No. 972-42). However, neither he nor Plaintiffs explain how he came to choose and consider only these particular studies. ASCOT and Navarese seem like obvious omissions, though without any stated methodology, there is no way to tell whether they should properly be excluded from his consideration or not.

In Dr. Quon's supplemental report, he discusses his own studies on the metabolic effects of statins, clinical data from Pfizer's Safety Updates, SPARCL, TNT, IDEAL, Preiss, Carter, and Cederberg. (Dkt. No. 1449-1). Again, Dr. Quon provides no indication as to how he chose studies for inclusion. The difference in Dr. Quon's methodology when conducting a literature review for publication and when preparing his testimony in this case is quite telling.

In Dr. Quon's 2011 literature review about the metabolic risks of statins, Dr. Quon cites nine studies that evaluate the effect of Lipitor on insulin sensitivity in humans.[18] (Dkt. No. 1383-20; Dkt. No. 1440-6 at 153). Of those nine studies, four found that Lipitor actually ***improved*** insulin sensitivity, four found that Lipitor had no effect on insulin sensitivity (including a paper co-authored by Dr. Quon in 2005), and only one study, the study by Dr. Quon and Dr. Koh published in 2010, found that Lipitor decreased insulin sensitivity. (Dkt. No. 1440-6 at 154). In his peer-reviewed published literature review, Dr. Quon described all of these studies and made the following statements about insulin sensitivity and atorvastatin after a complete review of the literature:

> It is not clear why atorvastatin has beneficial metabolic actions in some studies but not others.
>
> The effects of atorvastatin may be different between patients with and without metabolic syndrome and diabetes. However, when we compared effects of atorvastatin on metabolic parameters in patients with and without metabolic syndrome and diabetes, there were no significant differences.

(Dkt. No. 1441-3 at 11-12).

Despite Plaintiffs claims that Dr. Quon employed the same methodology in this 2011 literature review as he does in this litigation, Dr. Quon did not cite or discuss the metabolic studies that contradict his litigation opinion in his report. In his deposition, Dr. Quon stated that

[18] Plaintiffs cited this literature review as an example of the methodology he used to reach his opinions in this case. (Dkt. No. 1441-3 at 9).

he did not discuss these studies in his expert report because he "thought they were insignificant and flawed," (Dkt. No. 1440-6 at 141), or thought "there are probably alternative explanations for their data." (*Id*. at 146; *see also id*. at 151, 159).

In his peer-reviewed, published literature review, Dr. Quon wanted to show that "there's a range of opinions in the literature and that this is a controversial area," (Dkt. No. 1440-6 at 141-42), and he was "trying to put this in the context of the whole literature." (*Id*. at 143). He testifies that "the point" of a literature review is to "review the totality of the literature." (*Id*. at 156). But in his expert report in this case, when he is purportedly using the same methodology, Dr. Quon testified that he only provided "what [he] thought were the relevant pieces," (*id*. at 144), and "didn't put anything into [his] supplemental expert report that [he] didn't believe." (*Id*. at 146). He went on to state: "So I only wrote things that I believe. And I don't believe these studies."[19] (*Id*.)

Dr. Quon had a similar explanation for not including the results of his own studies, which showed that Lipitor had no effect on blood glucose levels:

> Q. Is there any particular reason why you didn't mention in your expert report that your study showed no difference in mean blood glucose levels?
>
> A. Because it's not relevant. What's –what's relevant is that you're causing insulin resistance, and insulin resistance is a known risk factor for diabetes.
>
> Q. So if a medication shows no increase in blood sugar levels compared to baseline, you would conclude that that's not relevant to determining whether or not the drug can increase the risk of Type II diabetes?

[19] When pressed to admit that eight of the nine studies cited in his 2011 literature review found no adverse effects on insulin sensitivity regardless of the dose of Lipitor used, Dr. Quon responded, "That's what they concluded, and this is perfect illustration of why meta-analysis is often bullshit. So if you just averaged all these [studies], you'd come to the wrong conclusion." (Dkt. No. 14409-6 at 155).

> A. No. I'm–***I'm pointing out all the factors that are in favor of this drug causing diabetes***, and in this particular study it happens to center around insulin resistance. If glucose also went up, that would be another factor. . . .

(Dkt. No. 1440-6 at 111-12). Thus, if a study showed increased blood glucose, he would include it because that is "in favor of this drug causing diabetes," but because blood glucose did not go up in the study, he excluded it from consideration because that piece of evidence was not "in favor of this drug causing diabetes."[20] Such cherry-picking of data is unreliable and "fails to satisfy the scientific method and *Daubert*." *Barber v. United Airlines, Inc*., 17 F. App'x 433, 437 (7th Cir. 2001); *accord Fail-Safe, L.L.C. v. A.O. Smith Corp*., 744 F. Supp. 2d 870, 889 (E.D. Wis. 2010) ("[I]t is readily apparent that Dr. Keegan all but 'cherry picked' the data he wanted to use, providing the court with another strong reason to conclude that the witness utilized an unreliable methodology."); *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liab. Litig*., 524 F. Supp. 2d 1166, 1176 (N.D. Cal. 2007) (excluding expert testimony where expert "reaches his opinion by first identifying his conclusion . . . and then cherry-picking observational studies that support his conclusion and rejecting or ignoring the great weight of the evidence that contradicts his conclusion").

Similarly, failing to adequately account for contrary evidence is not reliable or scientifically sound. *See McEwen v. Baltimore Washington Med. Ctr. Inc*., 404 F. App'x 789, 791-92 (4th Cir. 2010) (upholding exclusion of expert testimony where experts "failed to meaningfully account for . . . literature at odds with their testimony"); *In re Zoloft (Sertraline Hydrochloride) Products Liab. Litig.*, 26 F. Supp. 3d 449, 460-61 (E.D. Pa. 2014) ("The Court

[20] Dr. Quon similarly cherry picks data from the NDA data and Safety Updates, ignoring data that does not support his opinion. (*See* Dkt. No. 1440-6 at 239 ("I didn't include [that table] because it wasn't helpful."); *id.* at 229 ("I can't explain it. It could be data entry error. There's all sorts of things."); *id*. at 240 ("I think it's a chance finding."); *id*. at 241 ("I think these are just random, chance findings, again . . . "); *id*. at 242 ("Again, it's a chance finding, with low numbers of patients, that doesn't mean much.")).

finds that the expert report prepared by Dr. Bérard does selectively discuss studies most supportive of her conclusions . . . and fails to account adequately for contrary evidence, and that this methodology is not reliable or scientifically sound."), *reconsideration denied*, No. 12-MD-2342, 2015 WL 314149 (E.D. Pa. Jan. 23, 2015); *see also Burst v. Shell Oil Co.*, No. CIV.A. 14-109, 2015 WL 3755953, at *16 (E.D. La. June 16, 2015) (excluding expert testimony where, among other things, the expert "did not present a meaningful analysis in which he reconciled this conflicting group of studies" but "simply provides a literature review, at times supplemented by his own commentary and states a conclusion."). Furthermore, it is clear from Dr. Quon's deposition testimony that he has not "employ[ed] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999).

Plaintiffs argue that Dr. Quon's cherry-picking of data was caused by the Court's order in CMO 49. (*See* Dkt. No. 1395 at 27; Dkt. No. 1460 at 39-40). This argument is meritless. After oral argument on general causation, the Court ordered additional briefing and held additional oral argument on whether experts had offered sufficient evidence to support their opinions that Lipitor causes diabetes at all doses. (Dkt. Nos. 1149, 1206). The Court ultimately held that, at least in this context, dose did matter, and the experts had to support their causation opinions at various doses, which none of Plaintiffs' experts had done. (Dkt. No. 1197). At oral argument, Defendant adamantly argued that Plaintiffs should not get another bite at the apple. Expert discovery was over. Defendant argued that it was "not a surprise" that dose mattered in the case, that Plaintiffs had made a strategic decision to ignore it, and that the exclusion of experts on this basis happened "every day." (Dkt. No. 1206 at 17, 19). Over Defendant's strenuous objections, the Court reopened discovery to allow Plaintiffs' experts to serve supplemental reports

addressing dosage. (Dkt. Nos. 1197, 1206). However, the Court agreed not to allow Plaintiffs "an entire Daubert do over." (Dkt. No. 1206 at 41). The Court limited the experts to data and studies cited in the experts' prior reports or cited to the Court in the parties' supplemental briefing. (Dkt. No. 1197 at 12). The Court made clear that "[w]e're not reshuffling the deck and starting over again," but that experts could rely on anything they previously relied on and disclosed. (Dkt. No. 1206 at 55). Plaintiffs argue that this limitation by the Court prevented Dr. Quon from performing a systematic literature review and resulted in the cherry-picked studies in his supplemental report. (*See* Dkt. No. 1395 at 27; Dkt. No. 1460 at 39-40).

Plaintiffs' argument falls flat for several reasons. First, no such limitation existed for the experts' initial reports. Dr. Quon had full and free reign to conduct a systematic search of relevant literature in preparing his first report, as Dr. Singh did, yet he did not do so. These studies that Dr. Quon felt he must include in his peer-reviewed, published literature review appear nowhere in his first report. (*See* Dkt. No. 972-42). Second, the argument of counsel is contrary to Dr. Quon's own testimony. Dr. Quon testified that he only included studies that he "thought were relevant" and that he "believed," and only included data "in favor of this drug causing diabetes." (Dkt. No. 1440-6 at 144, 146, 111). He never once mentioned CMO 49 as a reason for not including studies or data that contradicted his opinion. Third, the record included contradictory data that Dr. Quon could have included in his supplemental report under CMO 49, but he failed to do so. For example, when discussing his own studies, he only cherry-picked the data that supported his conclusion (data regarding insulin sensitivity) and excluded data from consideration that did not support his conclusion (data showing no change in blood glucose levels). (Dkt. No. 1440-6 at 110-12). Therefore, the Court finds this argument meritless.

The Court finds that Dr. Quon has not reliably applied the "literature review" method to the facts of this case and has not employed the same level of intellectual rigor in reaching his conclusions in this case as characterizes his practice in the field. Thus, the Court excludes Dr. Quon's causation opinions under Rule 702.[21]

V. Dr. Roberts

As an initial matter, Dr. Roberts' supplemental report fails to comply with CMO 49. The Court was clear that it was not reopening discovery to allow experts have a complete "do over" or to "add justification" for their original reports. (CMO 49, Dkt. No. 1197 at 11). Rather the Court allowed supplemental reports for the sole purpose of addressing whether Lipitor causes diabetes at particular dosage levels, and ordered that "[f]or each dosage level on which the expert opines, the report must set for the facts and data that form the basis of the expert's opinion(s)." (*Id.*) Dr. Roberts does not do this. Instead, she discusses particular published studies and then simply states at the end that "[i]t is my opinion Lipitor can cause diabetes mellitus (DM) in dosages across the range of 10 mg, 20 mg, 40 mg, and 80 mg." (Dkt. No. 1449-3). There is no analysis whatsoever, much less a meaningful or reliable analysis, of whether particular dosages are capable of causing diabetes. (*See id.*). In particular, she does not discuss at all whether an association between particular dosages of Lipitor and diabetes even exists. The Court explained extensively in CMO 49, and above, why a causation opinion without regard to dosage is unreliable.

Dr. Roberts' other methodological flaws only compound her reliability problem. In her first report, Dr. Roberts does not state what, if any, methodology she used to reach her conclusions. (Dkt. No. 1247-15). In her supplemental report, she states that "the scientific

[21] This ruling does not prevent Dr. Quon from testifying about his own studies and research regarding the metabolic effects of statins.

evidence regarding the relationship between atorvastatin . . . and the development of diabetes appear to satisfy the Bradford Hill criteria for causation." (Dkt. No. 1449-3 at 13). Whether Dr. Roberts possesses the requisite expertise to provide an epidemiological opinion based on the Bradford Hill criteria is questionable. She readily admits that she is not an expert in epidemiology.[22] (Dkt. No. 1440-7 at 54). She cannot identify the limitations of different types of epidemiological studies and is not even able to give a basic definition of some types of epidemiological studies, such as a cross-sectional study. (*See* Dkt. No. 1440-7 at 53-54). She believes that observational studies provide better evidence than randomized control trials, (Dkt. No. 972-9 at 111), which is contrary to the widely accepted view in epidemiology. *See* RMSE at 555; (*see also* Singh Rep., Dkt. No. 972-6 at 6-7). She does not know the term "confounding by indication," how to adjust for it, or even whether it can be adjusted for in observational studies or is even a problem in randomized controlled trials. (*Id*. at 54, 55, 164). By contrast, Dr. Singh testifies that confounding by indication "is a well-recognized issue that epidemiologists . . . take into account when evaluating observational data," that the phrase is "very common" in the field, and that epidemiologists always address confounding by indication "to the extent possible," though most observational studies "cannot eliminate it." (Dkt. No. 1440-5 at 61). Without this basic knowledge regarding epidemiological studies, it is hard to see how Dr. Roberts can reliably apply the Bradford Hill method. *See* RMSE at 552 ("Assessing whether an association is causal requires an understanding of the strengths and weaknesses of the study's design and implementation.").

Furthermore, Dr. Roberts appears to confuse association and causation. When asked whether observational studies could "tell us about association but cannot prove causation," Dr.

[22] Dr. Roberts is a cardiologist.

Roberts testified, "I don't know." (Dkt. No. 1440-7 at 154). Dr. Roberts later testifies that "if you have studies that consistently show an association . . . one can be fairly certain, as certain as one can ever be in science, that statins cause the association that's seen." (*Id*. at 156). She reaches the same conclusion (that an association is sufficient for causation) later in her deposition, testifying that "I think there is clear-cut evidence that people who take Lipitor have an increased risk of diabetes . . . And the implication, therefore, is that Lipitor caused it." (*Id*. at 24-25). She also testifies that the difference between an increased risk of diabetes and causation is only a "semantic difference." (*Id*. at 25).

However, it is accepted by all parties in this case and well established in case law that an association is insufficient to prove causation.[23] *See, e.g., United States v. Valencia*, 600 F.3d 389, 425 (5th Cir. 2010) ("Evidence of mere correlation, even a strong correlation, is often spurious and misleading when masqueraded as causal evidence, because it does not adequately account for other contributory variables."); *Peters v. AstraZeneca LP*, 224 F. App'x 503, 507 (7th Cir. 2007) ("[A] correlation alone is not evidence of causation."); *Norris v. Baxter Healthcare Corp*., 397 F.3d 878, 885 (10th Cir. 2005) ("A correlation does not equal causation."). More importantly, it is the very premise of the methodology Dr. Roberts purports to use; the entire purpose of the Bradford Hill factors is to provide a framework or methodology for determining whether a particular association is causal. Dr. Roberts cannot reliably apply the Bradford Hill methodology if she misunderstands its basic premise.

In her deposition, Dr. Roberts seemingly forgot what methodology she employed to reach her opinions. When asked what methodology she employed to reach her causation opinion, Dr.

[23] Dr. Roberts also seemed to accept this fact as true in her first deposition, testifying that "increasing the risk and being a cause" are "not synonymous," and was seemingly only willing to state that Lipitor increased the risk of diabetes, rather than causing it. (Dkt. No. 972-9 at 84).

Roberts stated, "I read the articles. And I don't really understand the question. I don't—I didn't use any—I don't know what you mean by what method did I use to analyze them." (Dkt. No. 1440-7 at 20-21). Dr. Roberts never mentioned the Bradford Hill factors when asked this question, the methodology her report purports to use. (*See id.*). When asked whether she "set forth any criteria or methodology that [she] would use" as she looked at the various evidence and data, she responded, "No." (*Id*. at 24).

Regardless of whether Dr. Roberts used the Bradford Hill method or the literature review method that Plaintiffs' claim Dr. Quon used, the method was not reliably applied. Both require a systematic literature search, as Dr. Singh did in his first report, and as explained above. While Dr. Roberts stated that she "reviewed the medical literature that had any bearing on the question of dosage of Lipitor and increased risk of diabetes and also epidemiologic studies that showed an increased risk of diabetes in people who take statins compared to non-users of statins," Dr. Roberts had no explanation for how she identified such studies for her consideration. (Dkt. No. 1440-7 at 19). She did not conduct any kind of search, and it appeared to not even occur to her to conduct a search for relevant articles:

> Q. Did you do research seeking all the articles that were available related to the doses of statins between 10 milligrams and 80 milligrams?
>
> A. I don't understand the question.
>
> Q. Yes. Did you do any type of medical search for articles on the risk of diabetes associated with or not associated with the various doses of Lipitor?
>
> A. Do you mean like a Google search?
>
> Q. Google search or a med, medical online search.
>
> A. No. I mean, I try to stay pretty conversant with the medical literature so . . . . With regard to cardiology, so I pretty much knew what articles had come out.

> Q. So you didn't specifically go out and search for additional articles that you may not be aware of related to the various doses of statins and the risk of diabetes?
>
> A. Not that I recall.

(*Id*. at 19-20). As with Dr. Quon, ASCOT is a glaring omission for Dr. Roberts' first report. It is not a valid methodology for Dr. Roberts to simply pick the articles that she happened to remember or that supported her views, discuss them with a little commentary, and state an opinion. Because Dr. Roberts had no methodology for determining what studies to consider and which to disregard, apparently just choosing those that she remembered or found supportive of her opinion, because she fails to adequately account for contrary evidence, because she confuses association and causation, because she lacks the epidemiological expertise to evaluate epidemiological studies in an Bradford Hill analysis, and because she fails to provide any analysis at all as to whether particular dosages are capable of causing diabetes, the Court excludes Dr. Roberts' causation opinions as unreliable under Rule 702.

VI. Dr. Gale

Dr. Gale is a retired professor of diabetic medicine. (Dkt. No. 972-12 at 3). In Dr. Gale's initial report, he discusses several observational studies, clinical trials, and meta-analyses, (*id*. at 16-18), and offers the opinion that "[a]torvastatin increases the risk of diabetes in a sustained dose-dependent manner." (*Id*. at 4). While Dr. Gale did not state a particular methodology in his initial report, he testifies in deposition that he first looked at "whether there was an association between statin use and diabetes," and then he looked for "evidence of a causative association," considering "the clinical trial evidence," "the observational study evidence," and looking "for some of the evidence to support or refute a biological basis for such an effect." (Dkt. No. 972-1 at 36). In deciding what evidence to consider, Dr. Gale did not conduct a systematic review of

the literature, instead he "put [his] reliance on meta-analyses using powerful methodology." (Dkt. No. 972-1 at 217).

Dr. Gale did not submit a supplemental report in response to CMO 49 or otherwise provide opinions regarding whether particular doses of Lipitor cause diabetes. In his deposition, Dr. Gale was asked whether it was his opinion, to a reasonable degree of scientific certainty, that 10 mg of Lipitor increases the risk of type 2 diabetes. Dr. Gale did not provide such an opinion but responded that "a study adequately designed and powered to exclude that possibility has not been performed." (*Id*. at 253). Dr. Gale never considered the data by dose or whether particular doses of Lipitor could cause diabetes. (*Id*. at 55).

The Court finds that for the reasons stated in CMO 49 and stated above, Dr. Gale's opinion, which ascribes the risk observed at any dose of Lipitor or statin to all doses of Lipitor, unreliable. Therefore, the Court excludes his causation opinion under Rule 702.

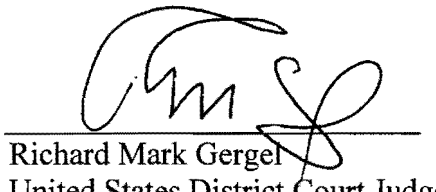
VII. Conclusion

For the reasons stated above, Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on the Issue of General Causation, (Dkt. No. 972), is GRANTED IN PART AND DENIED IN PART. The causation opinions of Dr. Quon, Dr. Roberts, and Dr. Gale are excluded under Rule 702. Dr. Singh's causation opinion with regard to 10 mg of Lipitor is excluded under Rule 702, and, based on his own testimony, he is unable to offer a causation opinion regarding Lipitor 20 mg or Lipitor 40 mg. The motion is **DENIED** as to Dr. Singh's Lipitor 80 mg causation opinion. Pfizer's motion to strike Dr. Roberts' supplemental report, (Dkt. No. 1271) is **DENIED AS MOOT**.

//

//

AND IT IS SO ORDERED.



Richard Mark Gergel
United States District Court Judge

March 30, 2016
Charleston, South Carolina