UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

In re: Baycol Products Litigation	MDL No. 1431
This Document Relates to:	AMENDED MEMORANDUM OPINION AND ORDER
All Actions	

Charles S. Zimmerman, Ronald S. Goldser, Robert R. Hopper and Stacy K. Hauer, Zimmerman Reed PLLP; Richard A. Lockridge, Bert Black, Robert K. Shelquist, and Yvonne M. Flaherty, Lockridge Grindal Nauen, PLLP; and Donald C. Arbitblit, Lieff Cabraser Heimann & Bernstein, LLP, for and on behalf of Plaintiffs.

Philip S. Beck and Adam Hoeflich, Bartlit Beck Herman Palenchar & Scott LLP; Susan A. Weber, James W. Mizgala, James R.M. Hemmings, Sherry Knutson, Nathan A. Huey and Elizabeth Curtin, Sidley Austin LLP; Paul J. Zidlicky, Frank R. Volpe and Eamon P. Joyce, Sidley Austin LLP; Catherine Valerio Barrad, Nitin Reddy, Thomas P. Hanrahan, Christine K. Son, Linda S. Peterson and J. P. Pecht, Sidley Austin LLP; Richard K. Dandrea, Eckert Seamens Cherin & Mellott, LLC; Peter W. Sipkins, Dorsey & Whitney LLP; Douglas R. Marvin, Williams & Connolly; and Joseph D. Piorkowski, Jr., The Piorkowski Law Firm, PLC for and on behalf of Bayer Corporation and Bayer AG.

Scott A. Smith and Tracy J. Van Steenburgh, Halleland Lewis Nilan Sipkins & Johnson, P.A. and Fred T. Magaziner, Dechert LLP for and on behalf of SmithKline Beecham Corp. d/b/a GlaxoSmithKline.

This matter is before the Court on the parties' motions to exclude certain expert testimony.

BACKGROUND

This action involves the prescription drug, Cerivastatin, which was

marketed in the United States under the brand name Baycol. Cerivastatin is a member of a class of drug known as statins that have been routinely prescribed to lower the lipid levels of individuals with high cholesterol, with the goal of decreasing the risk of cardiac diseases. Statins have been available since the late 1980's and have been widely prescribed.

Baycol was approved by the FDA in June 1997, but in August 2001, it was withdrawn from the market after thirty-one deaths in the United States were linked to Baycol use. Thereafter, thousands of lawsuits commenced throughout the country in state and federal court, asserting, *inter alia,* claims of strict liability, negligence, breach of warranty and medical monitoring. Given the number of cases filed in federal court, the Judicial Panel on Multidistrict Litigation (JPML) consolidated the cases in this Court by Order dated December 18, 2001 pursuant to 28 U.S.C. § 1407. Since that time, thousands of cases have resolved either by settlement or agreed stipulations of dismissal. Approximately 580 cases remain pending in this MDL proceeding, and discovery is near completion.

Before the Court are several Daubert motions to exclude certain expert testimony. Defendants seek to exclude portions of the expert testimony of the following proposed experts: Dr. John Farquhar; Dr. Harland Austin; Dr. R. Samuel Mayer; Dr. Charles Boult; Dr. Martyn Smith; Dr. Richard Kapit; Dr. Thomas Zizic; Dr. David Richman; Dr. Bruce Carlson; and Dr. Stephen Raskin. Defendants have

also brought two umbrella motions: motion to exclude expert testimony based on adverse event reports (AERs); and motion to exclude Plaintiffs' putative experts from invoking the testimony of other testifying experts.[1] Finally, Plaintiffs move to exclude, in part, the expert testimony of Dr. Janet Arrowsmith-Lowe.

STANDARD

Rule 702 of the Federal Rules of Evidence provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training or education, may testify thereto in the form of an opinion or otherwise if 1) the testimony is based upon sufficient facts or data, 2) the testimony is the product of reliable principles and methods, and 3) the witness has applied the principles and methods reliably to the facts of the case.

In Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), the Supreme Court set forth the standard for the admission of scientific expert testimony, noting the Rule 702 places emphasis on reliability and relevance. Thus, when faced with a proffer of scientific expert testimony, the court must engage in "a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue." Daubert, 509 U.S. at 592-593.

The Court then provided some general observations for the lower courts to

[1]These motions will be addressed within the context of the individual expert.

consider in making determinations as to whether the scientific knowledge is relevant and reliable, such as whether it has been tested, subjected to peer review and publication, what is the known or potential rate of error, and whether it is generally accepted. Id. at 593-595. "The inquiry envisioned by Rule 702 is, we emphasize, a flexible one. Its overarching subject is the scientific validity and thus the evidentiary relevance and reliability-of the principles that underlie a proposed submission. The focus, of course, must be solely on principles and methodology, not on the conclusions that they generate." Id. In its role as gatekeeper, the court should also keep in mind that "vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." Id. at 596.

In Kumho Tire Company, Ltd v. Carmichael, 526 U.S. 137 (1999), the Court extended the Daubert reasoning to experts who are not scientists.

> We conclude that Daubert's general principles apply to the expert matters described in Rule 702. The Rule, in respect to all such matters, establishes a standard of evidentiary reliability. . . It requires a valid . . . connection to the pertinent inquiry as a precondition to admissibility. . . And where such testimony's factual basis, data, principles, methods, or their application are called sufficiently into question, . . . the trial judge must determine whether the testimony has a reliable basis in the knowledge and experience of [the relevant] discipline.

Id. 526 U.S. at 149 (quoting Daubert, 509 U.S. at 590-592).

In addressing the reliability factor, the Supreme Court held that "[n]othing

in either Daubert or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146, 118 S.Ct. 512, 519 (1997).

> Applying the principles of Daubert, the Eighth Circuit held that generally
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> the factual basis of an expert opinion goes to the credibility of the testimony, not the admissibility, and it is up to the opposing party to examine the factual basis for the opinion in cross-examination. Only if the expert's opinion is so fundamentally unsupported that it can offer no assistance to the jury must such testimony be excluded.

Bonner v. ISP Tech., Inc., 259 F.3d 924, 929 -930 (8th Cir. 2001)(citing Hose v. Chicago Nw. Transp. Co., 70 F.3d 968, 974 (8th Cir.1996)). "Although it is common that medical experts often disagree on diagnosis and causation, questions of conflicting evidence must be left for the jury's determination." Id. (quoting Hose, 70 F.3d at 976).

ANALYSIS

1. Motion to Exclude Expert Testimony of Dr. John Farquhar

Dr. John Farquhar is a Professor Emeritus of Medicine at the Stanford University School of Medicine in Stanford, California. He has been a professor of medicine at Stanford since 1973, and was the Director of the Preventive Cardiology Clinic in the Stanford Medical Clinic from 1978 to 1996, while

maintaining an active clinical cardiology practice from 1962 to 2001. His principal areas of research and writing include epidemiology and cardiovascular risk factors; he has published over 200 articles in these areas. He has also received numerous awards and is a member of numerous medical organizations.

A. Comparative Toxicity of Statins

On behalf of Plaintiffs, Dr. Farquhar has submitted an expert report. In this report, Dr. Farquhar concluded, after reviewing available data from multiple sources, that to a reasonable degree of medical certainty, Baycol caused significantly greater muscle disease than other statins. Farquhar Report, ¶ 30. Defendants challenge the methodology used by Dr. Farquhar in reaching this conclusion.

In Section III of his Report, Dr. Farquhar discussed generally accepted epidemiologic methods that he concluded demonstrates that Baycol causes muscle injuries and that it is more toxic than other statins. Section III (C) discusses meta-analysis - a technique used to combine the results of several studies. Dr. Farquhar combined five early data sets and four later data sets of Spontaneous Reports (SR) of adverse events associated with Baycol and other statins. He asserted this method is supported in a recent article published in JAMA, which includes the passage: "Suggested roles for meta-analytic techniques include the establishment of associations between drugs and adverse effects, estimation of the frequency of

ADRs and identification of subgroups at increased risk for ADRs." *Brewer et al.,* "Post-Marketing Surveillance and Adverse Drug Reactions," JAMA (1999) 281:824-29 at 827.

Dr. Farquhar further reported that there is a consensus in the medical community that Baycol is more toxic than other drugs in the same class, and because several publications in scientific literature rely on adverse event reports to consistently conclude that Baycol is more dangerous than other statins, his compilations of adverse event reports form an appropriate basis for comparison of the risk of Baycol to other statins. Farquhar Report, ¶¶ 43-44.

One article was discussed extensively in Dr. Farquhar's Report. Id. ¶ 45. In February 2002, the New England Journal of Medicine (NEJM) published a letter to the editor which was authored by three officials of the United States Food and Drug Administration (FDA). *Staffa et al.*, "Cerivastatin and Reports of Fatal Rhabdomyolysis," NEJM (2002); 346:539-40. In this article, the authors reported the "reporting rate of fatal rhabdomyolysis in association with cerivastatin monotherapy is 1.9 per million prescriptions, 10 to 50 times as high as the rates associated with the other statins." The article also included the caveat

> Because of the underreporting of adverse reactions, the use of reporting rates as proxy measures has limitations. Only about one percent of all serious events are directly reported by physicians. There is a secular trend of increased reporting to the FDA over the past decade. However, the rate of reports of fatal rhabdomyolysis associated with the use of atorvastatin

> (approved for use within 6 months after the approval of cerivastatin) was far less than for cerivastatin. Thus, the increased reporting associated with the use of cerivastatin appears to be more than an artifact related to an increased awareness of statin-associated rhabdomyolysis or to secular trends in reporting.

Id. at 539-40.

While noting that "[r]eporting rates are not incidence rates" the authors nevertheless concluded that "on the basis of the finding of a markedly increased reporting rate of fatal rhabdomyolysis in association with cerivastatin, Bayer, with the concurrence of the FDA, moved to withdraw cerivastatin from the U.S. market." Id. Farquhar Report, ¶ 45. Dr. Farquhar noted that the *Staffa* article was peer reviewed before publication, and was cited with approval by the ACC/AHA/NHLBI Clinical Advisory on Statins in Circulation (2002); 106:1024-28 at 1025. Farquhar Report, ¶ 46.

Dr. Farquhar also cited to a study of adverse drug reaction reports for six pairs of similar drugs marketed at similar times. *Pierfitte et al.,* "Is Reporting Rate a Good Predictor of Risks Associated with Drugs?" British Journal of Clinical Pharmacology (BJCP) (1999); 47:329-21. The study calculated reporting rate ratios (RRRs) for each drug pair, finding relatively low differences in the reporting rates as to each drug. "These results tend to validate the basic assumption currently accepted in spontaneous reporting: the ratio of reporting rates approximates the ratio of actual risks (which would have been calculated on the

basis of the actual number of cases) given that the two compared drugs belong to the same therapeutic class and are used in similar conditions." Id. at 330.

Dr. Farquhar further noted that clinical trials conducted by Bayer are incomplete indicators of the risks of Baycol, and that his recalculation of the PacifiCare study, discussed below, shows statistically significant higher toxicity of Baycol than do pre-market release clinical trials. Farquhar Report ¶¶ 54-55. He further noted that Bayer's own compilation of published clinical trials show statistically higher toxicity of Baycol despite the inherent limitations of individual clinical trials. Id. ¶ 55. Dr. Farquhar concluded that "[b]ecause of the acknowledged inherent limitations of individual clinical trials, it is necessary to compile data in a meta-analysis in order to observe consistency in Baycol's higher risk of muscle injury compared to other statins, and to increase the precision of the estimate of such risk." Id.

In Section IV (A) and (B) of his report, Dr. Farquhar described his meta-analysis conducted of the five early and seven late spontaneous reporting data sets. Farquhar Report, ¶¶ 56-99. With respect to the meta-analysis of the five early data sets, Dr. Farquhar explained that he intended to answer two questions: 1) is Baycol, as monotherapy, relatively more likely to produce myopathy/rhabdomyolysis that the other five statins?; and 2) is Baycol relatively more likely to cause myopathy/rhabdomyolysis when used in combination with

gemfibrozil? Id. ¶ 58. As to the first question, Dr. Farquhar concluded the following: 1) that although the data sets were diverse in origin and outcome, there was a consistency in findings; 2) the data demonstrated consistency among studies in different settings and consistency among components within a single study; and 3) Baycol had a strong level of relative toxicity, seven-fold, compared to other statins. Id. ¶ 65. Similar conclusions were made with respect to the second question: 1) a consistency in findings were even greater with respect to combination therapy; and 2) strength of association greater for Baycol combination therapy compared to other statins. Id. ¶ 67.

A meta-analysis was also done with respect to seven data sets with the later lock point of August 7, 2001. These data sets provided reporting rates for rhabdomyolysis and fatal rhabdomyolysis. Id. ¶ 71. Based on his meta-analysis of these data sets, Dr. Farquhar again concluded that "[c]onsistency among meta-analyses adds to the weight of evidence pointing to Baycol's uniquely high toxicity in comparison to other statins." Id. ¶ 75. Dr. Farquhar also noted that the *Staffa et al.* analysis of the FDA's spontaneous reports for fatal rhabdomyolysis reveals reporting rates comparable to those reported in early and late lock point SR data sets compiled by Bayer. Id. ¶¶ 82-90.

In further support of his opinion that Baycol is more toxic than other statins, Dr. Farquhar discussed the "proportional reporting ratio" (PRR) method

which looks to the proportion of the outcome in question (instance of rhabdomyolysis) contrasted to other outcomes or adverse events. Id. ¶ 91. He stated that this method acts as a cross validation for the reporting rates described previously, as "the PRR is considered to be free of the uncertainty of inaccurate distribution (i.e. one statin is reported as toxic more than other statin - even if their rates of toxicity are the same)." Id. After conducting this analysis, Dr. Farquhar reported that for four time periods, the PRRs of Baycol monotherapy versus other statins were elevated. Id. ¶ 94. "The major point is that all SR data are consistent in both magnitude and statistical significance in defining Baycol monotherapy as being toxic compared to all other statins." Id. ¶ 95.

Dr. Farquhar also stated this his conclusions are supported by his recalculation of the PacifiCare study - a study conducted by Prescription Solutions at Bayer's request. Id. Section IV (C). Dr. Farquhar concluded that the PacifiCare study did not conform to generally accepted principles in the field of epidemiology. Id. ¶ 102. "When proper methods are applied, the PacifiCare data in fact show a substantially higher toxicity of Baycol, not only for combination therapy with gemfibrozil, but also in monotherapy." Id. The following paragraphs describe Dr. Farquhar's recalculation, taking into consideration corrections for "healthy person effect", "duration of exposure" and "misclassification of cases".

Finally, Section V of his report includes his analysis of Bayer-derived reports

on “Safety Findings from Clinical Trials”. Dr. Farquhar concluded that this data “shows that Baycol monotherapy was significantly more toxic in producing rhabdomyolysis at both, the 0.4 mg dose (RR=8.6, p=0.0054) and the 0.8 mg dose (RR8.8, p < 0.0001).” Id. ¶ 123.

Defendants argue that the proposed testimony of Dr. Farquhar comparing Baycol to other statins, and his opinion that Baycol was more toxic or dangerous than other statins should be excluded because the analysis upon which this opinion is based was not derived through accepted scientific methodology.

Defendants first argue that Dr. Farquhar’s analysis is improperly based on AERs, because the FDA and other courts have found that AERs should not be used to compare the safety of drugs.

AERs are reports required by the FDA when a prescription manufacturer receives information about adverse events reported by patients taking a particular prescription drug. 21 C.F.R. § 314.80(c). With respect to these reports, the FDA has published certain caveats, such as that AERs contain only those reactions voluntarily submitted, and that there is no certainty that the suspected drug caused the reaction, and most notably that “[n]umbers from these data must be carefully interpreted as reporting rates and not occurrence rates. True incidence rates cannot be determined from this database. Comparisons of drugs cannot be made from these data.” FDA Office of Postmarketing Drug Risk Assessment,

"Adverse Event Reporting System (AERS): Brief Description with Caveats of System" (Oct. 18, 1999), at 2. See also, U.S.Food & Drug Administration, Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment (March 2005) available at http://www.fda.gov.cder/guidance/6359OCC.htm (noting that comparisons of reporting rates may be valuable, but recognizing the substantial limitations that result from the inherent uncertainties in the numerator and denominator used, the FDA cautions that "[r]eporting rates can by no means be considered incidence rates, for either absolute or comparative purposes.")

Defendants further submit that other medical and scientific experts agree with the FDA that AERs cannot validly be used as proof of a relative risk between medications. For example, Defendants submit the expert report of Dr. Janet Arrowsmith-Lowe, who opines that "the comparison of reporting rates calculated from spontaneously reported adverse drug events is not generally accepted by the scientific and medical community as a valid methodology for estimating the relative risks of those events associated with individual drug products." Arrowsmith-Lowe Report ¶ 5. Defendants have also submitted the expert opinion of Dr. Brian Strom, who opines that the FDA's Medwatch system "cannot be used to make scientifically valid comparisons of incident rates between different pharmaceutical products." Strom Report ¶ 6. Plaintiffs' own expert, Dr. Harland

Austin, concedes that the AER database cannot be used to estimate drug risk. Austin Rep. ¶ 52.

The reliability of AERs has been addressed in several court opinions as well. For example, in McLain v. Metabolife Int'l, Inc., 401 F.3d 1233, 1250 (11th Cir. 2005), the court excluded plaintiff's medical expert report, in part, because it was based on AERs. Describing AERs as "reflect[ing] complaints called in by product consumers without any medical controls or scientific assessment" the court held such "[u]ncontrolled anecdotal information offers one of the least reliable sources to justify opinions about both general and individual causation." Id. See also DeLuca v. Merrell Dow Pharms., Inc., 791 F. Supp. 1042, 1051 (D.N.J. 1992) aff'd 6 F.3d 778 (3rd Cir. 1993) cert. denied 114 S. Ct. 691 (1994) (finding that AERs "are not of a type of data that are reasonably relied upon by experts in the fields of epidemiology and public health to make a determination of the causal relationship between a given substance and human birth defects"); Nelson v. Am. Home Prods. Corp., 92 F. Supp. 2d 954, 969 (W.D. Mo. 2000) (citing 314 NEW ENG. J. MED., 1589, 1591 (1996))(holding AERs not proof of causation).

With respect to the methodology employed in the meta-analyses of AER data, Defendants point out specific flaws or biases. For example, Defendants assert that in conducting the meta-analysis, Dr. Farquhar used data from the FDA US AERS, and the FDA Worldwide AERS, and did not attempt to learn if there was

any overlap in the data provided. Defendants further assert that AERs do not use standard definitions for terms. Dr. Farquhar took the terms rhabdomyolysis, myopathy or myositis from the AER data at its face value, without corroborating the information contained therein.

Defendants also assert that Dr. Farquhar did not take into account the "new drug" effect in which AERs are made more frequently during the first years a medicine is on the market. This effect is taken into account when clinical studies are performed, but Dr. Farquhar did not do so. He compared Baycol to both new drugs and those that had been on the market for a long time.

Finally, Defendants assert that in Dr. Farquhar's analysis, the number used for the numerator was the AERs, but the number used for the denominator came from the National Prescription Audit Plus database - which provides for the number of prescriptions for different statins in a given year. This number, however, does not include samples. Since Baycol was a new drug during the period in question, it was extensively sampled. Thus, Dr. Farquhar's calculations most likely over-state the RRR.

Defendants have put forth ample authority to demonstrate that a comparative analysis of drug toxicity - based on a meta-analysis of AER data - must be carefully scrutinized. Keeping this mind, together with the standard that expert testimony should be admitted unless it "is so fundamentally unsupported

that it can offer no assistance to the jury," the Court finds that Dr. Farquhar's opinion as to the comparative toxicity of Baycol to other statins must be excluded.

The Court has reached this conclusion after applying the tests for reliability set forth in Daubert. Contrary to Plaintiffs' position, Dr. Farquhar's meta-analyses of AER data, to compare the toxicity of Baycol to other statins, has not been tested or subjected to peer review and publication. Further, given the limitations inherent in AER data, there is insufficient evidence before the Court as to the known or potential rate of error, and no evidence has been submitted to demonstrate that such an analysis is generally accepted.

The Court has carefully reviewed all of the cited articles in Dr. Farquhar's report and finds none stand for the proposition that AER data can be used to conduct a comparative analysis of drug risks, or more specifically that Baycol is the most toxic statin. For example, the first article cited by Dr. Farquhar, *Thompson et al.*, "Statin-Associated Myopathy," JAMA 2003; 289:1681-90, the authors discussed skeletal muscle complaints associated with statins, as well as incidence, possible causes and approaches to skeletal problems. "[The review] also presents recent US Food and Drug Administration (FDA) data on the occurrence of statin-associated data." Id. at 1682. With respect to AER data, the authors noted that in their search of FDA AER data of statin-associated rhabdomyolysis, "cerivastatin (57%) was the most commonly implicated statin"

but included the further caveat that such "data rely on voluntary physician reporting and do not use a uniform definition of rhabdomyolysis. The effect of these vagaries on the results is unknown, but these data provide some insight into the magnitude of the problem." Id. at 1683. This article also sets forth rates of myalgia from clinical trials for Baycol and other statins, and the tables show Baycol has the second lowest myalgia rate of all statins. Id.

Similarly, the subject of the *Farmer* article was not to conduct a comparison of the relative risks of Baycol, but to expose weaknesses in "post-release regulation and surveillance of pharmacological agents with the potential to case rare, but potentially lethal adverse effects." *Farmer* "Learning from the cerivastatin experience," Lancet (2001); 358:1383-84. The focus on the *Hamilton-Craig* article similarly addressed the importance of post-marketing surveillance, and the need to report significant adverse drug reactions. *Hamilton-Craig* "Statin-Associated Myopathy," MJA (2001); 175:486 at 487. While the article included tables reporting adverse events for each statin attributable to myalgia, myopathy and rhabdomyolysis, the authors noted that the number of adverse event reports "does not provide information on the incidence of adverse effects in relation to numbers of prescriptions or patients treated." Id. Other cited articles address only rhabdomyolysis, not muscle ailments in general. See *Furberg et al.* "Withdrawal of cerivastatin from the world market" Current Controls in Cardiovascular Medicine.

(2001); 2:205-07 (commentary that references press reports that Baycol linked to rhabdomyolysis fatalities and non-fatalities); *Graham et al.*, "Incidence of Hospitalized Rhabdomyolysis in Patients Treated with Lipid-Lowering Drugs" JAMA (2004); 292: 2585 (focus only on rhabdomyolysis).

The Court also finds the *Staffa* letter does not support Dr. Farquhar's methodology in reaching his broad medical opinion that Baycol is the most toxic statin. The *Staffa* letter focused only on the reporting rate of rhabdomyolysis, and included the caveat that reporting rates are a crude measure of reports received by the FDA, and "since many factors can affect reporting and an unknown number of cases may not be attributed to the drug or reported to the FDA" reporting rates are not incident rates. *Staffa et al.*, NEJM (2002); 346:539-40.

With respect to the *Pierfitte* study, the Court recognizes that the authors found its analysis validated the hypothesis that the ratio of reporting rates approximates the ratio of actual risks. Nonetheless, the underlying data demonstrates that an AER analysis can be unreliable. The study focused on the RRR for six pairs of identical drugs, marketed at the same time. While for four of the six pairs, there was no statistically significant difference, the study did show a statistically significant difference between two of the drug pairs, one of which was a statin. *Pierfitte,* BJCP (1999); 47:329 at 330 (Table 1).

Plaintiffs argue that all of the Defendants' criticisms of the use of AER data

are overmatched by the magnitude of the excessive risks in the RRR for Baycol compared to other statins, citing *Bruce M. Psaty et al,* "Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions - Use of Cerivastatin and Risk of Rhabdomyolysis," JAMA (2004); 292:2625 and *Jennie Chang et al.* "Rhabdomyolysis with HMG-Co A Reductase Inhibitors and Gemfibrozil Combination Therapy," Pharmacoepidemiology and Drug Safety, (2004); 13:417. As the titles to these articles suggest, and a review of the contents reveal, these articles focus on reporting rates for rhabdomyolysis, not other muscle injuries.

Plaintiffs would have this Court allow Dr. Farquhar to opine on muscle injuries based solely on data and literature which focus on a specific disease, rhabdomyolysis. Plaintiffs have not provided the Court any evidence or authority upon which to support such a leap. The party seeking the admission of such testimony has the burden of demonstrating its reliability, and Plaintiffs have not met their burden in this regard. Failure to show the reliability of each step in an expert's methodology is fatal under Daubert. McClain, 401 F.3d at 1245.

In Leathers v. Pfizer, Inc., 233 F.R.D. 687 (N.D. Ga. 2006), the court excluded expert testimony that relied on adverse incident reports and medical articles. The proffered expert testimony was that Lipitor caused permanent side effects, such as muscular weakness, severe muscle pain, multiple myalgias,

myositis and a myopathic syndrome. The court found the expert's testimony unreliable, finding adverse incident reports reflect only reported data, not scientific methodology, and the medical literature did not support the opinion that Lipitor caused permanent injury. Leathers, 233 F.R.D. at 695 (noting medical literature consistently found that symptoms resolved after discontinuance of statin). Similarly, in this case, the medical literature does not support Dr. Farquhar's opinion comparing Baycol's toxicity to other statins, and the evidence concerning adverse event reports, standing alone, is unreliable.

Although this Court holds that Dr. Farquhar's expert opinion that Baycol is more toxic or dangerous than others statins must be excluded under Rule 702, such holding is not meant to prevent the admission of AER evidence at trial. As Plaintiffs point out, the AER data relevant to this case presented a very strong signal concerning Baycol and its association with rhabdomyolysis, and such evidence may be relevant at trial. It thus follows that Plaintiffs' experts may testify as to the existence of this signal. See In re: PPA Products Liability Litig., 289 F. Supp. 2d 1230, 1242 (W.D. Wa. 2003) (allowing expert testimony that was based in part on AER data, as the court found "significant the sheer volume of case reports, case series and spontaneous reports associating PPA with hemorrhagic stroke to women"). The ultimate determination as to the admissibility of AER evidence should be left to the trial court, however.

B. Recalculation of PacifiCare Study

Defendants also move to exclude Dr. Farquhar's recalculation of the PacifiCare study. Defendants assert that this study shows that Baycol was comparable in safety and effectiveness to other statins, when used in accordance with its label.

In his report, Dr. Farquhar claims that the PacifiCare study has bias due to the "healthy person effect" - those group members who have a greater tolerance to withstand the toxic effects of the exposure in question. In this case, patients who switched from a different statin to Baycol were more likely to be statin tolerant. To counter this effect, Dr. Farquhar made statistical adjustments that resulted in raising the relative risk of Baycol. Farquhar Report, ¶ 103. Dr. Farquhar also challenged the study because persons in the study were on the medicine for less time than those taking other statins and that the risk was therefore understated. Defendants argue this adjustment was based on an assumption, for which he offers no justification, that people who had adverse reactions will do so at a consistent rate over time they are on the medicine. As Defendants' expert Dr. Strom stated, adverse reactions to Baycol were more likely to occur shortly after taking the medicine. Id. ¶ 105.

Finally, Dr. Farquhar complains that the PacifiCare researchers were likely to misclassify cases. Id. ¶¶ 111-120. Defendants assert this assertion is based on

speculation.

It is generally accepted that bias in the conduct of a study can materially affect the result and that detection and accounting for bias are standard tools of epidemiology. *Michael J. Saks et al.*, Reference Manual on Scientific Evidence (2nd Ed. 2005-2006) at 504. In this case, Dr. Farquhar relied upon selection bias and information bias, well-known types of bias that are within his expertise as an epidemiologist, to challenge the PacifiCare study. Specifically, Dr. Farquhar challenged the study first because he believes the PacifiCare study did not negate selection bias due to the "healthy person effect" and because the study did not account for exposure of duration. See Reference Manual on Scientific Evidence, at 514, n. 85 (health status must be accounted for). Plaintiffs note that Lawrence Posner, Bayer's Head of Regulatory Affairs, also recommended that adjustments concerning duration of exposure be made to the PacifiCare study. See Supplemental Rebuttal of John W. Farquhar, M.D. in response to the report of Janet Arrowsmith-Lowe, ¶ 11. The Court finds that Dr. Farquhar is qualified to offer his opinions as to the accuracy of the PacifiCare Study, and that such opinion is reliable.

Dr. Farquhar went beyond challenging the study, however. He also recalculated the study by making statistical adjustments; the basis of which come from adverse event data. As discussed previously, however, such data has

substantial limitations that result from the inherent uncertainties in the numerator and denominator used. Accordingly, Dr. Farquhar's recalculation of the PacifiCare study is not scientifically reliable, and is excluded.

2. Motion to Exclude Expert Testimony of Dr. Harland Austin.

Dr. Harland Austin is a biostatistician and professor of epidemiology at Emory University School of Public Health in Atlanta, Georgia, and has worked in these fields for the last twenty-seven years. He received a Masters in Statistics in 1976 from the Department of Applied Mathematics and Statistics at the State University of New York, Stony Brook, and a Doctorate of Science in Epidemiology in 1983 from the Harvard School of Public Health. He is the author or co-author of approximately 70 peer-reviewed publications and book chapters. He was retained by Plaintiffs to evaluate the design, conduct and analysis of the PacifiCare Study. Austin Report, ¶ 13. He also conducted an independent analysis of the FDA AERS database. Id.

Defendants move to exclude Dr. Austin's testimony about the relative risk of monotherapy Baycol based on his analysis of adverse event reports and his recalculation of the PacifiCare study.

A. Testimony on Relative Risk

Dr. Austin conducted an independent review of AERs, computing an RRR and a PRR. He opined that spontaneous reporting rates of rhabdomyolysis and

myopathy are appreciably higher for Baycol monotherapy compared with monotherapy for other statins. Id. ¶ 18. Table 1 in Dr. Austin's report summarizes spontaneous reports of rhabdomyolysis and myopathy occurring among Baycol and all statin users. From this data, Dr. Austin reached the conclusion that "[s]pontaneous reporting rates of rhabdomyolysis and myopathy are appreciably higher for Baycol monotherapy compared with monotherapy for other statins." Id. ¶ 18. Dr. Austin also conducted a PRR analyses, described as "a contrast of the proportion of adverse events of interest (e.g. rhabdomyolysis) reported for persons using a drug of interest (say drug X) divided by the corresponding proportion for persons using a referent drug (say drug Y)." Id. ¶ 21. The results of this analysis are summarized in Table 2. From the data provided, Dr. Austin computed the PRR for rhabdomyolysis for Baycol users is about 15, when compared against Lipitor, and 9 when compared with all other statins. Id. ¶ 25. "These findings almost certainly are not attributable to chance." Id.

Defendants challenge Dr. Austin's testimony as to the relative risks of Baycol, again arguing AER data cannot support such expert opinions. Defendants assert that in reviewing the AER data, he did nothing to eliminate any biases in the data, biases he acknowledged, and then compounds this error by making RRR and PRR calculations based on unfounded assumptions.

Plaintiffs assert that Dr. Austin conducted an independent analysis of the

FDA AER database. Plaintiffs acknowledge that Dr. Austin did not have all the data to support his conclusions, but assert that Dr. Austin had other ways to address these concerns. For example, he explained that confounding "is not likely a problem because persons using various cholesterol lowering drugs are likely to be roughly comparable with respect to the determinants of myopathies." Id. ¶ 20.

The Court finds that Dr. Austin did not address the undisputed substantial limitations inherent with AER data, discussed in the previous section. Thus, for the same reasons Dr. Farquhar's opinion that Baycol is more toxic or dangerous than other statins is excluded, Dr. Austin's testimony concerning his AER analysis is similarly excluded.

B. Recalculation of the PacifiCare study

With respect to the PacifiCare study, Dr. Austin has opined that the study has many limitations, the most important of which is the failure of the investigators to perform the proper statistical analysis, which caused them to underestimate the association between monotherapy Baycol use and the risk of myopathy. Id. ¶ 14. He further opined that the study investigator also failed to confirm the diagnosis of myopathy through review of medical charts, which is likely to result in many false positive cases. Id. Adjusting for these limitations, Dr. Austin opined that the study is consistent with the spontaneous reports and provides support for the opinion that monotherapy Baycol use increases myopathy

risk. Id. ¶ 16. Dr. Austin noted that the PacifiCare study was undertaken because of the strong signal apparent, both in the RRR and the PRR, that Baycol monotherapy was associated at a higher rate of occurrence of rhabdomyolysis than monotherapy with other statins. Id. ¶ 26. The remainder of his report discusses specifics as to the design, findings and limitations of the PacifiCare study.

Dr. Austin began by discussing the design of the study, and its conclusion that "there was no increase in the risk of myopathy for Baycol monotherapy compared with monotherapy on the other HMG inhibitors." Id. ¶ 31. He then noted a number of inaccuracies contained in the study. Id. ¶¶ 32-47.

Dr. Austin concluded that the PacifiCare study was not well written and its methods were not described clearly. Id. ¶ 48. He further criticized the study by noting it was "much too small to provide meaningful information on rhabdomyolysis" because the study investigated only "myalgia". As a result, he found the study did not provide assurance that monotherapy Baycol was unrelated to rhabdomyolysis or other serious forms of myopathy. Id. ¶ 49. He further noted that certain biases were not addressed, such as misclassification of cases or exposure, failure to use person-time in the analysis, and selection bias. Id. ¶¶ 53-71.

Dr. Austin then computed estimates adjusted for confounding and biases he described previously in his report. He inflated the monotherapy for Baycol

reporting rate by 30% for the failure of the investigators to eliminate false positives by medical record review and by 10% for the combination of non-differential misclassification of exposure, sampling and switching, which resulted in proportionately more Baycol person-time being contributed by subjects with a longer history of statin use. Id. ¶ 74.

Defendants move to exclude Dr. Austin's testimony regarding the PacifiCare study, and his conclusions about the relative risk of Baycol use arising from his analysis of that study. Defendants assert that Dr. Austin's attempt to correct the PacifiCare data failed to follow the basic scientific method, which is to first generate hypotheses and then test them to see if they can be falsified. Defendants assert that Dr. Austin instead skewed the PacifiCare data simply to fit his pre-conceived conclusion that the risks associated with Baycol monotherapy is higher than the risks associated with other statins. Defendants further challenge Dr. Austin's corrections of the PacifiCare study by noting that Dr. Austin did not independently review the underlying data, and that his assumptions that the study did not take into consideration certain biases are based on guesswork. Defendants also challenge the fact that Dr. Austin inflated the relative risk of Baycol monotherapy by 40% while keeping the relative risk of the other statins constant.

Plaintiffs respond that Dr. Austin applied accepted methodologies to demonstrate how various flaws in the PacifiCare study led to an understatement of

the Baycol monotherapy risk for muscle disorders relative to the risk with other statins. With respect to Dr. Austin's corrections for misclassification, in which he raised the relative risk for Baycol by 40%, while keeping the other statins constant, Plaintiffs respond that because Dr. Austin was calculating the relative risks for Baycol, not rates, it was appropriate that he did not correct the relative risks for the other statins, because such calculation would not effect his correction with respect to Baycol. Plaintiffs further respond that Dr. Austin explained at length the 30% correction for misclassification of disease, and the 10% correction for misclassification of exposure, referring to paragraphs 56 through 58 of Dr. Austin's report.

Defendants respond that Plaintiffs have not met their burden in demonstrating that Dr. Austin's methodology comports with sound science. It is not enough to state he used "accepted and valid methodologies." With respect to the use of nondifferential misclassification, the example used by Plaintiffs on pages 6-7 of their brief uses incidence rates that are known. In this case, however, the incidence rates of myopathy are not known. As the report is based on unsupported assumptions and recalculations, Dr. Austin's testimony regarding the PacifiCare study should be excluded.

The Court has carefully reviewed Dr. Austin's report, as well as his deposition testimony and supporting documents. Based on that review, it appears

that Dr. Austin's recalculation of the PacifiCare study is based on a number of assumptions, and that Dr. Austin did not demonstrate that the bases for such assumptions are reliable.

This is especially apparent with respect to Dr. Austin's attempt to correct the PacifiCare study due to misclassification of cases. For this recalculation, Dr. Austin had to rely on a number of assumptions, and such assumptions were based on the "supposition" that there existed a higher association between Baycol and myopathy. See id., ¶ 56 ("Suppose Baycol use were related to an increased occurrence of myopathy more so than the other statins, but not to the occurrence of other less serious muscle problems."); id. ¶ 57 ("Suppose that the rate of a disease is higher among exposed persons (Baycol users) compared with unexposed persons (users of other statins)."); id. ¶ 58 ("Assuming the RR of myopathy for Baycol users compared with users of other statins is between 2 and 4 and considering a range from 95% true cases to only 50% true cases, I estimate a correction factor of about 1.26 (the average correction factor in the table below).") See also Austin Dep. at 262-263. The problem, in this case, is that these assumptions are based on an analyses of AER data, and the Court has determined that such analyses are unreliable. It thus follows that to recalculate a study, based in part on an unreliable methodology, would render the recalculation unreliable. The Court further notes that Dr. Austin's recalculation theory has not been tested,

subjected to peer review, and it has not been established that it is generally accepted.

The Eighth Circuit has cautioned against expert opinions that are "reasoned from an end result in order to hypothesize what needed to be known but was not." Sorenson v. Shaklee Corp., 31 F.3d 638, 649 (8th Cir. 1994). The Court recognizes that experts may, at times speculate, "but too much speculation is fatal to admission." Group Health Plan, Inc. v. Philip Morris USA, Inc., 344 F.3d 753, 760 (8th Cir. 2003). In this case, Dr. Austin testified at his deposition that he did not look at the underlying data for the PacifiCare study, and admitted he could do a better analysis if he had reviewed the underlying data. Instead, he made assumptions based on AER data that this Court has already found to be unreliable. The Court thus finds that Dr. Austin's recalculation of the PacifiCare study does not meet Daubert standards, and must be excluded.

3. Motion to Exclude Expert Testimony of R. Samuel Mayer, M.D.

Dr. R. Samuel Mayer is the Medical Director of Inpatient Rehabilitation at the Johns Hopkins Hospital and Clinical Associate in the Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine. He is certified by the American Board of Physical Medicine and Rehabilitation, the American Board of Electrodiagnostic Medicine, and the American Board of Independent Medical Examiners. He has published 17 peer-reviewed papers and

abstracts, and three book chapters, many related to the area of abnormal muscle tone and the area of epidemiology of disability. One abstract was a case series of three patients with rhabdomyolysis after taking cyclosporin and simvastatin. In addition to his clinical practice and research, he is also a professor at the Johns Hopkins University School of Medicine where he is a course director for Physical Medicine and Rehabilitation and instructor in Introduction to Clinical Medicine.

Dr. Mayer has submitted an expert report on behalf of Plaintiffs, which addresses the toxic effects of Baycol on muscle cells, the methods for diagnosing toxic myopathy, functional limitations that result from myopathy and the prognosis for recovery after Baycol has been withdrawn.

Defendants challenge two opinions contained within that report: 1) that Baycol causes long-term or permanent muscle damage, even after discontinuation of the drug, regardless of a lack of verification by laboratory data; and 2) Baycol is less safe than other statins and causes muscle damage more frequently and with greater severity than other statins, especially when taken with gemfibrozil or cyclosporin. Defendants argue these opinions are unsupported by scientific findings.

A. Comparative Toxicity of Statins

Dr. Mayer also intends to offer an opinion that Baycol was more dangerous than other statins, basing such opinion on AER data, the metabolic profile of

Baycol and its withdrawal from the market. As has been discussed previously, this Court finds that opinions as to Baycol's comparative toxicity cannot be made on the basis of AER data, or on the meta-analysis of AER data conducted by Dr. Farquhar.

With respect to Dr. Mayer's reliance on Baycol's "bioavailability", Defendants argue that there is no scientific support for this theory. Dr. Mayer admitted at his deposition that he was not aware of any study which showed a connection between Baycol's bioavailability and its comparative toxicity, and that he is not qualified to give opinions about a drug's comparative safety based on the drug's metabolic profile . Mayer Dep. at 258, 270.

Plaintiffs argue that Dr. Mayer is relying on other experts as the basis for these opinions, and that it is the cumulative effect of all experts' knowledge that completes the picture. Plaintiffs have provided no support for this position, however. If an expert is not qualified to opine in a particular area, and Dr. Mayer admits he is not qualified to provide opinions about a drug's comparative safety, such testimony is excluded under Daubert.

B. Long term effects from Baycol

Dr. Mayer has offered the opinion that Baycol causes long-term or permanent muscle damage, even after discontinuation of the drug, regardless of a lack of verification by laboratory data. Plaintiffs assert that this opinion is

supported by Dr. Mayer's clinical observations and by scientific and medical literature. As to Dr. Mayer's clinical experience dealing with statin-induced myopathy, Dr. Mayer testified at his deposition that while he prescribed statins to patients in his clinical practice, he did not recall ever having prescribed Baycol. Mayer Dep. 35:17-18. Further, he testified that he only treated one or two patients suffering from statin-induced myopathy who were taking Baycol, because Baycol was not on the formulary in his health care system. Id. 36:12-37:3. Thus, to the extent Dr. Mayer opines definitively that Baycol causes long-term or permanent muscle damage, his own clinical experience cannot support such an opinion.

In his report, Dr. Mayer states that "[c]erivastatin causes a continuum of muscle damage. . . . In many individuals, their symptoms will abate within days to weeks after discontinuance of cerivastatin. In others, a more profound amount of muscle death occurs, and muscle weakness develops. These individuals typically take months to recover, and may suffer permanent damage." Id. ¶ 17. Later in his report he states "[m]yopathy causes significant, and often long-lasting, functional limitations." Id. ¶ 30. In his deposition, Dr. Mayer testified that "statins can cause myopathy that does not involve cell death of muscles, and, consequently, does not raise the level of CK." Mayer Dep. 85:21-86:6. Defendants move to exclude testimony consistent with these statements.

The Court finds that none of the cited scientific and medical literature in Dr. Mayer's expert report directly address the issue of whether Baycol causes long term injury, even after discontinuation of the drug, and with no elevated CK levels. Rather, the cited literature address statins in general and none focus on long term affects.

For example, one of the pieces of medical literature cited by Dr. Mayer in support of his opinions is *Phillips et al.*, "Statin-Associated Myopathy with Normal Creatine Kinase Levels, Ann. of Intern. Med. (2002); 137(7):581-586. This article describes a study involving four patients taking statins. "The objective of the trial is to determine whether patients with muscle symptoms and normal creatine kinase levels while taking statins could distinguish statin therapy from placebo." Id. at 581. The study found that all four patients developed muscle symptoms during statin therapy despite normal creatine kinase levels. Id. The study further found that "symptoms and histologic changes occurred only during statin use . . . [T]he pathologic abnormality reversed upon discontinuation of statin therapy." Id. at 583.

Plaintiffs argue that while the 2002 *Phillips* article focused on patients without persistent problems, the study does not contradict Dr. Mayer's opinions, and subsequent articles from *Phillips* actually support Dr. Mayer's conclusion that myopathy persists in some patients. For example, in the 2004 *Phillips* article,

Plaintiffs note that one of the patients studied took Baycol and was still experiencing weakness more than 5 years after taking Baycol. *Phillips et al.* "Statin myotoxicity is associated with changes in the cardiopulmonary function." Atherosclerosis. (2004): 177:183 at 185. And more recently, Phillips and others published an article that, although it focused on rhabdomyolysis, recognized that there are persistent symptoms in some patients following statin therapy. *Antons et al*. "Clinical perspectives of statin-induced rhabdomyolysis." Am. J. Med. (2006):119:400-409.

The Court rejects Plaintiffs' characterizations of the Phillips articles. First, it is clear that Dr. Mayer did not rely on either the 2004 or 2006 articles, as they were published after he submitted his expert report. Second, as the focus of these articles did not address or conclude that Baycol causes permanent myopathy, they cannot form the basis of such an opinion.

Dr. Mayer also discussed an abstract published in Arthritis & Rheumatology to support his hypothesis that a patient's pain or weakness from statin therapy can persist after termination of statin use. *Hildebrand et al.*, "The Natural Course of Statin Induced Myopathy" Arthritis & Rheumatism (2003); 48(9) Suppl:730. The purpose of this study was to "define the time course, severity, and long term sequalae of patients who have experienced statin-induced myopathy." Id. After reviewing the medical records of 217 patients, the researchers noted that 30

patients taking a statin presented with muscle complaints, and of those in which the statin was discontinued (26/30), muscle symptoms resolved two months after discontinuation in 11 patients, and after 9 months, 16 patients returned to baseline. Id. From these results, the authors conclude "Although previously published case reports suggest significant morbidity with HMG-CoA reductase inhibitor myotoxicity, our findings indicate a benign clinical course with discontinuation of the offending statin and supportive care." Id. Subsequently, this abstract was published. See, *Hansen et al.*, "Outcomes in 45 patients with statin-associated myopathy." Archives Internal Med. (2005); 165:2671-2676. After reviewing 437 patients identified with ICD codes potentially representing cases of statin-associated myopathy, 45 patients were diagnosed as having statin-induced myopathy. The conclusion of this study revealed that "[p]atients with statin-associated myopathy experienced full resolution of muscle pain on cessation of statin-therapy." Id. at 2671.

Despite the study's conclusion, Plaintiffs note that of the 45 patients described in the study, 34% reported resolution of symptoms after 6 months and 7% after 14 months. Plaintiffs argue that this data supports Dr. Mayer's opinion that myopathy induced by Baycol can be long-term. Although the study sample was small, the Court agrees that the fact that a few patients did not report resolution of symptoms until 14 months after discontinuation of statin therapy

lends support to a medical opinion that statins may cause injuries that subsist for a period of time. This study did not, however, identify the statins involved, thus the study provides no link to a definitive opinion that Baycol in particular causes such an injury.

Dr. Mayer also relied on an AZT study in rendering his expert opinion that drug-induced myopathies, in general, can produce long-term muscle weakness in some patients. Mayer Dep. 201:19-20; *Chalmers et al.* "Prognosis in AZT myopathy." Neurology (1991); 41:1181-84. The study did not look at statins, rather it focused on the occurrence of myopathy in HIV positive patients taking AZT. Dr. Mayer also referred to studies of steroid induced myopathy, and experiments involving astronauts after returning from space flight in support of his opinion that Baycol can cause long term muscle weakness. Mayer Rep. at ¶ 29.

Plaintiffs assert that when faced with a dearth of information on a specific topic, doctors may reach out to the medical literature and extrapolate to the particular issues they seek to examine. In this case, as there is little information available as to Baycol's toxicity, Plaintiffs argue it was reasonable for Dr. Mayer to rely on the AZT study, steroid studies and the astronauts experiments. In support, Plaintiffs cite to Brasher v. Sandoz Pharmaceutical. Corp., 160 F. Supp. 2d 1291 (N.D. Ala. 2001), in which the court found it reasonable for the experts to rely on animal studies which showed the vasoconstrictive properties of Parlodel, and on

medical textbooks and treatises that identify bromocriptine, Parlodel's active ingredient, as a risk factor in stroke and myocardial infarction, in rendering an expert opinion that Parlodel caused the plaintiff's strokes.

Brasher lends no support for what Plaintiffs are attempting to do here, using studies (such as the AZT study) involving completely different classes of drugs to support its expert's opinions concerning statin-induced myopathies. As Dr. Mayer has not explained how one might reliably extrapolate from such studies a conclusion that statins, and Baycol in particular, causes permanent muscle injury, the Court finds such reliance misplaced.

Finally, Dr. Mayer opines that muscle strength returns at the rate of about three percent per week, and that after 33 weeks most patients would be mostly recovered. Defendants argue the actual literature cited by Dr. Mayer shows complete resolution of muscle symptoms in two months and in a range of two weeks to five months.

Defendants urge the Court to follow the decision in Leathers, supra which involved the statin Lipitor. In Leathers, the parties disputed whether Lipitor can cause the permanent, milder form of diffuse muscle ailment that the plaintiff claimed to have. Plaintiff first argued that general causation was already established, because the medical community recognizes that Lipitor and statins in general cause muscle-related ailments. 233 F.R.D. at 691. Defendants disputed

this contention, arguing the medical community, in fact, recognizes that discontinuing the statin will correct such muscle ailments. Id. After reviewing the articles and adverse incidence reports of record, the court found

> [t]he statin side effect recognized in the medical community is a temporary one that ends when the patient stops taking the drug. Plaintiff attempts to extrapolate this temporary side effect to establish general causation of a much more serious, permanent illness. However, Daubert decisions "warn against leaping from an accepted scientific premise to an unsupported one." (citation omitted).

Id. The court thus subjected plaintiff's expert report to the Daubert analysis, and found the expert's testimony that Lipitor caused plaintiff's permanent injuries was not reliable in that adverse event reports and the medical articles do not support such opinion "and do not create a scientifically valid causal link between Lipitor and statin-induced myopathy." Id. at 695. The court further noted that "[r]esearch addressing the relationship between Lipitor (and, more generally, statins) and Plaintiff's alleged injury is still in an immature stage and does not possess the level of reliability required by Daubert." Id.

In this case, like in Leathers, the parties dispute whether the statin at issue can cause persistent or long term muscle injury. After carefully reviewing all relevant articles and studies of record in this case[2], together with Dr. Mayer's

[2]Without knowing what medical literature was reviewed by the court in Leathers, this Court is hesitant to place much reliance on the Leathers court's ultimate finding that the medical literature did not support the expert's opinion that statins in general can cause permanent or long-term injury.

qualifications and experience, this Court finds Dr. Mayer's expert testimony is sufficiently relevant and reliable to the extent that he testifies consistent with the record - that while the vast majority of patients' muscle ailments resolve after discontinuation of statin therapy, there is a some indication that a few patients' muscle ailments did not resolve immediately.

Plaintiffs have put forth no support for Dr. Mayer's opinion that Baycol, or any statin, can cause permanent injury. To the extent that Dr. Mayer would testify definitively that Baycol, in particular, causes permanent or long term injury, such testimony must be excluded. See In re: Ephedra Prod. Liab. Litig., 393 F. Supp. 2d 181, 193 (S.D.N.Y. 2005) (recognizing that it is one thing to prohibit an expert from testifying causality "to a reasonable degree of scientific certainty" and that it is another to allow an expert to testify as to the scientific plausibility of a particular hypothesis of causality).

4. Motion to Exclude Expert Testimony of Dr. Richard Kapit

Dr. Richard Kapit is a medical doctor, and for nearly 30 years, he has worked in various capacities for the U.S. government. For 16 years he was a clinical reviewer at the FDA, where he reviewed data on clinical trials and medical use of drugs and biologicals. He also made recommendations to the FDA about the safety and efficacy of unapproved and approved pharmaceuticals, and about the adequacy of Investigational New Drug Applications, New Drug Applications,

Biologics Licensing Applications and postmarketing surveillance reports.

On behalf of Plaintiffs, Dr. Kapit has provided an expert report in which he offered several opinions. Defendants move to exclude certain of these opinions.

A. Comparative Toxicity of Statins

Dr. Kapit opined that after reviewing "hundreds of pages of IND and NDA documents about Baycol, internal company documents not part of regulatory submissions and documents generated outside the company, [he] found information demonstrating that Baycol was substantially more toxic to muscles that other statins to which Bayer compared its drug." Kapit Rep. ¶ 70. He further stated that "Cerivastatin is particularly unusual in its propensity to cause severe reactions in muscle tissue. . . " id. ¶ 72, and that Baycol was many times more dangerous to muscle tissue than any other statin. Id. ¶ 75. Defendants move to exclude these opinions as they are primarily based on comparisons of adverse event reports. See id. ¶ 74 (pre-marketing information) and id. ¶¶ 113-132 (post-marketing information). Defendants assert that in his deposition, Dr. Kapit conceded that in a large number of AERs, there is probably no relationship between the drug and the adverse event. Kapit Dep. 236:6-8. He also admitted that AERs cannot be used to calculate incidence rates. Id. 238:11-15.

Plaintiffs respond that Dr. Kapit relied on more than AER data in reaching his conclusions regarding Baycol's comparative dangerousness. He relied on

internal company documents and external data, animal studies, clinical trials, multiple AER databases and studies of AERs showing relative reporting rates among drugs in the same classification. More importantly, in this case Dr. Kapit's testimony is meant to illustrate the vast amount of information available to Bayer indicating the dangers of Baycol, and Dr. Kapit's specialized knowledge of the pharmaceutical industry and FDA regulatory scheme lays bare Defendants' failure to act in the face of numerous warning signs.

The Court has carefully reviewed Dr. Kapit's report, and finds that his opinion that Baycol was more toxic or more dangerous than other statins must be excluded for the same reasons discussed at length above. AER data and analyses have not been a generally accepted method by which to compare drugs, and the relevant medical and scientific literature cited by Dr. Kapit does not support such comparisons.

B. Opinions as to the Adequacy of Bayer's Submissions to the FDA

Defendants also move to exclude those portions of Dr. Kapit's report that criticize Bayer's submissions to the FDA and the FDA's approval of Baycol. For example, Dr. Kapit discussed an internal memo prepared by a Bayer epidemiologist, S. Niemcryk, in which Niemcryk commented that AER data obtained from the FDA "indicate that patients receiving monotherapy, cerivastatin substantially elevates risk for rhabdomyolysis compared with other statins." Kapit

Rep. ¶ 117. In the following paragraph, Dr. Kapit stated "[a]n ethical pharmaceutical manufacturer in possession of such information and analysis about one it [sic] its drugs should have immediately advised the FDA of the findings and asked for guidance from the Agency", but that Bayer did not inform the FDA of Niemcryk's findings. Id. ¶¶ 118, 119. In his deposition, Dr. Kapit admitted that a pharmaceutical company has no legal obligation to provide such internal data. Kapit Dep. 173. Dr. Kapit also criticized Bayer's submissions concerning an animal toxicity investigation. Kapit Rep. ¶¶ 88-90. He further provided criticisms of the FDA's prescription drug approval process, Kapit Dep. 126:24-127:22; that FDA reviewers are prone to overlook information; id. ¶ 19; and speculated that the FDA reviewers who approved Baycol made incorrect assumptions about Baycol. Id. ¶ 42. Defendants assert that to the extent such opinions are offered to support a claim that a plaintiff's injuries result from Bayer's failure to provide different or better information to the FDA is preempted by federal law. Buckman Co. v. Plaintiffs Legal Comm., 531 U.S. 341 (2001).

In Buckman, the Supreme Court held that any state tort law claim based on a "fraud on the agency" theory against the FDA is preempted by federal law. Id. 531 U.S. at 348. The basis for this ruling was that such claims would inevitably conflict with the FDA's responsibility of policing fraud. Id. at 350. In addition, allowing such claims to go forward would cause applicants to fear that their

disclosures to the FDA, although deemed appropriate by the administration, would be deemed insufficient in state court - causing applicants to flood the administration with a deluge of information that it neither wants or needs. Id. at 350-351. See also Webster v. Pacesetter, Inc., 259 F. Supp. 2d 27, 36-37 (D.D.C. 2003) (excluding evidence of what was told to the FDA because such evidence would lead the jury to speculate as to what the FDA may have done if the facts were different).

Plaintiffs assert that Defendants misinterpret Buckman, as that case addressed only state-law fraud claims arising from a duty that runs to the agency itself. Buckman does not, however, apply to state-law torts such as failure to warn, arising from duties that run to the medical community. For example, in In re: St. Jude Medical, Inc. v. Silzone Heart Valves Products. Liability. Litigation., No. MDL 01-1396 JRT/FLN, 2004 WL 45503 at *3 (D. Minn. Jan. 5, 2004), the court distinguished Buckman, noting that Buckman applies only to causes of action that depend entirely on the regulatory relationship between the federal government and the FDA, not to causes of action based in traditional state tort law. See also Kittleson v. Sandoz Pharm. Corp., No. 98-2277 JMR/FLN (D. Minn. Spt. 20, 2001) (P. Ex. B) (Buckman is premised exclusively on the allegation that the FDA was itself the victim of fraud).

Defendants reply that in this case, Dr. Kapit seeks to testify that Defendants

are liable to plaintiffs because they should have provided different information to the FDA, and that such testimony should be excluded based on Buckman.

The difficulty with this issue in the present context is that there is no specific claim or complaint before the Court. A similar situation was addressed in Bouchard v. American Home Products Corp., 213 F. Supp. 2d 802 (N.D. Ohio 2002). In Bouchard the court held that, based on the Buckman decision, any evidence offered only to show that the FDA was misled or that evidence was intentionally concealed from the FDA would be excluded. Id. at 812 (emphasis added). The court also held, however, that if the plaintiff's claims were, in fact, based on direct fraud against her and her physician, rather than the FDA, then evidence as to what was or was not provided to the FDA may be relevant. Id. (citing Globetti v. Sandoz Pharm. Corp. No. CV98-TMP-2649-S, 2001 WL 419160 (N.D. Ala. Mar. 5, 2001); Eve v. Sandoz Pharm. Corp., No. IP 98-1429-C-Y/S, 2002 WL 181972 (S.D. Ind. Jan. 28, 2002)).

Thus, to the extent Dr. Kapit's testimony is offered only to show that the FDA was misled, or that information was intentionally concealed from the FDA, the testimony must be excluded. The Court will leave to the respective trial courts the admissibility determination of such testimony to the extent it is offered to support a claim that the medical community, treating physicians or patients were misled by Bayer's alleged failure to submit information to the FDA.

C. Opinions as to Bayer's State of Mind and Ethical Opinions

Defendants further move to exclude Dr. Kapit's proposed testimony concerning Bayer's state of mind, see Kapit Rep. ¶ 27, 70, 72(d), 72(g), 73, 85(c), and 86, and the motives underlying business decisions. See id., ¶¶ 72(d), 77, 123, 129, 133-34. Defendants further challenge Dr. Kapit's speculations that most drug companies would have proceeded to the second phase of the development of Baycol, see id. ¶¶ 39-41, 92, his speculations that certain statements made by Bayer to the FDA "likely played a role in the Agency's allowing the clinical investigation program to go forward", id. ¶ 46, speculating that statements made by Bayer may have given the FDA certain impressions about Baycol, id. ¶ 69, and that "Stenger's note implies that the sales people were hurting, worried about the safety of Baycol. Id. ¶ 85(f). Defendants also move to exclude Dr. Kapit's testimony to the extent he offers his personal views on the ethical obligations of Bayer and other pharmaceutical companies. See Kapit Rep. ¶¶ 14, 104, 68, 82(a), 96, 98 and 85(h).

Personal views on corporate ethics and morality are not expert opinions. See In re: Rezulin Prod. Liab. Litig., 309 F. Supp. 2d 531, 544 (S.D.N.Y. 2004); In re: Diet Drugs Prod. Liab. Litig., 2001 WL 454586 at *9 (E.D. Pa. Feb. 1, 2001) (excluding opinions of medical ethics expert, as such opinions only marginally relevant to pharmaceutical companies conduct in manufacturing and marketing

drugs, where pertinent issues involved obligations of the company in testing, surveying and labeling medications). Further, expert testimony that is merely speculation or pure conjecture based on the expert's impressions of the physical evidence must be excluded as not based on any reliable methodology or scientific principle. J.B. Hunt Transport, Inc. v. Gen. Motors Corp., 243 F.3d 441, 444-45 (8th Cir. 2001). See also, In re: Rezulin, 309 F. Supp. 2d at 546 (expert opinions as to the intent, motives or states of mind of corporations, regulatory agencies and other have no basis in any relevant body of knowledge or expertise.).

Plaintiffs concede that an expert witness' speculation as to the motivation of Defendants is outside the realm of Rule 702. In addition, Plaintiffs agree that an expert witness' personal ethical leanings are inappropriate. Plaintiffs thus agree that Dr. Kapit should be precluded from offering opinions as to Defendants' intentions and from using the word "ethics" and its cognates. Plaintiffs disagree, however, with Defendants over the substance of Dr. Kapit's opinions regarding Defendants' so-called ethical conduct to the extent that Dr. Kapit's testimony establishes the standard of care for pharmaceutical manufacturers. Plaintiffs further argue that "[a] close reading of Dr. Kapit's report indicates that the term "unethical" is often used as a synonym for irresponsible or even reckless." Plaintiffs' Opposition Brief, p. 11.

Defendants do not dispute that generally, an expert may offer testimony as

to the appropriate standard of care. But to the extent that Plaintiffs' intend to offer Dr. Kapit's opinions about Defendants' supposed ethical obligations in the guise of an opinion on the standard of care, Defendants move the exclusion is nonetheless appropriate.

The Court finds that while Dr. Kapit may be allowed to testify as to the standard of care for pharmaceutical companies, he may not infuse his personal views as to whether Bayer acted ethically, irresponsibly or recklessly. Further, his expert testimony to the extent that he speculates as to Bayer's motive, intent or state of mind, or speculates as to motives of the FDA or what other drug companies would do is excluded.

D. Testimony Concerning Foreign Regulatory Matters

Finally, Defendants seek to exclude those portions of Dr. Kapit's report concerning regulatory actions in foreign countries, as such evidence is irrelevant. See Harrison v. Wyeth Labs, 510 F. Supp. 1 (E.D. Pa. 1980) (in addressing forum non conveniens motion, court held evidence as to safety of drugs in another country are properly the concern of that country); Deviner v. Electrolux Motor, 844 F.2d 769 (11th Cir 1988) (excluding evidence concerning Swedish law to avoid jury confusion); Hurt v. Coyne Cylinder Co., 956 F.2d 1319, 1327 (6th Cir. 1992) (foreign legal standards are excludable in products liability cases); Sherry v. Massey-Ferguson, Inc., 1997 WL 480893 at *2 (W.D. Mich. June 5, 1997) (finding

that while foreign legal standards and requirements would unnecessarily confuse the jury, evidence as to foreign tractor design admissible).

Plaintiffs intend to introduce Dr. Kapit's opinions concerning foreign regulatory actions to demonstrate Defendants had notice of Baycol's dangerous side effects - not that Defendants violated foreign law. Plaintiffs argue the cases cited by Defendants are distinguishable. For example, they argue that Harrison has no application in this case because it addressed a forum non conveniens motion. Plaintiffs further argue that Deviner and Hurt do not hold that evidence regarding foreign regulation was irrelevant; the evidence was excluded only to avoid jury confusion. Should Dr. Kapit be allowed to testify as to foreign regulatory actions, no jury confusion issues arise.

To the contrary, the Court finds that allowing the admission of evidence of foreign regulatory actions, in a case that is governed by domestic law, would likely cause jury confusion. Given that notice is not dependent on governmental action, and to avoid jury confusion, the Court finds Dr. Kapit's testimony concerning foreign regulatory actions must be excluded.

5. Motion to Exclude Expert Testimony of Dr. Bruce Carlson

Dr. Bruce Carlson is a Professor in the Department of Cell and Developmental Biology at the University of Michigan Medical School and a Research Professor and Director of the Institute of Gerontology at the University of

Michigan. He received a B.A. degree from Gustavus Adolphus, an M.S. degree in Ichthyology from Cornell and M.D., Ph.D. degrees from the University of Minnesota in 1965.

The overall theme of his research over the years has been the regeneration of limbs and muscles, and over the last 15 years, his research concentrated on problems of mammalian muscle regeneration and aging, and the biology of denervated muscle. He has published approximately 200 articles and chapters, authored 9 books, and was the editor of 13 additional books.

Dr. Carlson has been offered as an expert on behalf of Plaintiffs in the fields of clinical research and as a generic expert to opine as to the science of myo-anatomy and pathology and the effects of toxins on muscle degeneration and regeneration. In his expert report, Dr. Carlson opined that Baycol, whether used in monotherapy or in combination with other drugs, is responsible for a much higher incidence of muscle pathology and a death rate 16-80 times greater than that of other statins. Carlson Rep. ¶ 8. He further stated that Baycol associated muscle pathology is manifest along a spectrum of severity. Id. ¶ 9. He noted that many individuals that have suffered myopathic effects from Baycol are elderly, and that as a group, elderly individuals are more susceptible to muscle damage, and they repair muscle damage more slowly. Id. ¶ 10. Exercise can also cause muscle fiber damage, and that use of Baycol can result in increased muscle

damage after exercise or heavy work. Id. ¶ 11.

In his lengthy expert report, Dr. Carlson also made a number of additional observations and statements. Defendants move to exclude only the following: 1) Baycol is the most myotoxic statin (id. ¶ 8); 2) Baycol causes long-term damage even after discontinuation of the drug (id. ¶¶ 15, 17 and 51); 3) Baycol-induced myopathy can occur in the absence of clinical symptoms or corroborating laboratory data (Supplemental Report ¶ 4); and 4) Bayer should have studied and publicized myotoxicity tests of Baycol (Carlson Rep. ¶ 14).

A. Comparative Toxicity of Statins

Defendants assert that Dr. Carlson does not have expertise in comparing drug risks, therefore he is not qualified to testify regarding epidemiological and pharmacological properties of statins, and admits as much in his deposition. Carlson Dep. 143-47. Defendants further assert he has not conducted any independent research and is merely parroting the conclusions of other experts. Defendants also argue that Dr. Carlson has no experience working with AER data, and that he has never even seen an AER. Under these circumstances, Dr. Carlson is not qualified to offer opinions as to the comparative risks of Baycol.

Plaintiffs respond that Dr. Carlson's opinion that Baycol is not as safe as other statins is obvious, as Baycol is the only statin to be removed from the market. This particular opinion is also based on the expert opinions of Drs.

Farquhar and Austin, myotoxicity studies conducted by Bayer and adverse event data, as well as scientific and medical literature.

This Court has already excluded the expert opinions of Drs. Farquhar and Austin as to Baycol's comparative toxicity. Thus, reliance on AER data in this context, or on the opinions of Drs. Farquhar and Austin, is inappropriate. Contrary to Plaintiffs' assertions, the scientific and medical literature does not support opinions as to the comparative toxicity of statins. At most, relevant to this case, such material demonstrates the strong signal generated by AERs which associated Baycol use and rhabdomyolysis.

Dr. Carlson also stated he relied on studies conducted by Bayer in forming his opinion that Baycol is less safe than other statins. These studies, attached as Exhibits F and G to Plaintiffs' submission, do not support an opinion that Baycol is less safe, as the information relied on by Dr. Carlson was taken out of context. The 2001 study in fact states:

> There were considerable differences in the cytotoxicity of these statins. The highest toxicity was observed for cerivastatin[]. Simvastatin, fluvastatin and lovastatin behaved quite similarly [], whereas atorvastatin [] and especially pravastatin [] were markedly less cytotoxic. There is, however, a marked spread in the HMG-CoA reductase inhibitory activity of these compounds - cerivastatin and atorvastatin being by far the most active statin with IC 50 values in the low nanomolar range. When related to their pharmacological activity, it became obvious that the myotoxic potential of cerivastatin, simvastatin, fluvastatin, and lovastatin was in a comparable relation to the pharmacological activity (between 30 and 300 times IC50 of the HMG-CoA inhibition)"

Plaintiffs' Ex. G at 9-10 (emphasis added).

Accordingly, the Court finds that Dr. Carlson's opinion as to the comparative toxicity must be excluded as such opinion is not based on reliable science.

B. Long Term Muscle Damage

Dr. Carlson offered the following opinion in his expert report:

> On the basis of clinical and research data, cerivastatin can cause a spectrum of myopathy from mild to severe. This can be exacerbated by the concomitant use of certain other medications, by exercise or hard work, or even by the fact that a patient is elderly or female. The regenerative repair of damaged muscle can be compromised by factors such as drug-induced damage to satellite cells, fibrosis, damage to associated tissues (e.g. blood vessels or nerves), or advanced age. Based on a reasonable degree of medical certainty, I feel that as a result of these factors some individuals will experience or have experienced prolonged recovery from muscle pathology or suffer(ed) permanent muscle damage as the result of their use of cerivastatin alone or in combination with other agents.

Carlson Rep. ¶ 15.

Defendants seek to exclude Dr. Carlson's opinion that Baycol can have long–term adverse effects, as the basis for this opinion is not independent research, but reliance on unrelated studies, including animal research and muscle transplant cases. Defendants argue that Dr. Carlson's testimony in this regard represents an unsupported leap, and should be excluded. He conceded at his deposition that there is nothing in the scientific literature to support this opinion regarding long-term effects of Baycol. Carlson Dep. at 230-231, 303-304. Plaintiffs respond that it was reasonable for Dr. Carlson to extrapolate from the

literature and studies in existence to form opinions as to Baycol's long-term effects.

An expert may rely on inferences, analogies and extrapolation as long as the gaps between steps is not too great. In re: Ephedra, 393 F. Supp. 2d at 189. With respect to the animal studies conducted by Dr. Carlson, none involved the use of statins. Rather they involved muscle regeneration in animals generally. Carlson Dep. 19:17-23; 155:5-22. The Court finds that the gap between these animals studies and Dr. Carlson's opinions concerning long-term effects of Baycol is too great. Reliance on these studies is thus inappropriate. With respect to the studies conducted by Bayer, Exhibits F and G, neither address long-term effects of Baycol.

As discussed in the section addressing Dr. Mayer's expert opinions, the scientific and medical literature does not definitively support the opinion that Baycol causes long term or permanent injury. Rather, existing literature supports the finding that while most patients' muscle ailments resolve after discontinuation of statin therapy, there is some indication that a few patients' muscle ailments did not resolve immediately. Dr. Carlson's experience, qualifications and the information he relied on to render his opinion that Baycol can cause long-term or permanent injury do not lead to a different conclusion. Thus, like Dr. Mayer, Dr. Carlson's testimony that Baycol causes long-term or permanent injury must be excluded. He can, however, testify that with respect to statins in general, studies

indicate a small number of patients whose muscle ailments did not resolve immediately.

C. Baycol Induces Myopathy Even Where There is a Lack of Clinical Symptoms or Elevated CK Test Results.

In his supplement report, Dr. Carlson discusses generally the process of muscle fiber damage caused by exposure to statins, and other extrinsic factors, such as exercise. Supp. Report. ¶ 4. He states that as exposure to statins occurs over an extended period of time, "muscle fiber damage would be much less likely to occur as a single synchronous event than in small increments over a longer periods of time." Id. He then concludes that "such a sequence of events (small incremental muscle fiber damage over extended periods of time) would not necessarily result in large increases in plasma creatine kinase (CK) levels, because at any one time only a relatively small number of muscle fibers would be degenerating and releasing their cytoplasmic contents into the bloodstream." Id.

Defendants seek to exclude the opinion of Dr. Carlson that Baycol causes myopathy even where there is a lack of clinical symptoms or elevated CK test results. Plaintiffs assert that Defendants are misstating Dr. Carlson's testimony in this regard. Dr. Carlson opined that there is a continuum of injury that starts with one muscle cell and goes all the way to rhabdomyolysis. Dr. Carlson is not offered as a general causation expert - he is simply making a statement with regard to continuum of injury. The Court agrees. With regard to the cited portions of the

report, Dr. Carlson is simply addressing the phases of muscle fiber damage, and Plaintiffs have sufficiently demonstrated that he has the requisite qualifications to provide such an opinion.

D. Ethics Opinion

Defendants further move to exclude Dr. Carlson's proposed testimony concerning his personal opinions that Bayer was unethical. Specifically, Bayer moves to exclude Dr. Carlson's opinion that "it is difficult to understand why Bayer did not conduct or did not publicize results of thorough myotoxicity tests of cerivastatin in preclinical or clinical trials." Carlson Rep. ¶ 14. Defendants assert that Dr. Carlson is not an expert on FDA regulations, and does not know the standards for preclinical studies of new drugs. Dr. Carlson admitted at his deposition that he did not review the information provided to the FDA by Bayer prior to its approval, and that he did not review the FDA medical officer's review of Baycol after its new drug application was approved. Carlson Dep. 107-108. Without knowing definitively what preclinical or clinical studies were conducted, Dr. Carlson was not in the position to offer the opinion that Bayer did not conduct or publish certain studies. His opinion in this regard thus lacks foundation. The Court agrees.

Without knowing what information was provided to the FDA in support of the new drug application for Baycol, Dr. Carlson has not established a proper

foundation for his opinion that "Bayer did not conduct or publicize results of thorough myotoxicity tests of cerivastatin in preclinical or clinical studies."

In addition, the Court finds such testimony is simply Dr. Carlson's personal opinion as to the way Bayer approached preclinical and clinical testing. Similar testimony was excluded in the decision in the Rezulin multidistrict litigation. In Rezulin the court characterized testimony challenging the manner in which the pharmaceutical company presented data in a new drug application as speculative. Id. 309 F. Supp. 2d at 542-544.

> Such speculative testimony, contrary to plaintiffs' argument, cannot serve as the predicate for any purported industry ethical standard. Even if expert testimony on the ordinary practices of a profession or trade were appropriate to enable the jury to evaluate the conduct of the parties against the standards of ordinary practice in the industry, it still must comport with the reliability and helpfulness requirements of Rule 702. At their core, however, the witnesses' opinions regarding ethical standards for reporting or analyzing clinical trial data or conducting clinical trials articulate nothing save for the principle that research sponsors should be honest. Even if charitably viewed as a standard, the testimony nevertheless is so vague as to be unhelpful to a fact-finder.

Id. at 543.

The Court finds that Dr. Carlson's opinion with respect to how Bayer conducted preclinical and clinical testing not only lacks foundation, but is also speculative and will not assist the fact-finder. Accordingly, such testimony will be excluded.

6. Motion to Exclude Portions of the Testimony of Dr. Thomas Zizic

Dr. Thomas Zizic is an Associate Professor of Medicine at John Hopkins University School of Medicine in Baltimore, MD, and has been for the past 20 years. He is also currently Co-Director of Chesapeake Medical Research and has a private practice in Rheumatology. He reports that his principal subjects of research have been osteoporosis, osteonecrosis, the study of connective tissue diseases and a variety of other diseases that have muscle signs and/or symptoms. He has published approximately 100 articles and abstracts in peer reviewed journals, and several chapters in medical textbooks. For the last 15 years he has treated patients with statin-associated muscle disorders.

Dr. Zizic was asked to provide opinions on a number of subjects, including the cause and effect relationship between exposure to Baycol and muscle disease and disorders, and how statins in general act at the cellular level. Defendants move to exclude only that portion of Dr. Zizic's expert testimony that Baycol causes persistent or chronic muscle injury even in the absence of elevated CK levels, and that Baycol is the most toxic of all statins.

For the reasons stated above, the Court finds that Dr. Zizic's testimony that Baycol can cause persistent or chronic muscle injury must be qualified as follows: that while most patients' muscle ailments resolve after discontinuation of statin therapy, there is some indication that a few patients' muscle ailments did not resolve immediately.

With respect to Dr. Zizic's opinion that Baycol is the most toxic of statins, based on AER data and the scientific and medical literature, such testimony is excluded for the reasons previously stated.

7. Motion to Exclude Expert Testimony of Dr. David Richman

Dr. David Richman is a Professor in the Department of Neurology at the University of California at Davis School of Medicine in Davis, California. He graduated from Johns Hopkins University School Medicine in 1969, and has been board certified in neurology since 1976. His principal subject in research is myasthenia gravis, a neuromuscular disorder. Dr. Richman stated that expertise in muscle function and disease is integral to this field, and that he has devoted a substantial portion of his career to the study of muscle function and disease. Richman Report ¶ 4.

He has submitted an expert report on behalf of Plaintiffs, and Defendants challenge the following opinions contained within that report: 1) that Baycol is more toxic than other statins (Richman Rep. ¶ 11, Richman Dep. 134); 2) the theory that statins may induce persistent myopathies and rhabdomyolysis-related muscle damage even after statin use has been discontinued (Richman Rep. ¶¶ 11, 17, 20 and 35); 3) the theory that rhabdomyolysis may be diagnosed retrospectively (Richman Rep. ¶ 23, 25, Richman Dep. 25); and 4) that Baycol affects cell membranes differently from other statins (Richman Dep. 52-58).

A. Comparative Toxicity of Baycol

Defendants assert that Dr. Richman does not have expertise in epidemiology, therefore he is not qualified to offer opinions as to the comparative toxicity of Baycol. Furthermore, Defendants argue his opinions as to the comparative toxicity of Baycol to other statins is based on AER data and on a number of case reports, none of which involve a comparison of statins.

Plaintiffs respond that Dr. Richman's opinion as to the comparative toxicity of Baycol is based on reliable methodologies and should not be excluded. Specifically, Plaintiffs assert the opinion that Baycol is more toxic than other statins is supported by the medical literature, and by Dr. Richman's years of clinical experience.

The Court has reviewed the bases for Dr. Richman's opinion on the comparative toxicity of Baycol, including the case reports, and finds that Plaintiffs have not demonstrated that this opinion is supported by sound methodology. As previously discussed in this Memorandum Opinion, comparative analyses of the toxicity of statins, based on AER data, is not reliable. In addition, the case reports discussed in Dr. Richman's export report do not address toxicity comparisons, and Dr. Richman has not demonstrated how his review of a discrete number of case reports would support such an opinion. Accordingly, Dr. Richman's expert opinion that Baycol is the most toxic statin must be excluded.

B. Statin-Induced Persistent Injury

Defendants move to exclude Dr. Richman's opinion concerning statin-induced persistent injury on the basis that it is untested and speculative. Plaintiffs respond that this opinion is based on Dr. Richman's overall understanding after reading medical records of individual patients, the medical literature, as well as his own experience. He also relied on the Hildebrand article, discussed above, in reaching his conclusions that statins can cause persistent injury, even after discontinuation of the medication. Dr. Richman also relied on *England, J.F. et al.* "Mitochondrial myopathy developing on treatment with the HMG CoA reductase inhibitors - simvastatin and pravastin" 25 Austl. N.Z. J. Med. 374-75 (1995), which indicated that in three patients that had consented to a repeat muscle biopsy, "the microscopic and biochemical mitochondrial abnormalities were still present one year after stopping the drug."

As discussed above, existing medical literature, including the *England* article, indicates that while most patients' muscle ailments resolve after discontinuation of statin therapy, there is some indication that a few patients' muscle ailments did not resolve immediately. Thus, Dr. Richman is not precluded from testifying that statins may cause persistent injury, as long as such testimony is qualified with the statement that most patients' symptoms resolve after discontinuation of statin-therapy.

C. Retrospective Diagnosis of Rhabdomyolysis

Defendants also move to exclude Dr. Richman's opinion that "[i]n the event that the CK level is not measured in a timely manner, rhabdomyolysis may be diagnosed retrospectively on the basis of clinical information, including exposure to statin or other muscle toxin, complaints of muscle weakness, and/or brownish discoloration of urine resulting from the presence of myoglobin released by ruptured muscle cells." Richman Rep. ¶ 23. Defendants also move to exclude any testimony that a patient can have rhabdomyolysis even after the patient's CK level has dropped to normal range. Richman Dep. 25. Defendants assert no studies support these theories. Rather, such theories were generated solely for this litigation by extrapolation from the medical literature.

Plaintiffs respond that Defendants are distorting Dr. Richman's testimony in this regard. At his deposition, Dr. Richman stated that "at some point in time, the CK would be elevated" and "because CK is cleared from the blood relatively quickly . . . you could miss the elevation in an individual case if you only had a couple of time points." Richman Dep. 22:24-25. Relying on an article that appeared in the Journal of Internal Medicine, Dr. Richman further testified that a patient suffering from rhabdomyolysis, after the CK had been cleared from the bloodstream, would still have rhabdomyolysis, as there is still injury to the muscle at that point. Richman Dep. 24-25; *Mogyorosi*, "Rhabdomyolysis and Acute Renal

Failure Due to Combination Therapy with Simustatin and Warfarin," Journal of Internal Medicine, 1999; 246:599-602. Dr. Richman testified that in the event CK levels are not drawn in a timely manner, and the CK levels have returned to normal, a doctor could still diagnose a patient with rhabdomyolysis by looking at the symptoms the patient has recently suffered and other diagnostic evidence, such as dark urine. Plaintiffs further argue that rhabdomyolysis is not a synonym for elevated CK levels, and that while elevated CK levels is an easy-to-measure indicator of rhabdomyolysis, it is not the only way to diagnose the disease.

The Court has reviewed the relevant medical literature relied on by Dr. Richman, and finds none support his theory that rhabdomyolysis can be retrospectively diagnosed without evidence that CK levels were contemporaneously elevated as stated in paragraph 23 of his report. Rather, the relevant medical literature provides that an elevated CK level is a diagnostic criteria. See, eg., *Warren, et al., "*Rhabdomyolysis: A Review" Muscle & Nerve, 2002:332-347, at 334 (noting that many cases of rhabdomyolysis are subclinical and can only be detected by an elevated serum CK); *Ravnan et al*, "Cerivastatin-Induced Rhabdomyolysis: 11 Case Reports" Pharmacotherapy 2002:22;534-537 (rhabdomyolysis has been defined by smaller increases in creatine kinase ($\geq$ 5 times the upper limit of normal); *Mogyorosi*, (no suggestion that rhabdomyolysis can be retrospectively diagnosed absent contemporaneous elevated CK levels).

The motion to exclude this aspect of Dr. Richman's report, and any testimony related thereto, is granted.

Defendants also take issue with Dr. Richman's opinion that strength testing is a method to diagnose the presence and severity of muscle injury. Richman Rep. ¶ 25. While recognizing that the report discusses "muscle injury," Defendants argue that Dr. Richman is really opining that strength testing can be used to diagnose statin-induced myopathy. Plaintiffs respond that Dr. Richman is not suggesting that rhabdomyolysis or statin-induced myopathy can be diagnosed retrospectively on the basis of exposure to a statin and strength testing. His testimony regarding strength testing is that it could be used together with other combinations of factors. The Court finds that Plaintiffs have properly characterized Dr. Richman's opinion with respect to strength testing. See id. Qualified in the manner described by Plaintiffs, testimony concerning strength testing is admissible.

D. Baycol May Affect Cell Membranes Differently Than Other Statins

At his deposition, Dr. Richman testified that "the ability of statins to get into the muscle cell differs, and Baycol being the most effective in getting into the muscle cell." Richman Dep. 52:19-21. He further testified that "I think it's very likely that Baycol has more of an effect on the membrane of the muscle cell. And that could explain why there's more rhabdomyolysis with Baycol." Id. at 53:5-8.

Defendants move to exclude this testimony, arguing its sole basis is extrapolated from a single sentence from the Davidson article, which reads "[t]he noted myotoxicity and subsequent withdrawal of cerivastatin from the worldwide market in August 2001 has demonstrated that the safety of statins is not a class effect." M.H. Davidson, Controversy surrounding the safety of cerivastatin, 1 Expert Opin. Drug Saf. 207-12 (2002).

Plaintiffs respond that in addition to the Davidson article, Dr. Richman's opinion concerning how Baycol affects cell membranes is based on his 30 plus years of experience as a physician and muscle expert. It is Defendants' position, however, that as there is no consensus in the medical community as to the exact mechanism by which statins affect muscle cells, testimony that Baycol affects muscle cells differently should be excluded.

The Court agrees with Plaintiffs that Dr. Richman's testimony in this regard is logically and reliably based on his years of experience directly related to muscle injury, the *Davidson* article, the relevant medical literature discussing the association between Baycol and rhabdomyolysis, and the fact that Baycol was withdrawn from the market due to the increased reporting of rhabdomyolysis after Baycol use. The motion to exclude this aspect of Dr. Richman's testimony is denied.

8. Motion to Exclude Expert Testimony of Dr. Charles E. Boult

Dr. Charles Boult is a geriatrician practicing at Johns Hopkins Hospital. He earned his medical degree from Wayne State University School of Medicine in 1974, received a master of public health from the University of Minnesota in 1989 and received a master of business administration form the University of Michigan in 2000. He practiced emergency medicine from 1978 to 1981 and since then has held a full-time academic position that includes patient care in hospitals, nursing homes, rehabilitation facilities and outpatient settings.

Dr. Boult has provided an expert report on behalf of Plaintiffs that addresses aging generally, and his opinions that aging "is accompanied by several biologic processes that change the ways the body functions, increase its vulnerability, and impair its response to injury and its potential for recovery." Boult Rep. ¶ 18. He opines that: 1) clinical criteria independent of objective findings permit the post hoc diagnosis of muscle injury allegedly caused by Baycol; and 2) Baycol causes muscle pain after patients have stopped taking the medicine. Id. ¶¶ 23 and 26.

Defendants challenge portions of Dr. Boult's expert report.

A. Opinion that Baycol Causes Persistent Myopathy.

Defendants assert no study shows a causal link between Baycol and persistent or chronic muscle injury after the patient stops taking the medicine.

Plaintiffs respond that Dr. Boult will testify that while most Baycol-induced myopathy resolves within a few weeks, that is not always the case. Plaintiffs

further assert that the articles relied on by Dr. Boult do not contradict this opinion and that recent articles support it.

In addition to the articles addressed previously in this Memorandum Opinion, Dr. Boult also relied upon *Argov*, "Drug Induced Myopathies" Current Opinion in Neurology 2000; 13:541-545. In this article, the author notes that "stopping the medication will usually result in return of serum CK to normal levels" and that myalgia unrelated to activity "is almost always associated with elevated serum CK. Withdrawal of the drug usually leads to full recovery." Id. at 542. The author also noted that "I have seen several patients in whom recovery was very slow and incomplete and who continued to complain of muscle aches long after the drug was stopped. This clinical experience has been reported to me by other neuromuscular experts also, but has not been formally reported." Id.

Plaintiffs note that a recent article confirms that patients suffer persistent statin-induced myopathy, citing to *Dobbin, M.H.* "Underappreciated Statin-Induced Myopathic Weakness Causes Disability." Neurorehabilitation and Neural Repair 2005; 19:259-263. This study found a likely causal relationship between disabling myopathy and statin use. The author noted that no studies of statins included strength testing, therefore the incidence of weakness with or without muscle symptoms and elevated enzymes is unknown or perhaps overlooked. Id. at 259. With respect to the test subjects observed, by three months after discontinuance of

the statin, all recovered proximal strength. Id.

Defendants do not challenge the opinion that statins can cause persistent myopathy while the patient is taking the statin, however. Rather, they move to exclude the opinion that Baycol causes persistent myopathy after the patient has stopped taking the medicine, and the Dobbin study confirms this position. Id. at 260-261.

Consistent with its prior rulings herein, the Court finds that Dr. Boult can testify consistent with the record - that while most statin-induced myopathy resolves within a few weeks after discontinuance of the statin, there is evidence that some patients' symptoms do not resolve immediately.

B. Diagnosis of Statin-Induced Myopathy in the Absence of Clinical Evidence

Defendants also challenge Dr. Boult's opinion that, even without objective findings, one may diagnose a patient as having Baycol-induced myopathy if: 1) the muscle pain is severe enough to cause significant functional limitations; 2) the symptoms began after the statin was ingested; and 3) the symptoms diminish or remain the same after the statin is discontinued. Boult Rep. ¶ 23.

In his deposition, Dr. Boult admitted his clinical criteria have not been scientifically accepted or addressed in the medical literature. Boult Dep. 252. In addition, Dr. Boult also admitted that a differential diagnoses is the core methodology for diagnosing statin-induced myopathy. Id. at 134.

Plaintiffs respond that the three criteria listed above are consistent with the medical literature, and that this opinion is offered as to general causation, not to specific causation. Further, Plaintiffs assert that Dr. Boult is not advocating exclusion of a differential diagnosis from a case-specific opinion and that individual patient information will need to be evaluated.

That is not what Dr. Boult included in his report, however. He stated "[p]eople who meet this criteria are likely to have moderate-to-severe statin-induced myopathy." Accordingly, the motion to exclude that portion of Dr. Boult's report in which he opines that even without objective findings, one may diagnose a patient as having Baycol-induced myopathy if the patient meets three clinical criteria is granted.

C. Comparative Toxicity Opinion

Although not included in his report, Dr. Boult testified at his deposition that the percentage of patients who acquired muscle damage from cerivastatin was greater than the percentage of people who suffered muscle damage with other statins, Boult Dep. 86:5-8, and patients had a more likely chance to suffer moderate to severe myopathy with cerivastatin. Id. 182:3-12. The basis for these statements is the *Staffa* article referred to previously. For the reasons stated above, with respect to the unreliability of AER data, such testimony is scientifically unreliable and is excluded.

D. Adequacy of Labeling

Also in his deposition, Dr. Boult offered opinions that Bayer should have warned doctors that clinical trials of Baycol did not sufficiently test the effects of the drug on the elderly. Boult Dep. 121:14-122:5; 79:17-80:4; 111:22-112:7. This opinion is also alluded to in his report. Boult Rep. ¶ 20 (discussing the need, in general, to provide complete information from the pharmaceutical manufacturer about the effects of age, disease and other drugs on the prescribed drug's likelihood of causing adverse effects.).

Defendants assert that the only relevant question as to labeling was whether the labeling complied with FDA regulations. Defendants further assert Dr. Boult does not claim any expertise in whether adverse event data should be included in labeling. Defendants also point out that Dr. Boult did not actually review Baycol clinical trial data, nor did he review the Baycol marketing materials. Boult Dep. 62:20-63:3 and 123:16-18. In fact, in both the 1997 package insert and the 2000 amended package insert, both refer to geriatric use and that the 2000 insert notes that one study of 0.8 mg noted that women over 65 with low body weight have a higher risk of myopathy.

Plaintiffs respond that labeling is highly relevant in this case as Baycol was marketed to the elderly and opinions as to the label's warnings for this particular population is clearly relevant. In support of their position, Plaintiffs cite to the

opinion issued by Judge Bechtle in the Fen-Phen case, in which the court held that physicians may opine on the medicine and science regarding the risks and benefits and compare that knowledge to what was disclosed in the label. In re: Diet Drugs, 2000 WL 876900 (E.D. Pa. June 20, 2000). The court held "[the doctors] are qualified to render an opinion as to the label's completeness, accuracy, and – it follows from that – the extent to which any inaccuracies or omissions could either deprive a reader or mislead a reader of what the risks and benefits of the diet drugs in issue are or were at the time the labeling was published." Id. at *11. This ruling was subsequently adopted after remand. Smith v. Wyeth-Ayerst Laboratories, 278 F. Supp. 2d 684, 702 (W.D.N.C. 2003).

The Court agrees that Dr. Boult is qualified to render an opinion regarding the completeness or accuracy of the Baycol label based on his knowledge of the risks of Baycol and his own clinical experience. He is not, however, qualified to render an opinion as to whether the Baycol labeling complied with FDA regulations. Thus, any testimony consistent with such opinion is excluded.

9. Motion to Exclude Expert Testimony of Dr. Martyn Smith

Dr. Martyn Smith is a toxicologist and has been a professor of toxicology in the Division of Environmental Health Sciences, School of Public Health, University of California Berkeley since 1992. He received a Bachelor of Science Degree in Biology from Queen Elizabeth College, University of London in 1977 and a Ph.D.

in Biochemistry from the Medical College of St. Bartholomew's Hospital, London in 1980. For the past fifteen years he has been a full member of the Society of Toxicology, and he has been a reviewer or a member of the editorial boards of several peer-reviewed journals. He has also authored or co-authored hundreds of articles, book chapters and abstracts about toxicological matters.

In his expert report, Dr. Smith offers a number of opinions. Defendants move to exclude the following: 1) Baycol is the most toxic commercially available statin (Smith Rep. ¶ 6(a); 2) Baycol is more susceptible to drug-drug interactions because of its dual metabolic profile (Id. ¶ 29-32); the mechanism of statin-induced myopathy (Id. ¶ 19-23); and 4) whether Bayer and its scientists acted ethically.

A. Comparative Toxicity of Baycol

Dr. Smith first opined that Baycol is at least 10 times more toxic than other statins. In support of this opinion, Dr. Smith cited a number of articles that have previously been discussed in this Memorandum Opinion, for example the *Staffa* letter, *Farmer*, *Thompson* and *Hamilton-Craig*. Smith Rep. ¶¶ 7-10. For the reasons state above, these articles do not support a comparative toxicity opinion.

In addition, Dr. Smith relied on two animal studies in rendering his comparative toxicity opinion. Id. ¶ 16-18. Defendants assert that Dr. Smith improperly extrapolates data from flawed animal studies. The first study cited,

Matsuyama K. et al., "Evaluation of myopathy risk for HMG-CoA reductase inhibitors by urethane infusion method." Biol. Pharm. Bull. 25:346-350 (2002), is flawed because the scientists conducting the study infused animals with urethane, an anesthetic that has the potential to cause myotoxicity, like all statins. Dr. Smith admitted at his deposition that there is no data to say whether urethane interacts with all statins in the same way. Smith Dep. 100. Also, Defendants argue the dose given to the rats was not comparable to the dose prescribed for humans - that the rats were given a dose two thousand times the dose that would be given a human.

Dr. Smith also relies on the *Matzno* study, which examined the myotoxicity in rats muscle cells *in vitro*. *Matzno et al.*, J. Lipid Research 55, 795-802, 2003. Defendants argue that like the *Matsuyama* study, this study did not adjust the dose of the drug. Dr. Smith admitted in his deposition that studies done in a test tube must be cautiously interpreted, and that the scientific community would consider such tests potentially unreliable. Smith Dep. 123-124.

Plaintiffs respond that given Dr. Smith's background and expertise, he properly based his opinions on the total data picture, provided by animal, *in vivo, in vitro* and human studies. Plaintiffs argue that Dr. Smith does not extrapolate from the animal studies that Baycol is the most toxic of statins in humans, rather he opines that Baycol is the most toxic *in vivo and in vitro* and that the scientific

community considers Baycol to be the most toxic of statins. Plaintiffs assert that there is no general rule that animal studies are unreliable. See Glastetter v. Novartis Pharm. Corp., 252 F.3d 986, 991 n.5 (8th Cir. 2001)(refusing to discount the value of animal studies *per se*); Bonner, 259 F.3d 924 (affirming the admissibility of expert, whose opinion was based in part on *in vivo* studies.)

Plaintiffs also argue that the differences in doses is irrelevant and unpersuasive. Dr. Smith does not base his opinion on the extrapolation of the results of high-dose animal studies to humans - he bases his opinion on the comparison of high-dose animal studies between statins. Animal studies can also form the basis for an opinion if they are interpreted with the proper care and precision. Dr. Smith knows this, and did this in forming his opinions.

The Eighth Circuit has recognized that because of the dose-response differential between animals and humans, extrapolating to humans from animal studies can be problematic. Sorenson., 31 F.3d at 646, n. 12. Expert opinion testimony has been excluded when the expert fails to take into account the critical differences in animal data and human experiences, including but not limited to extrapolation in dosing. See, eg., Soldo v. Sandoz Pharms., Inc., 244 F. Supp. 2d 434, 546 (W.D. Pa. 2003)(citing Joiner, 522 U.S. 136); Bourne ex rel. Bourne v. E.I. Dupont de Numbers and Co., 189 F. Supp .2d 482, 496 (S.D.W. Va. 2002). In this case, Defendants have demonstrated that in both animal studies cited, no

adjustments were made for dosing, and in the *Matsuyama* study, no control addressed the use of urethane, a compound which in itself can cause myotoxicity. The Court is not persuaded by Plaintiffs' argument that Dr. Smith, in relying on the animal studies, was simply opining that *in vitro* and *in vivo*, Baycol was the most toxic. The inclusion of such an opinion would only be relevant in this case if the jury were to infer from such studies that Baycol is the most toxic in humans. Accordingly, the Court finds that Dr. Smith's testimony concerning the animal studies does not provide a scientifically reliable basis for his opinion that Baycol is the most toxic statin.

B. Baycol is more susceptible to drug-drug interactions because of its dual metabolic profile.

Defendants next challenge Dr. Smith's opinions that Baycol's dual metabolic profile makes drug-drug interactions more likely and that an increase in cell death more likely than not plays a critical role in the mechanism of statin-induced myopathy. Smith Rep. ¶¶ 29-32. In his deposition, Dr. Smith admitted that his opinions regarding Baycol's dual metabolic profiles are untested and that he has not seen any writing supporting his theory. Smith Dep. 176.

Defendants further note that Plaintiffs' Rebuttal Expert, Dr. Sandy Pang, disagreed with Dr. Smith's theory concerning dual pathways. "I think it is better to have more than one pathway. Then you . . . if you inhibit one enzyme, the

other compensates for the inhibition." Pang Dep. 153:17-20. Dr. Pang goes on to state, however, "[b]ut of course if you have two enzymes, the incidences of drug-drug interactions, as Dr. Smith pointed, out, becomes higher because you have two different components that could be interacted with." Id. 153:23-154:1.

Plaintiffs respond that in reaching this opinion, Dr. Smith reviewed the data and reports of Bayer scientists, and analyzed them using his own expert knowledge of molecular toxicology. This opinion is well-reasoned and he explains at length how he reached this conclusion. The Court agrees.

Dr. Smith is an experienced toxicologist. In his report, Dr. Smith provides a thorough explanation for his opinion that Baycol's "dual metabolic pathway" increases the risk of drug interaction. Defendants do not challenge the methodology used in reaching this opinion. Rather, Defendants simply argue that Dr. Smith could point to no peer-reviewed articles that support his theory. Having failed to demonstrate that Dr. Smith's opinion as to Baycol's dual metabolic pathway is so fundamentally unsupported that it can offer no assistance to the jury, the motion to exclude this portion of Dr. Smith's expert testimony is denied.

C. Mechanism of Statin-Induced Myopathy

Dr. Smith further opines as to the mechanism of statin-induced myopathy. Smith Rep. ¶¶ 19-23. Defendants move to exclude this portion of his report, arguing it is merely unfounded hypothesis. Dr. Smith conceded that the

mechanism of statin injury is not fully known and that "additional work is required to demonstrate definitively" the mechanism of statin-induced myopathy. Smith Dep. 58:2-5; Smith Rep. ¶ 23. Defendants assert that as the opinion is not generally accepted in the scientific community, it should be excluded under Daubert.

Plaintiffs respond that there is a consensus in the medical community that statins cause rhabdomyolysis and other muscle injury. The fact that the exact mechanism of statin-induced myopathy is not yet known does not affect the admissibility of Dr. Smith's opinion. The Court agrees. Other courts have recognized that science is constantly evolving, and the fact that a theory is new or in the process of becoming generally accepted does not prevent its admission in court. Ruiz-Trioche v. Pepsi-Cola Puerto Rico Bottling Co., 161 F.3d 77, 85 (1st Cir. 1998). Dr. Smith's opinion regarding the mechanism of statin-induced myopathy is well-reasoned and based on relevant scientific literature as well has his years of experience in toxicology. Accordingly, Defendants' motion to exclude this opinion is denied.

D. Opinion as to Whether Bayer and its Scientists Acted Ethically.

Dr. Smith also criticized Bayer for inadequately evaluating the potential toxicity of Baycol. Smith Rep. ¶ 12. He further claimed that Bayer's scientists were concerned about Baycol's narrow safety margin very early in the development

process but that their warnings went unheeded. Id. ¶ 14. Defendants argue these opinions are inadmissible because they are either legal argument or based on speculation. Defendants add that similar testimony was excluded by Judge Bernstein of the Pennsylvania Court of Common Pleas in Galdi v. Bayer Corp., Pa. Ct. Cmn. Pls. July Term 2002, Case No. 4892, Trial Tr. 3/12/04 at 37:2-4. (Defendants Ex. H). Defendants argue that Bayer's motives are classic jury questions, not one for experts. See In re Diet Drugs, 2000 WL 876900 at *9.

Plaintiffs respond that Dr. Smith is qualified to testify as to the proper toxicological methods to interpret data. Moreover, Dr. Smith's testimony that Bayer toxicologists were concerned about the steep dose-response curve and narrow safety margins is not an inference the jury is capable of making without his expert assistance. Finally, Dr. Smith is not speculating as to what Bayer's toxicologists knew, as they state directly in their reports what they knew.

The Court finds that Dr. Smith's opinion criticizing Bayer for inadequately evaluating the potential toxicity of Baycol, and asserting that Bayer ignored warnings is legal argument that does not qualify as expert testimony under Rule 702. The Rezulin court held that proposed expert testimony that the pharmaceutical manufacturer interfered with scientific freedom, and suppressed scientific inquiry, pertains to "lay matters which a jury is capable of understanding and deciding without the expert's help. It is no more than arguments and

conclusory statements about questions of fact masquerading behind a veneer of technical language." In re: Rezulin, 309 F. Supp. 2d at 553. The same is true in this case. Bayer's motives as to how it proceeded with evaluating Baycol's toxicity, and its reactions to its toxicologists's warnings are issues that can be decided by the jury, without expert assistance.

Finally, Defendants seek to exclude Dr. Smith's opinion that Baycol is not an "ideal statin" - as represented to the FDA by Bayer. Smith Rep. ¶ 24. Defendants argue that at his deposition, Dr. Smith conceded that no statin is ideal. Smith Dep. 168. Thus, any opinion on this issue must be an attempt to demonstrate that Bayer misled the FDA. Defendants further argue that federal law preempts any state-law fraud on the FDA claims. Buckman, 531 U.S. at 353.

Plaintiffs respond that Dr. Smith is in no way stating that Bayer misled the FDA, he is simply pointing out the inaccuracy of Bayer's scientists' statement to underscore his expert opinion regarding the toxicological shortcomings of Baycol.

Although Dr. Smith does not expressly state that Bayer misled the FDA by describing Baycol as an "ideal statin", the Court is nonetheless concerned that such an inference could be made by a jury. Where such testimony can cause jury confusion as to the nature of the plaintiff's claims, exclusion may be appropriate. Bouchard v. Am.Home Prods. Corp., 213 F. Supp. 2d 802, 811 (N.D. Ohio 2002). On the other hand, Dr. Smith is qualified to testify as to the medical facts and the

risks and benefits of statins. In re: Diet Drugs, 2000 WL 876900 at *11. His testimony concerning what could be considered an "ideal statin" may be relevant at trial. This issue is best left to for the trial court's determination, depending on what issues will be tried. The motion to exclude this testimony is thus reserved.

10. Motion to Exclude Expert Testimony of Stephen Raskin

Dr. Stephen Raskin is a cardiologist. He has been board certified in Internal Medicine since June 1976, with a subspecialty in Cardiovascular Diseases since 1977. He is currently an Associate Clinical Professor of Medicine at the University of California, San Francisco Medical Center, and since 1977 has served as the Director of Coronary Care at Alameda Hospital in Alameda, California.

In addition to providing an expert opinion, Plaintiffs assert that Dr. Raskin will also provide factual evidence that the information given physicians by Bayer in an educational/marketing setting was materially different from the information known to Bayer at the same time.

In his expert report, Dr. Raskin opined that based on his review of information known to Bayer, he and other physicians were not informed about key and very material concerns relating to Baycol's efficacy and safety. Raskin Report ¶ 6. Dr. Raskin opines that Bayer actually misrepresented the risks of muscle toxicity with Baycol, and that had he known of Baycol's risks, he wouldn't have prescribed Baycol to his patients, and would not have participated on Baycol's

Clinical Advisory Panel. Id. ¶ 26.

A. Comparative Toxicity of Baycol

Defendants move the Court to exclude Dr. Raskin's opinion as set forth in paragraphs 12 and 26 of his report, in which he states that Baycol was more dangerous than other statins. Defendants argue the underlying bases of this opinion, AER data and analyses of such data, are not reliable under Daubert.

Plaintiffs respond that Dr. Raskin relied on more than AER data in reaching his conclusions regarding Baycol's comparative dangerousness. He relied on his expertise as a practitioner, as a statin drug researcher, his review of internal Bayer documents, as well as AER data. Plaintiffs further note that Dr. Raskin has experience working with AER data, and is aware, and took into consideration, biases that arise from such data.

In reviewing Dr. Raskin's report, it is clear that his conclusions concerning the comparative toxicity of Baycol are based on AER data. See Raskin Rep. ¶ 10 (discussing FDA adverse event report); id. ¶ 11 (increase in adverse event reporting); id. ¶ 13 (Bayer scientists discussing AER data); id. ¶ 14 (discussing adverse event reporting rates); id ¶ 15 (same); id. ¶ 17 (same); id. ¶ 22 (discussing Bayer chart comparing confirmed U.S. rhabdomyolysis cases according to FDA data). As this Court has determined such data not a reliable foundation for the opinion as to the comparative toxicity of statins, such testimony is

excluded.

B. Adequacy of Baycol Labels

Defendants also move to exclude those portions of Dr. Raskin's report in which he opines that Bayer should have used AER or other post-marketing surveillance data to change the warnings on the Baycol label and to provide some form of comparison to other statins. Raskin Rep. ¶¶ 14, 15, 17 and 23, Raskin Dep. 109:21-25.

Defendants assert that Dr. Raskin's proposed testimony concerning the adequacy of Baycol labeling must be excluded as he has no expertise in FDA rules and regulations concerning labeling, and such testimony is contrary to FDA regulations, which specifically prohibit comparison data on labels. 21 C.F.R. § 201.57(g)(4) and (c)(3)(v)(2003) and 21 C.F.R. § 314.126(e)(2004). Defendants further assert that Dr. Raskin's opinion as to the Baycol label derive entirely from another expert's report, Dr. Kapit, and his review of federal regulations.

Plaintiffs respond that Dr. Raskin may testify to the state of scientific and medical evidence of risk of a pharmaceutical product and to the question of whether information provided on a label adequately describes the risk. In re Diet Drugs, 2000 WL 876900, at *11 (refusing to preclude expert opinions of physicians comparing facts in evidence with the status of the content shown on

the labeling of the diet drugs). Also, Dr. Raskin is an expert on statin therapy, was a past member of Bayer's Advisory Panel on Baycol, and is thus well qualified to render an opinion as to the label's adequacy. Plaintiffs further argue that as a prescribing physician, Dr. Raskin can testify based on personal knowledge as to whether a warning label adequately warned of risks of the product, asserting similar testimony was found admissible in Stahl v. Novartis Pharmceutical.Corp., 283 F.3d 254 (5th Cir. 2002).

In Stahl, the district court allowed the treating physician to testify as to whether the label at issue adequately warned him of the known risks associated with the drug Lamisil. Id. at 265. In this case, however, Dr. Raskin is not testifying as the treating physician, nor is he proposing to testify as to whether the label warned of known risks. Rather, his testimony is offered as an expert witness who is proposing to testify, *inter alia*, that the Baycol package inserts should have included AER data. In this regard, Dr. Raskin is not qualified to render such an opinion. See In re: Diet Drugs, 2000 WL 876900, at *12 (finding physicians not qualified to speak as experts in the field of the requirements of the federal regulations regarding labeling and warnings for FDA approved drugs.) Thus, to the extent that Dr. Raskin would testify that Baycol package inserts should have included AER data, such testimony is excluded.

C. Personal Opinions

Defendants further move to exclude Dr. Raskin's proposed testimony concerning his personal opinions that Bayer was unethical, Raskin Rep. ¶¶ 12, 16, 17 and 18, opinions concerning Bayer's state of mind, and the motives underlying business decisions, id. ¶¶ 6, 10, 21 and 26, speculation as to other physicians' knowledge, id. ¶¶ 6, 12, 19, 21, 25, and 26, and an argumentative narrative of Baycol's history. See, Id. ¶¶ 13, 14, 18, 24 and 26.

For the most part, Plaintiffs do not contest this aspect of Defendants' motion to exclude. In its opposition brief, Plaintiffs only respond that Dr. Raskin is not offering opinions as to Bayer's motive, knowledge, intent or state of mind. As Defendants point out, however, comments within his expert report could be construed as such. For example, Dr. Raskin notes "[p]erhaps in response to the growing reports of rhabdomyolysis in patients taking Baycol, in February, 1999, Bayer requested information from the FDA." Id. ¶ 10. This statement clearly infers a motive for Bayer's conduct. The question of corporate intent is one for the jury, not for an expert. In re: Diet Drugs, 2000 WL 876900, at *9.

As discussed above, an expert may not testify as to ethical issues or to his personal views. Nor can Dr. Raskin testify as to what other physicians knew or would have done with different information. In re: Diet Drugs, at *11 (holding that physicians' qualifications do not render them qualified to testify about what all doctors generally consider in making prescription decisions). Accordingly, to

the extent that Dr. Raskin offers personal opinions as to ethical issues, motive, intent, knowledge or state of mind of Bayer and its employees, and about what other physicians knew or would have done with different information, such opinions are excluded.

11. Motion to Exclude Expert Testimony of Dr. Janet Arrowsmith-Lowe

Plaintiffs assert that Defendants have proffered the expert testimony of Dr. Janet Arrowsmith-Lowe on subjects such as the FDA approval process, post-approval reporting requirements and labeling requirements. Plaintiffs characterize Dr. Arrowsmith-Lowes' report as a slim document with only vague and conclusory statements about "adequacy" and "appropriateness" without barely a shred of explanation about how such conclusions were reached. Her deposition provided little clarification.

By this motion, however, Plaintiffs only seek to exclude her testimony that in her opinion, Bayer did not need to report to the FDA its analysis of adverse event conducted by Dr. Kuno Sprenger. Dr. Sprenger and associates compared the number of rhabdomyolysis reports for Baycol with other statins. Plaintiffs assert that at her deposition she agreed that such an analyses was scientifically valid as a method to determine if there was a signal for some problem with Baycol, but then opined that the results of the Sprenger analysis did not have to be reported to the FDA pursuant to 21 C.F.R. § 314.80(c)(2)(ii) (requiring the sponsor of a drug to

submit periodic reports that contain a history of actions taken since the last report because of adverse experiences, such as labeling changes or studies initiated). Plaintiffs argue this opinion is "simply wrong" and should be excluded.

In response, Defendants argue that Plaintiffs cannot challenge an expert because they disagree with the expert's conclusions. Rather, Plaintiffs must challenge the qualifications or methodology of the expert, and in this case, Plaintiffs have done neither. Courts must focus on the principles and methodology, not on the expert's conclusions. Kudabeck v. Kroger, 338 F.3d 856, 860 (8th Cir. 2003). In addition, Defendants demonstrate that Dr. Arrowsmith-Lowe's provided similar expert testimony in Galdi v. Bayer Corp., Case No. 04892 (Pa. Ct. Com. Pl. Mar. 10, 2004); Haltom v. Bayer Corp., No. 02-60165-4 (Nueces County, Tex. Mar. 12, 2003).

Plaintiffs have not challenged Dr. Arrowsmith-Lowe's qualifications, and do not challenge her methodologies outright, except to complain that her expert report is only eight pages long and provides vague and conclusory statements.

The Court has reviewed Dr. Arrowsmith-Lowe's expert report in this case, and finds her expert opinion is relevant, and will assist the jury in understanding the FDA's rules and regulations relevant to the drug approval process. Given her experience as a practicing physician, and her eleven years experience with the FDA as a medical review officer, she is also qualified to present an opinion. The

Court agrees that Plaintiffs are improperly moving to exclude Dr. Arrowsmith-Lowe's conclusion that the Sprenger analyses did not need to be reported to the FDA pursuant to 21 C.F.R. § 314.80(k), without challenging her qualifications or methodology. Plaintiffs will have the opportunity at trial to challenge her conclusions. Accordingly, the motion to exclude is denied.

IT IS HEREBY ORDERED THAT:

1. Defendants' Motion to Exclude Plaintiffs' Putative Expert Witnesses from Invoking the Testimony of Other Testifying Experts [Doc. No. 4114] is GRANTED to the extent set forth in this Memorandum Opinion and Order.
2. Defendants' Motion to Exclude Expert Testimony Based on Adverse Event Reports [Doc. No. 4116] is GRANTED to the extent set forth in this Memorandum Opinion and Order.
3. Defendants' Motion to Exclude Expert Testimony of John W. Farquhar, M.D. [Doc. No. 4128] is GRANTED to the extent set forth in this Memorandum Opinion and Order.
4. Defendants' Motion to Exclude Expert Testimony of Harland Austin, M.D. [Doc. No. 4092] is GRANTED to the extent set forth in this Memorandum Opinion and Order.
5. Defendants' Motion to Exclude Expert Testimony of R. Samuel Mayer, M.D. [Doc. No. 4102] is GRANTED to the extent set forth in this Memorandum

Opinion and Order.

6. Defendants' Motion to Exclude Expert Testimony of Richard M. Kapit, M.D. [Doc. No. 4100] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

7. Defendants' Motion to Exclude Expert Testimony of Bruce Carlson, M.D. [Doc. No. 4096] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

8. Defendants' Motion to Exclude Expert Testimony of Thomas M. Zizic, M.D. [Doc. No. 4112] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

9. Defendants' Motion to Exclude Expert Testimony of David Richman, M.D. [Doc. No. 4106] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

10. Defendants' Motion to Exclude Expert Testimony of Charles E. Boult, M.D. [Doc. No. 4094] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

11. Defendants' Motion to Exclude Expert Testimony of Martyn Smith, Ph.D. [Doc. No. 4110] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

12. Defendants' Motion to Exclude Expert Testimony of Stephen Raskin, M.D.

[Doc. No. 4104] is GRANTED to the extent set forth in this Memorandum Opinion and Order.

13. Defendants' Motion to Exclude Expert Testimony of Janet Arrowsmith-Lowe, M.D. [Doc. No. 4124] is DENIED to the extent set forth in this Memorandum Opinion and Order.

Dated: July 16, 2007

s/Michael J. Davis
Michael J. Davis
United States District Court