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. 74** **This Order relates to all cases.**

This matter is before the Court on Pfizer's Motion to Exclude the Testimony of Plaintiffs' Regulatory Expert G. Alexander Fleming. (Dkt. No. 975). 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, that Defendant failed to adequately warn about the alleged risk of developing Type 2 diabetes while taking Lipitor, and that Defendant misrepresented Lipitor's effectiveness for primary prevention in women.

Dr. Fleming is Plaintiffs' regulatory expert. He has a medical degree from Emory and is board certified in internal medicine and in endocrinology and metabolism. (Dkt. No. 975-2 at 5). He spent twelve years at the FDA. For eight of those years, he was responsible for the regulation of diabetes drugs and other metabolic drugs. (*Id.*). After leaving the FDA, Dr. Fleming became the Senior Vice President for Global Regulatory Affairs at the company Worldwide Clinical Trials, which later became Ingenix Pharmaceutical Services. (*Id.* at 6). Then in 2002, he co-

founded Kinexum LLC and has been its CEO ever since. (*Id.* at 7). Kinexum is a consulting company that helps corporations advance their products (drugs, medical devices, dietary supplements, gene therapies, etc.) to commercialization. (*Id.*). He has published on diabetes treatment and federal regulation of drugs and medical devices.

Dr. Fleming opines that

- "The manufacturer of a drug, not the FDA, holds primary responsibility for ensuring that its drug label fully and accurately discloses the risks and benefits of its drug. . . .";
- "The clinical trial data submitted with the NDA contained reasonable evidence of an association between Lipitor and clinically meaningful increased hyperglycemic abnormalities. Based on this data, Pfizer had a duty to add language to the Warnings section of the Lipitor label . . . . [T]hese data triggered an additional obligation on Pfizer's part to undertake additional testing in long-term clinical trials regarding the risks of hyperglycemia and new onset diabetes";
- "Pfizer had a duty to inform the FDA about the Japanese label update in June 2003. . . .";
- "The ASCOT data did not establish the efficacy of Lipitor in women for primary prevention, and, notwithstanding FDA's agreement with Pfizer's proposed language for the July 2004 label update concerning ASCOT, Pfizer's label was inappropriate and misleading. In this case, Pfizer ignored the clinical and regulatory imperative to identify subpopulations for which the benefit to risk relationship is questionable or not favorable."

(Dkt. No. 975-2 at 10-11). By previous order, the Court has excluded Dr. Fleming's opinion that the Lipitor label was misleading with regard to ASCOT. (CMO 72, Dkt. No. 1511 at 32). Pfizer moves to exclude each of Dr. Fleming's remaining opinions as unreliable for various reasons. (Dkt. No. 975). Plaintiffs have filed a response, (Dkt. No. 1048), and Plaintiffs have filed a reply. (Dkt. No. 1093).

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. Discussion

A. New Drug Application (NDA) Data

In CMO 72, the Court held that "any claim that a drug label should be changed based on information previously submitted to the FDA is preempted" because, under federal law, a manufacturer cannot unilaterally change a label based on such information. (CMO 72, Dkt. No. 1511, at 7). Thus, for the reasons explained in CMO 72, Plaintiffs claim that Defendant had a duty to add language to the Warnings section of the Lipitor label based on the information submitted to the FDA with its New Drug Application (NDA) is preempted. Therefore, Dr.

Fleming's testimony to this effect is irrelevant. To the extent that it has any marginal relevance, it would be confusing and misleading to the jury to hear testimony on the allegedly misleading nature of the Lipitor label based on the NDA data when such allegations cannot be the basis of Plaintiffs' claims. Therefore, Dr. Fleming's testimony that "[b]ased on this [NDA] data, Pfizer had a duty to add language to the Warnings section of the Lipitor label" is excluded under Fed. R. Evid. 402 and 403.

Furthermore, Dr. Fleming's opinions regarding the NDA data relies heavily on Dr. Jewell's analysis of the NDA data. (*See, e.g.*, Dkt. No. 975-1 at 94 ("I am relying on [Dr. Jewell's] analysis of the signal provided by the adverse event reporting to the NDA."); *id.* at 97 (admitting reliance on various calculations by Dr. Jewell); *id.* at 99-100 ("It starts with Dr. Jewell's analysis, and then my interpretation is that this is reflecting an increased risk of diabetes."); *id.* at 109 ("I'm relying on Dr. Jewell here."); *see also* Dkt. No. 975-2 at 31 (discussion Dr. Jewell's analysis)). By separate order, the Court has excluded Dr. Jewell's analysis of the NDA data as unreliable. (CMO 54, Dkt. No. 1258; CMO 67, Dkt. No. 1412). Therefore, Dr. Flemings testimony based on this analysis is unreliable and must be excluded under Rule 702. *See United States v. Nacchio*, 555 F.3d 1234, 1241 (10th Cir. 2009) ("Under *Daubert*, any step that renders the expert's analysis unreliable . . . renders the expert's testimony inadmissible.") (internal quotations omitted); *accord Paz v. Brush Engineered Materials, Inc.*, 555 F.3d 383, 388 (5th Cir. 2009); *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1245 (11th Cir. 2005); *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 267 (2d Cir. 2002).

B. ASCOT

By an earlier order, the Court has already excluded Dr. Fleming's opinion that the Lipitor label was misleading with regard to the ASCOT data. (CMO 72, Dkt. No. 1511, at 36).

However, this is not Dr. Fleming's only opinion with regard to ASCOT. He also opines that "[t]he ASCOT data did not establish the efficacy of Lipitor in women for primary prevention" and that "Pfizer ignored the clinical and regulatory imperative to identify subpopulations for which the benefit to risk relationship is questionable or not favorable." (Dkt. No. 975-2 at 10-11).

This first statement is based on Dr. Wells' reanalysis of the ASCOT data; Dr. Fleming did not conduct his own analysis. (Dkt. No. 975-2 at 35-39; *see also* Dkt. No. 975-1 at 216 ("I don't consider myself an expert. I think Dr. Wells is very credible, and I accept his analysis.") Defendant argues that Dr. Fleming cannot simply "parrot[] the opinion of another Plaintiffs' expert." (Dkt. No. 975 at 8).

An expert may rely on any "facts or data," including another expert's analysis, that experts in the particular field "would reasonably rely on . . . in forming an opinion on the subject." Fed. R. Evid. 703. Here, Dr. Fleming may rely on Dr. Wells' reanalysis of the ASCOT data to support his opinion that, based on this data, Pfizer should have identified "subpopulations for which the benefit to risk relationship is questionable or not favorable." The Court has considerable discretion under Rules 403 and 611 to limit cumulative evidence. To the extent that Dr. Fleming's testimony regarding Dr. Wells' opinion is needlessly cumulative or wastes time, Defendant may make such an objection at trial, and the Court will rule on it then.

Defendant has not made any specific objection to Dr. Fleming's opinion that "Pfizer ignored the clinical and regulatory imperative to identify subpopulations for which the benefit to risk relationship is questionable or not favorable." (*See generally* Dkt. No. 975). Thus, the Court does not address it further.

Finally, Defendant moved to exclude Dr. Fleming's statement that "[i]n my opinion, the benefit to risk relationship for the use of Lipitor in women for primary prevention is not favorable." (Dkt. No. 975 at 31-33). Plaintiffs state that this statement "is not one of the opinions Dr. Fleming seeks to offer." (Dkt. No. 1048 at 15 n.6). Thus, the matter is moot.

C. Current Label

In a footnote of his report, Dr. Fleming states

> In 2011, the FDA mandated an update to the "WARNINGS AND PRECAUSTIONS" section for all statins, except for pravastatin. The updated warning, effective in February 2002, indicated , for the first time, that: "Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including LIPITOR." In my opinion, the current Lipitor label, which continues to carry the "class" label quoted above, continues to fail to adequately warn[] doctors and their patients: 1) that Lipitor has been shown to have a statistically significant increase in the incidence of diabetes, particularly among women; 2) that doctors should monitor their patients' glucose levels and consider alternative therapy; and 3) that the overall risks of adverse events, including diabetes, outweigh the benefits, particularly for women at low risk for cardiovascular events.

(Dkt. No. 975-2 at 32 n.29). Dr. Fleming does not provide any further explanation or the basis of this opinion in his report. (*See id*; *see also* Dkt. No. 975-1 at 289 (agreeing he does not provide any reasons beyond what is stated in the footnote itself)). He testified in deposition that he believes the basis for the first recommended warning is a trial in the NDA data that reports an increasing rate of glucose abnormalities for patients on Lipitor. (Dkt. No. 975-1 at 291-93). When asked whether he reviewed the "totality of available evidence on this issue to reach that conclusion," Dr. Fleming replied, "No, I don't think so." (*Id.* at 293).

With regard to the second recommended warning, Dr. Fleming testifies that he is "not suggesting that there be an explicit recommendation to monitor," just that heightened awareness of the risk would result in more monitoring. (*Id.* at 295). He

testifies that "this footnote is somewhat cryptic, and if I were to do it over again, I would not provide these [warnings] so much as reasons that the label is defective." (*Id.* at 296).

The third recommendation is based on an opinion about overall risk benefit, which Plaintiffs state Dr. Fleming does not intend to offer at trial. (Dkt. No. 1048 at 15 n.6). In the end, Dr. Fleming testifies that what he really "intended to say here" is that the warning should have used the term "diabetes" rather than HbA1c and fasting glucose. (Dkt. No. 975-1 at 297-98).

By Dr. Fleming's own admission, he does not provide any basis in his report for the opinions in this footnote. Nor could he articulate a basis for these opinions at deposition. (Dkt. No. 975-1 at 290-98). While Dr. Fleming may have only intended to state that the warning should have included the term diabetes, this is not the opinion stated in footnote 29. Regardless, his report does not set out the basis for either opinion. Thus, the Court excludes this opinion for failure to comply with Rule 26. Furthermore, because Dr. Fleming has not provided a basis for his opinion, the Court cannot assess whether "the testimony is based on sufficient facts or data" or whether "the testimony is the produce of reliable principles and methods." Fed. R. Evid. 702. Plaintiffs have the burden of establishing the admissibility of expert testimony. *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 199 (4th Cir. 2001). They have failed to establish the reliability of this opinion under Rule 702. Therefore, this opinion is excluded under Rule 702 as well.

D. Japanese Label Change

Dr. Fleming opines that "Pfizer had a duty to inform the FDA about the Japanese label update in June 2003" regardless of whether it agreed with the label change. (Dkt. No. 975-2 at 10, 32-35). Defendant argues that this opinion should be excluded because Dr. Fleming is not an expert on the Japanese regulatory system and because Dr. Fleming has not independently

reviewed the bases of Japan's decision to require a label change. (Dkt. No. 975 at 21). However, such arguments miss the point. Dr. Fleming does not claim to be an expert on the Japanese regulatory system. (Dkt. No. 975-1 at 172-73). Nor does he claim to have conducted a thorough review of the labeling decision in Japan. (*See id.* at 195 ("I think it's clear I have not evaluated their process and their data."). He does not offer the opinion that the Japanese decision was correct. Indeed, he testifies that he does not have the necessary information to determine whether the labeling change in Japan was justified. (*Id.*).

Dr. Fleming offers the opinion that *under FDA regulations in the United States*, Pfizer had a duty to tell the FDA that there was a labeling change in Japan, regardless of whether they agreed with the change. (Dkt. No. 975-2 at 34-35). Defendant has not attacked Dr. Fleming's expertise as an FDA regulatory expert, which is the expertise relevant to this opinion. Therefore, Pfizer's Rule 702 motion is denied with regard to Dr. Fleming's opinion regarding the Japanese label change.

Defendant also argues that all evidence regarding the Japanese label change, including Dr. Fleming's opinion, should be excluded under Rule 403. (Dkt. No. 975 at 28). This argument is the subject of a separate motion in limine, (Dkt. No. 1163), and the Court declines to address it here. This issue is reserved until the Court rules on pre-trial motions in limine.

E. Dr. Fleming's Consulting Work for Pfizer

Dr. Fleming has "occasionally advised Pfizer" but not regarding Lipitor. (Dkt. No. 975-2 at 7). Dr. Fleming received confidential information from Defendant through this consulting work. (Dkt. No. 975-1 at 59). Defendant argues that Dr. Fleming "should not be permitted to bolster his qualifications by referencing [this work], and he should certainly be prevented from

testifying regarding any information Pfizer provided him during the course of that consultation." (Dkt. No. 975 at 35-36).

Any confidential information received by Dr. Fleming and the details regarding the drugs at issue in Dr. Fleming's consulting work are not relevant to this litigation and are not admissible. However, the simple fact that Dr. Fleming provided consulting services to Pfizer and the general nature of his engagement goes to his credibility and is admissible.

F. Background Section of Dr. Fleming's Report

Finally, Pfizer argues that the Background Section of Dr. Fleming's report, which discusses cholesterol, statins, and diabetes, (Dkt. No. 975-2 at 11-17), should be excluded because he was not named as an expert in these areas. Defendant also argues that the brief "FDA Commercial and Regulatory History for Lipitor," should be excluded because it is not a full, detailed history. To the extent that any of this information served as part of the basis for Dr. Fleming's opinions, he was required to it in his report under Rule 26. Dr. Fleming is also allowed to explain the basis of his opinions at trial. To the extent that Dr. Fleming goes beyond providing context and the basis for his opinions at trial, Defendant may make an objection at that time. The Court reserves for trial ruling on the admissibility of any such particular statements.

IV. Conclusion

For the reasons stated above, Pfizer's Motion to Exclude the Testimony of Plaintiffs' Regulatory Expert G. Alexander Fleming, (Dkt. No. 975), is **GRANTED IN PART AND DENIED IN PART**. The Court has previously excluded Dr. Fleming's opinion that the Lipitor label was misleading with regard to the ASCOT data. (CMO 72, Dkt. No. 1511, at 36). Dr. Fleming's opinions regarding the NDA data are **EXCLUDED** under Rules 402, 403 and 702.

Dr. Fleming's opinions stated in footnote 29 of his report are **EXCLUDED** for failure to comply with Rule 26 and under Rule 702. The motion is otherwise **DENIED**.

AND IT IS SO ORDERED.

Richard Mark Gergel
United States District Court Judge

May 6, 2016
Charleston, South Carolina