UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

In re: Baycol Products Litigation	)	File No. MDL 1431 (MJD/SRN)
	)	Minneapolis, Minnesota
	)	January 30, 2007
	)	9:00 a.m.

BEFORE THE HONORABLE MICHAEL J. DAVIS
UNITED STATES DISTRICT COURT JUDGE

(DAUBERT HEARING)

APPEARANCES

For the Plaintiffs:	CHARLES ZIMMERMAN, ESQ. RICHARD LOCKRIDGE, ESQ. RANDY HOPPER, ESQ. DONALD ARBITBLIT, ESQ. BERT BLACK, ESQ.
For Defendant Bayer:	PHILIP BECK, ESQ. ADAM HOEFLICH, ESQ. TAREK ISMAIL, ESQ. JAMES MIZGALA, ESQ. KEN BAUM, ESQ.
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P R O C E E D I N G S

IN OPEN COURT

THE COURT: Let's call this matter.

THE CLERK: This matter is In re: Baycol, Multidistrict Case No. 01-1431. Counsel, could you please state your appearances for the record.

MR. ZIMMERMAN: Good morning, Your Honor. Charles Zimmerman for the Plaintiffs' Steering Committee.

THE COURT: Good morning.

MR. LOCKRIDGE: Good morning, Your Honor. Richard Lockridge for the Plaintiffs' Steering Committee.

THE COURT: Good morning.

MR. HOPPER: Good morning, Your Honor. Randy Hopper for the Plaintiffs' Steering Committee.

THE COURT: Good morning.

MR. BLACK: Good morning, Your Honor. Bert Black for the Plaintiffs' Steering Committee.

THE COURT: Welcome.

MR. ARBITBLIT: Good morning, Your Honor. Donald Arbitblit of Lieff, Cabraser, Heimann & Bernstein for the Plaintiffs' Steering Committee.

THE COURT: Welcome.

MR. BECK: Good morning, Your Honor. Phil Beck for Bayer.

THE COURT: Good morning, Mr. -- I like the beard.

MR. BECK: Thank you.

MR. HOPPER: I am having an influence on him, Your Honor.

MR. HOEFLICH: Good morning, Your Honor. Adam Hoeflich for Bayer.

THE COURT: Good morning, Adam.

MR. ISMAIL: Good morning, Your Honor. Tarek Ismail on behalf of Bayer.

THE COURT: Welcome.

MR. BAUM: Good morning, Your Honor. Ken Baum on behalf of Bayer.

THE COURT: Welcome.

MR. MIZGALA: Good morning, Your Honor. James Mizgala on behalf of Bayer.

THE COURT: Good morning, Jim.

MR. MAGAZINER: Good morning, Your Honor. Fred Magaziner on behalf of GSK.

Your Honor, with Your Honor's permission, I am going to leave sometime after the status conference and Mr. Smith is going to stay for the Daubert hearing.

THE COURT: All right.

MR. SMITH: Good morning, Your Honor. Scott Smith for GSK.

THE COURT: Good morning.

Anyone else want to be introduced?

MR. HOEFLICH: No, Your Honor, but before we begin, Ms. Weber is not here today because of health issues. She, of course, would want to be here if she could.

THE COURT: Keep me informed --

MR. HOEFLICH: We will.

THE COURT: -- on her condition.

Mr. Zimmerman.

MR. ZIMMERMAN: Thank you, Your Honor.

THE COURT: Someone's BlackBerry --

MR. BECK: We turned ours off.

MR. ZIMMERMAN: I'll check mine when I go back. I thought I turned it off, Your Honor.

Good morning, Your Honor. We are here for a two-part hearing. I think we're having a joint status -- or the status conference first and then we'll move into the Daubert hearings. I'm Charles Zimmerman on behalf of the Plaintiffs.

Yesterday I think the Court issued Pretrial Order 156, which answers some of the questions contained in the report about a deadline. I don't know if you want us to go over those when we get into the body of the status conference.

But the first item of business on the report is the status of cases and the first thing I think it's important to report is that there are approximately 1,116

active plaintiffs in the proceedings who have -- I'm sorry.

There are approximately 1,700 Baycol cases that remain active, down from 14,800 filed in the litigation. The active cases include approximately 1,200 cases filed in or removed to federal court, down substantially from 9,100.

Obviously those statistics tell us a lot about the last year that we've been working with the discovery, case-specific discovery, and that the number of cases that remain active are down dramatically.

I expect when we summarize Phase III and IV, where we are, we will see that those numbers will shrink dramatically, probably in the same proportion, if not greater.

The report of Phase I and Phase II is contained at paragraph B, which indicates that in Phase I we are down to 39 plaintiffs, down from 60 as of November 7, 2006.

What that means is with the completion of that discovery in Phase I, there remain 39 cases for which I do not -- I believe no further activity with regard to case-specific discovery will now be taking place and they would remain for whatever resolution through remand and trial would exist in the transferor court should this Court at the appropriate time remand those cases.

In Phase II we have 99 cases, down from 150. I don't know if it's as of that same date, but it's down to 99

cases.

In effect what we have here, Your Honor, is about 138 cases from Phase I and Phase II that remain after the case-specific discovery is almost completed in II, I believe.

Is it totally completed or is there actually expert reports -- I mean, there's expert discovery, I think, in II left --

MR. HOEFLICH: Yes.

MR. ZIMMERMAN: -- to complete. So there may be some more whittling down of those 138 cases.

In Phases III and IV, Your Honor, we just got the schedule. We have 373 cases in Phase III and 546 cases where discovery and case-specific work has to be done in Phase IV.

It is more likely than not, in fact, it's highly probable, that these numbers will be whittled down into the same sorts of percentages we've seen out of Phase I and Phase II.

What I would report to Your Honor is this, and this is something that's --

THE COURT: Would everyone turn off their BlackBerrys and their cell phones.

MR. ZIMMERMAN: Let me make sure mine is off, Your Honor. It should be off, but we'll make sure.

THE COURT: Thank you.

MR. ZIMMERMAN: What I've asked my staff to do is sort of look at what's out there if we were kind of to project going forward and although the -- I don't want to put these on the record at the present time, Your Honor, although I would be happy to talk about them informally, because I don't want anybody to think that we can make total judgments about someone else's case.

We see that the number -- that there will be some additional rhabdo cases coming out of Phase III and IV at least in terms of the records that have been produced, the medical records or the reports that have been produced. It's our view there will be somewhere in the nature of 20 to 25 rhabdo cases coming out of Phase III and IV.

Defendants may object to that characterization of those being rhabdo or not and that will go through the mediation process or the process that at least would apply to a rhabdo case, but that's sort of what we're looking at coming out of Phases III and IV, approximately a total between 20 and 25 rhabdo cases.

And we see about 200 cases generally where there are some kind of elevated labs, elevated CK levels, elevation beyond the upper limits of normal where we at least have objective sorts of evidence that there could be some seriousness associated with the alleged injury.

I just throw that out there, Your Honor, so we understand what the order of magnitude is and the idea that we're trying to look at the cases going forward before all the case-specific discovery plays out to see what we're sort of looking at. And that seems to be what we're looking at, so the Court has some idea of the order of magnitude.

MR. HOEFLICH: Your Honor, the only point I would add is that if Mr. Zimmerman has rhabdomyolysis cases he would like us to look at, please feel free to provide them to us.

In Phases I and II we're aware of one rhabdo case and we are progressing well in settlement discussions. That's a case that was not filed in the District of Minnesota. It was filed in a transferor court. We hope we will be able to resolve it soon.

MR. ZIMMERMAN: And we support that, Your Honor. We agree there is one coming out of Phase I and II, and we understand that's close to resolution or at least it's in a program to be resolved.

MR. HOEFLICH: Yes.

MR. ZIMMERMAN: And we are looking at approximately 20 to 25 coming out of III and IV, allegedly, and we will get those people into -- we will get you the names at least so you have them and we can begin that process sooner rather than later.

MR. HOEFLICH: In addition, as we have committed to the Court and as I committed to the Court at the November status conference, we continue to look at rhabdo cases that we're aware of.

At the November status conference I believe we had settled at that point 3,052 cases for roughly $1.154 billion. As of today's status conference we have now settled 3,067 cases. So we are making progress.

If Mr. Zimmerman has more cases, we'll be happy to look at them and we will do our -- we will endeavor our very best to resolve those cases, Judge.

THE COURT: All right.

MR. ZIMMERMAN: Of course that's the next item and I think it's appropriate to move to that, Your Honor, because now we have, under C, Pretrial Order 156 which sets a scheduling order for Phases II and III and a procedure for remand that is contained within the order.

And also at the bottom of that order there is this -- also this paragraph that addresses mediation saying that the orders with regard to mediation protocol for the rhabdo cases set forth in prior pretrial orders remains in full force and effect, with the idea that if we have alleged rhabdos in the Plaintiffs' group of cases, we want to get them into the program as quickly as possible and resolve those cases, which brings us back, then, now to number II,

which is the results of the settlement.

The only thing I wanted to add to that, Your Honor, is really a congratulations to everybody. Settling 3,067 cases and 941 cases in this MDL is no small task and it took a lot of work and it took a lot of focus and it took Bayer stepping up and initiating the program and the Plaintiffs participating in it over a period of significant amount of time. It's a great success.

It sometimes gets lost in all of the other things we're dealing with, but I just congratulate Bayer and I congratulate the Plaintiffs and I congratulate everyone involved with the process, including this Court, for getting 3,067 cases settled and 941 cases in the MDL settled for a substantial consideration. It's a marvelous accomplishment and it shouldn't ever be lost sight of as we continue in the adversary proceedings with regard to the nonrhabdo cases.

MR. HOEFLICH: Judge, for the record and because we know the Court has taken the step of putting the transcripts online for people to see, let me just let people know what we've done in terms of settlement and what the amounts are at this point.

To date Bayer has settled 3,067 cases with a total value of $1,154,343,835. Of this total, 941 cases have been determined to be subject to the MDL assessment with a total value of $350,409,334.38.

As of the last status conference in November, Defendants had settled 3,052 cases with a total value of $1,151,613,835. Of that total, 937 cases had been determined to be subject to the MDL assessment with a total value of $350,121,334.38.

In addition, 141 cases have been submitted to the MDL mediation process and we thank the Court for its assistance with that.

THE COURT: All right.

MR. ZIMMERMAN: I like to roll those numbers off, but I guess I was happy that you could do it.

I don't know about the 141 that have been submitted to the MDL process. That doesn't mean they're still in the process, that just means they were resolved within that process?

MR. HOEFLICH: Correct. I believe that's a cumulative number of what's been submitted.

MR. ZIMMERMAN: Okay. Thank you. Again, a hearty congratulations to everybody involved. It's a remarkable result.

THE COURT: Well, Mr. Zimmerman, if I can interrupt for a second. I would like to again congratulate both the Plaintiffs and the PSC and the Defendants on resolving as many cases that they have. I think I've been a cheerleader for you for three years telling you that this is

a process that is different than any other MDL that's come down the pike.

It's a new paradigm that Bayer brought to the table and I think Plaintiffs should look at it that they have resolved a number of cases without having to go through litigation, expensive litigation, in this matter and the plaintiffs have been paid fair settlements.

When you have that many plaintiffs' attorneys being involved in a settlement process, you know that Bayer has so many people coming at them for different figures and that the appropriate figures for the appropriate injuries have been paid out; and I've said that from the beginning when I saw the process started.

And it's important that you've come to realize, as the PSC, that a tremendous amount of money has been paid out in this litigation. It's been quietly paid out, no big headlines. But it's not necessary for people to be compensated and have a headline follow that.

And so I compliment your leadership for the PSC. You've done a tremendous job. I've said that from the beginning. And your stewardship of this MDL in a new paradigm has been quite remarkable.

And certainly Bayer has come to the table with a new philosophy of -- if the people that are on the phone would put their phones on mute so we don't have to listen to

them rattle their papers and cough, that would be appropriate.

Mr. Beck and his team has done a tremendous job for the Defendants and it's just been a marvelous experience for me and I hope we can wind this down by January of 2008 and go our merry way.

Mr. Beck.

MR. BECK: Your Honor, if I may. I would also join Mr. Zimmerman in thanking the Court for your guidance. When you said you were a cheerleader, I had a mental image more of kind of a drill sergeant. I think there was some more than gentle prodding that went into the process.

But on behalf of Bayer, I must say that we're delighted with how it worked out. Obviously my client ended up paying a great deal of money, but it was money to people who had demonstrated side effects that could be associated with the use of our medicine.

We were able -- with every single person who came to us wanting to discuss settlement, we were able to resolve the cases so far without having to go through a trial and contest liability with one exception early on.

It's been an unusual couple of years for me where I have had one MDL where I had one trial and 3,067 settlements and then I've recently been involved in another MDL where I have had six trials and no settlements.

So it is a different paradigm, partly because of the nature of the side effect that's at issue and a lot of things went into that, but not least of which was the Court's guidance as well as the cooperation and leadership shown by the PSC in getting what I think we all think are fair settlements through the process rather than getting them all gummed up and opting instead for contested litigation on every case.

So we appreciate the work done by the PSC and their leadership and we thank you for that.

MR. ZIMMERMAN: And if I just might make one more comment, Your Honor. I was in New York at a seminar in December and I actually had the opportunity to congratulate Bayer directly through their general counsel. Is it George Lykos? And I stood up in public in a large group of people and congratulated Bayer for doing the right thing and stepping up, because that was his topic, about doing the right thing.

And it's been through a lot of reflection because obviously we battled over the nonrhabdo cases in this court for some time, but it was a very enlightening moment, I think, for both George and I to see us as adversaries stand up and congratulate one another for doing the right thing even though at times our reasonable minds differed on how other parts of the litigation should follow.

But for the main we all did a good job and it's through the Court's stewardship for sure and through the great advocacy on both sides, but we did the right thing for the people and we're very proud of that as we stand here today.

We've got some issues left. We'll get them done this year, I'm confident we will, and the chips will fall where they may, but this was an outstanding MDL and I'm proud to be a part of it.

The next and last topic is trial settings. There are no trial settings for cases in the MDL. That's pretty obvious.

A trial in the Lollar case has been set for October 15, 2007 in Monroe County, Mississippi. Good luck down there to everybody. I don't know too much about that case. I don't even know where Monroe County, Mississippi, is, but I guess we'll find out.

Then there's the class action in Oklahoma that is scheduled for trial in June of 2007. The PSC is working with class counsel down there and I don't know if there's anything really to report on it other than it's proceeding.

No Baycol cases have been --

THE COURT: Is that really going to trial?

MR. ZIMMERMAN: It is scheduled to go to trial, Your Honor. My guess --

THE COURT: Or is it going to be continued again?

MR. BECK: Right now it's scheduled to go to trial and we're proceeding on the assumption that it will, but it has been continued several times and that could happen again.

THE COURT: What about the Lollar case, any knowledge of that case? Is that in a lower court?

MR. HOEFLICH: It's scheduled now, Judge. I don't know all that much about it or whether the trial date will stick, but we will keep the Court informed.

MR. ZIMMERMAN: I don't know if counsel can enlighten us, but I did read just yesterday of a settlement in a case involving the attorneys general that I did not have on my radar screen. I knew there were claims out there and there was a class -- was it a class? -- or an attorney general settlement that I read about the other day and I don't know what the status of that is.

MR. HOEFLICH: Your Honor, we were not -- Mr. Beck and I were not involved in that either, but if Mr. Zimmerman has questions about it, he can communicate with me and I'll get him what information is publicly available.

MR. ZIMMERMAN: All I know is there was some settlement involving a group of attorneys general and that's all I know. It just came over my Internet site.

THE COURT: Regarding Baycol?

MR. ZIMMERMAN: Baycol having to do with -- something having to do with the economic cost or something of the drug, but again, I'm not familiar with it and I have to do more research on it.

MR. BECK: Your Honor, I know probably what Mr. Zimmerman knows as it came over my screen as well. All I know is that there was some sort of claims and that 22 different state attorney generals settled with Bayer for a total of $8 million. So whatever the claims were, they went -- 22 state claims went away for a grand total of $8 million. That's all I know.

THE COURT: All right. If you get any more information on that, why don't you pass it my way.

MR. ZIMMERMAN: I will be happy to do that and we will certainly do that, Your Honor.

That is the -- concludes the status conference with the exception of the Daubert motions, which are going to be heard by the Court. Unless the Court has any further questions, we could probably move right into that.

I want to make one other statement, however, and that is that we will -- the PSC is committed, now that we see so much of the landscape with regard to the nonrhabdo cases, to encourage people to go through the discovery or make their decisions early if they're not going to go through the discovery so we can get to the nub of the matter

and perhaps even ramp up the schedule that is in Pretrial 156 to make this happen even faster.

That's our commitment to the Court and to counsel, to try to on a voluntary basis do something to make sure that people get -- are aware of the realities that are out there and what is going on, what has happened in Phase I and Phase II, and to get the cases separated from those that are really going to be remanded at the end of the day or be prepared for remand and they are really going to stand behind for case-specific discovery and those that are not.

We just want to save wear and tear on everybody, if possible, and we stand committed to do that through this Phase III and IV.

THE COURT: I appreciate that.

Anything else from the Defense?

MR. HOEFLICH: No, Your Honor. Thank you. Thanks, Bucky.

THE COURT: Fred, anything for GSK?

MR. MAGAZINER: No, Your Honor.

THE COURT: All right. We'll get situated for the Daubert arguments. Mr. Beck, I think you're going to go first; is that correct?

MR. BECK: Your Honor, yes, although I believe that the Plaintiffs had requested that they be given 20 minutes or so to make some general remarks about Daubert

motions. We have no objection if they want to do that. Whatever -- we'll weave ours into the specific motions.

THE COURT: Good morning, Mr. Lockridge.

MR. LOCKRIDGE: Is that all right, Your Honor, if we do that?

THE COURT: That's fine with me. And I apologize for not including you in my compliments for the PSC because you are co-lead counsel and everything that I said about Mr. Zimmerman applies to you. Your leadership and stewardship in this matter has been invaluable for the Court.

MR. LOCKRIDGE: Well, thank you, Your Honor. I appreciate that, of course.

I would like to make some very preliminary comments and then I would like Don Arbitblit from the Lieff Cabraser firm also to make a few minutes of some preliminary comments because these are comments which really go to all of the motions, and I think it will only take a few minutes.

At the outset, of course, we feel that we have probably the finest set of experts that have ever been put together in any case and we are exceptionally proud of them.

And I wanted to briefly address the overall Daubert issue simply to emphasize a few things because Daubert is so typically used by the defendants as an attempt to prevent experts from testifying, but the reality is that

the actual Daubert case is very interesting.

When one goes back and reads it, the Supreme Court said Rule 702 must be read in the context of a liberal thrust of the Federal Rules of Evidence and must be interpreted consistently with the general approach of relaxing the traditional barriers to opinion testimony.

So I think it's clear that barring testimony, expert testimony, is the exception rather than the rule and obviously we hope the Court will keep that in mind. The real threshold for admissibility is not how persuasive the evidence might be, but rather the reliability of the evidence.

And also as discussed in Daubert and subsequently, I might note, of course, in Kumho Tire and others, the courts, including the Supreme Court, really seem to be saying that Daubert and the so-called gatekeeping rule is not a substitute for defendants vigorously cross-examining the experts at trial and, if they want, presenting contrary instructions or having the court give carefully crafted instructions to the jury.

Of course, Daubert specifies two requirements, admissibility -- for admissibility, reliability and relevance. Obviously relevance is not an issue here. And for reliability, as the Court knows, it's to look at such factors as scientific methodology; that is, as the Eighth

Circuit actually said in the Turner vs. Iowa Fire Equipment case, the evidence must be grounded in the methods and procedures of science. And that's what we have here.

Now, obviously I'm aware of the progeny of Daubert and Kumho Tire where courts do, in fact, look at the conclusions of various experts, but I want to emphasize that of course we welcome the Court to look at the substance and the conclusions of our experts.

Now, there will not be forward-looking clinical studies here because they're not available because obviously Baycol was pulled from the market. So what we have primarily is extremely qualified experts examining and looking at studies, sometimes Bayer's studies, looking at the literature, sometimes relying on other experts and sometimes relying on AERs, as we're going to get to, and relying on other things.

And that is really the test here. I would submit that the real test is that simply we have to prove, we have to establish that the evidence is reliable and that we used scientifically valid methodologies.

And I think it's clear that in every single case our world-renowned experts have done that, Your Honor. I would ask you to always keep that in mind as you are listening to Mr. Beck's extensive arguments here this morning.

If I could, Your Honor, I would like to have Don Arbitblit from the Lieff Cabraser firm now say a few words also.

THE COURT: You may. Good morning.

MR. ARBITBLIT: Good morning, Your Honor. Thank you for the opportunity to address the issues on this hearing.

I've been -- just for a brief background, I've been involved in the Baycol litigation since its inception, although I have not appeared before Your Honor before. I have worked extensively on my firm's individual cases and, as others have, I have managed to resolve the rhabdomyolysis cases with defense counsel. Again, I too appreciate the spirit with which defense counsel came to those negotiations and we worked very well together.

I expect that during the course of today we will see that there are some disagreements, but I also think that there are some agreements that will be presented today. And I thought as part of the road map for where we are going I would explain what I see, working with our experts and counsel, as the principal issues and what is and is not in dispute.

As I see it, there are a number of key issues, a small number of key issues. One is whether Baycol is more toxic to muscles than other statins and a second one is with

respect to statin myopathy, which is conceded to be a real phenomenon and is not in dispute, how is it diagnosed and how long does it last.

And as to each of those substantive questions that are always going to come up in the procedural mechanism of a Daubert hearing, we will present the evidence as to those, but briefly what we would expect the evidence to show is that there is a consensus that Baycol is more toxic than other statins.

It started in August 2001 with the withdrawal of the drug and the scientific community has spoken with one voice since that time. We have and will present and have submitted to the Court recent literature that validates and confirms the existence of that consensus time after time after time. Without exception Baycol is called the most toxic statin, the statin that causes the most muscle injury.

And so it's important in the sense that clearly we've come three years since these reports were served and there's an issue that the Court undoubtedly has to face as to what is the impact of subsequent research.

Our view of it is that our experts were on the right track with what they had at the time. They came to the right decisions based on reliable methodology and the available evidence and that time has only confirmed and validated what they said then.

There's a consensus that Baycol is the most toxic statin and we'll be presenting the evidence in peer-reviewed studies on that subject and that will include published epidemiology studies finding Baycol with a 6- to 10-fold increased risk of hospitalized rhabdomyolysis, as well as evidence about Bayer's own clinical trials.

In terms of reliability, the clinical trial evidence has not been the focus of the pleadings on the defense side. They've tended to focus on the relative reporting ratio study with the goal of undermining it by saying it's all about adverse event reports and therefore somehow unreliable.

Well, it's important that those are just one piece of the puzzle. They're not the whole puzzle. They are a piece of it. The clinical trial evidence that's cited in Dr. Farquhar's report that shows an 8-fold increase in rhabdomyolysis on published clinical trials is in his report, but it's not the focus of what Bayer is attacking.

I think it's important to understand, in my reading of the case law and the Reference Manual on Scientific Evidence, that even isolated case reports may be permissibly considered by an expert in the context of other evidence.

This is not a case where the adverse event reports are the sole or even main evidence. They do take up a lot

of space and time because there's a lot of data, but clinical trial evidence is in the record, not only Dr. Farquhar's analysis, but the analysis of defense consultant Dr. Strom's assistant, Mr. Loutanbach, who performed a very similar calculation to Dr. Farquhar on the published clinical trials and came up with a very similar result, showing a high rate of confirmed rhabdomyolysis for Baycol in published studies, as well as a piece of data that I found surprising when I saw it and that has not been published, which is a comparison of 19 pooled clinical trials that are called short-term studies in which the relative risk for myalgia was 1.76 statistically significant for Baycol versus placebo.

That has never been published. Instead what is in the literature is 2.5 versus 2.3, essentially no difference, and that's been cited time after time because it's in the PDR, the label and the Physicians' Desk Reference, based on a subset of clinical trials, only U.S. studies, only 3,000 people; whereas, the 19 studies that Bayer submitted in 2001 to European regulators consisted of almost 9,000 people and larger samples are considered more stable and reliable. So that's clinical trial evidence. That analysis was done by Dr. Strom's assistant. He's a defense witness.

And it's important that as part of the evidence that we don't focus just on the relative reporting rate

study. Now, with respect to that study, it's also important that --

MR. BECK: Your Honor, I don't want to be impolite, but I was told that they wanted a few minutes to talk about Daubert standards and now we're --

THE COURT: We are going into argument already. You will have certainly enough time to --

MR. ARBITBLIT: Thank you, Your Honor. I will move on to one last point where I think we will have some agreement because having taken the deposition of the defense expert on the subject of duration of injury and how it's diagnosed, the Plaintiffs' experts and the defense experts agree on a number of points, Your Honor, but most importantly, as Your Honor has held, differential diagnosis is the way to determine causation in a toxic exposure case such as this.

As far as how it's diagnosed, the criteria used by the various experts are quite similar and compatible. The issue of duration has advanced in the literature and, as conceded by the defense expert at his deposition, that there's a range of time that CK is a marker. It's not the injury itself. When CK normalizes, that doesn't necessarily mean the injury is over and that the range of injury is subject to individual variation.

THE COURT: All right. Thank you.

MR. ARBITBLIT: Thank you, Your Honor.

THE COURT: Mr. Beck.

MR. BECK: Your Honor, I need just a moment or two to arrange the technology here.

(Pause.)

MR. BECK: I think we're all set now if you're ready for me, Judge.

THE COURT: Mr. Beck, you asked for an hour and a half; is that correct?

MR. BECK: Yes, Your Honor.

THE COURT: I put that on the timer and the yellow light will come on with 30 minutes to go so you will know that you have 30 minutes.

MR. BECK: Where is this yellow light, Your Honor? Oh, here it is. I see. Thank you.

Your Honor, I'm going to discuss several motions together and then Mr. Ismail will do that with some other motions this afternoon. For the ones that I'm going to be discussing, I'm going to be focusing very much on questions of methodology.

We are not here to argue about the academic credentials of any of the experts and we're also not here simply to dispute the conclusions that the experts have come to.

Rather, the motions that I'm going to be

discussing focus on whether the experts in this particular case in the opinions they've rendered in this case have followed scientific methodology such that their conclusions have sufficient reliability to be put before a jury under Daubert.

The motions that I'm going to be discussing are the adverse event report motion and there the question is -- a couple of important questions. One is whether adverse event report data can be used to show comparative drug safety, so the safety of one statin versus another. And we believe that it cannot.

And that is particularly so given point number two, which is that the adverse event report data that they rely on relates mainly to one condition, which is rhabdo, and then they rely on it to draw drug safety comparisons concerning a different condition, which is myalgia or aches and pains.

As Your Honor has heard this morning during the status conference, we've done a pretty good job, all of us involved, in cleaning out the rhabdo cases and we're left with the nonrhabdo cases.

So they are using here in the adverse event reports information concerning rhabdo and then drawing conclusions of comparative drug safety concerning different conditions that are not rhabdo. So that's one of the

motions.

A couple of the other motions that I'll be addressing concern Drs. Farquhar and Austin and both of them -- there is substantial overlap there, Your Honor. We believe that they have misused the adverse event report data, so there will be overlap with that motion.

And also we believe that they have improperly manipulated the epidemiological study that actually was done by PacifiCare that showed that when Baycol was used at 4 milligrams, the normal dose and was not used along with gemfibrozil that, number one, there was no increase in the incidence of rhabdo, but also, number two, no increase in or difference in the incidence of myopathy.

And they have taken criticisms of that study, which they're certainly entitled to advance, but then purported to basically redo the analysis in an unscientific way in reaching the opposite conclusion. So we'll be focusing on their methodology there.

And then, Your Honor, what I'm actually going to talk about first is the problem that we have with several of their other witnesses where they have not relied on other experts, as I think it was Mr. Lockridge said, but instead they have parroted or adopted wholesale the conclusions of other experts, chiefly Dr. Farquhar.

And all of these are related and that's why I

would like to discuss them as a group. And I will actually start with the last one I mentioned, what we think of as the parroting motion.

As I said, this is not a case where there are several steps in an analytical chain and an expert says I am assuming that proposition B is true -- in my A, B, C, D chain of reasoning I'm assuming that proposition B is true and the basis for my assumption that it's true is Dr. Hoeflich's report and it rises or falls with Dr. Hoeflich's report, but I'm assuming it's true for my purposes.

That, I think, is appropriate for an expert to do. As the Plaintiffs say, not every expert can be -- can have expertise in every possible field. But they're not doing that here.

And if they do something like that, when you've got that kind of a situation, then if Dr. Hoeflich doesn't show up, their analysis gets thrown out the window. It either gets stricken or they're not allowed to put it in, depending on the sequence of how the testimony comes in.

Or if Dr. Hoeflich does show up to establish proposition B, I get a chance to cross-examine Dr. Hoeflich and show that he's the charlatan that he is and that his analysis is deeply flawed and that he's got biases and that sort of thing. And so the jury gets to hear Dr. Hoeflich

and the basis for that part B, that assumption that the other expert is entertaining.

But here what we've got are a whole series of experts who are adopting as their own conclusions that were reached, as I said, principally by Dr. Farquhar concerning relative risk of different statins based mainly on the adverse event reports.

And then these experts are purporting to take these conclusions and say that they are their conclusions without having done the analysis and without any basis other than Dr. Farquhar's opinion. We gave examples in our brief. I'll just highlight a couple of those for you.

I'm going to show first some testimony from Dr. Smith. He's a toxicologist and he wrote an opinion that says that Baycol when administered along with another drug called -- well, it's Plavix, but it's got a hard to pronounce generic name. He says that Baycol along with Plavix has an interaction and increases risk. And so here's -- that's his opinion, he claims, and here's what he says as to the basis of that:

"Paragraph 32, The most serious interactions between Baycol and other drugs appear to be with gemfibrozil and clopidogrel. What's clopidogrel?

"Well, I forget as I sit here today. It's also a commonly prescribed drug, but I forget for what condition.

"What's your basis for this statement?

"That that -- the report by Dr. Farquhar.

"Okay. Did you do a literature search or did you find any other support for that statement other than Dr. Farquhar's report?

"There are many reports, of course, with gemfibrozil.

"Right.

"The clopidogrel is from Dr. Farquhar's report."

MR. BECK: So here we have a toxicologist who is proposing to render an expert opinion that Baycol and clopidogrel are particularly toxic when taken together. He doesn't even know what the drug is and his only basis is that Dr. Farquhar says so.

Now, Dr. Farquhar may or may not pass Daubert muster on that and Dr. Farquhar, if he does pass Daubert muster, may or may not stand up to cross examination on that, but Dr. Smith shouldn't be allowed to just adopt as his own a conclusion that is based 100 percent on Dr. Farquhar and that he doesn't even understand.

We've got a similar situation with Dr. Raskin. He's a cardiologist and he offers opinions on comparative drug risks based on the adverse event reports, and here's what he says:

"Have you ever published an article, Dr. Raskin, in which you make comparative statements between two drugs

using spontaneous adverse event data?

"No, sir.

"Have you done any research in which you make comparative statements between two drugs using spontaneous adverse event data?

"No, I haven't.

"Has anyone ever asked you to undertake an investigation into the comparative safety of two drugs using spontaneous adverse event data?

"Only for the purposes here to review this data. No, I haven't done a study."

MR. BECK: And then he goes on.

"So the only investigation you made into how potential biases affect the reporting rate of adverse events for statins is to review the reports of Dr. Farquhar and Dr. Strom, correct?

"That is correct."

MR. BECK: As I said, we have other examples in the brief, but I think that those two are illustrative.

And the concern that we have, Your Honor, is that by having these other experts claim Dr. Farquhar's opinion as their own, the Plaintiffs' lawyers are trying to accomplish two things. One is -- and this surprised me when I reviewed the papers -- that they're actually trying to shield Dr. Farquhar's opinions from Daubert review.

To be sure they're going to stand up and say that Dr. Farquhar is the most qualified person in the world and he passes Daubert muster. But they also say in their brief that even if he doesn't, even if this Court finds that Dr. Farquhar's methodology is so flawed that he should not be allowed to present his analysis to the jury, they say, well, that's okay because the other experts are entitled to adopt his conclusions as their own because experts can rely on inadmissible evidence.

And they cite no support for the proposition that if a court excludes as unreliable one expert's conclusion that another expert can come along and rely on that. And I can't believe that ploy is going to work.

What they also hope to do -- would you like to say something?

MR. ARBITBLIT: Mr. Beck, I would like to waive that argument if it were made in the papers. Your Honor, I would not --

MR. BECK: Then we don't need to take any more of my time. If that argument was made, which it was, they've now waived it.

MR. ARBITBLIT: I would not have made that argument. And having worked with Dr. Farquhar, I'm prepared to stand on the merits of his opinion. And if it's not admitted by the Court, then I would not expect any other

expert in this litigation to rely on it.

MR. BECK: Good. So that's done.

What they're also doing through this mechanism of having other experts adopt Dr. Farquhar's conclusions is they shield Dr. Farquhar from cross examination.

When defending Dr. Farquhar's analysis in their briefs, they say that the criticisms that we make go to the credibility of the analysis rather than its admissibility and that that's an issue for searching cross examination. I think that some of the remarks that Mr. Lockridge made this morning were along the same lines.

But if other experts can simply adopt Dr. Farquhar's conclusions without having done the analysis or, in the case of the toxicologist, without even knowing what drug he is talking about, then the conclusions come in without any cross examination of the methodology or the bias of the person who came up with the conclusions.

And, Your Honor, that -- this is not just some hypothetical concern. Many of us at both of the tables have been involved in the Vioxx litigation over the last year. And I don't want to suggest that what happens in Vioxx should drive what happens in this proceeding, but they make a point in their papers of saying Dr. Farquhar was found qualified to testify by Judge Fallon in the Vioxx cases and then they quote at length Dr. -- Judge Fallon's opinions

saying that Dr. Farquhar could testify there.

It is interesting. Judge Fallon found that Dr. Farquhar was qualified to testify. He had a much different analysis than he has here. They list him in every case as one of their experts and they never call him.

And instead -- I keep getting ready to cross-examine Dr. Farquhar and I never get to and instead what happens is other experts come in and they purport to rely on Dr. Farquhar even though Dr. Farquhar doesn't present himself for cross examination.

And we think that in this case that it's very important that the Plaintiffs not be able to backdoor Dr. Farquhar's conclusions in through other experts, that they put him up -- if he passes Daubert, which we don't think he does, that they put him up to testify as to his own conclusions rather than having somebody else act as his mouthpiece.

We have serious questions for Dr. Farquhar, including who really wrote his report, you know, what involvement the lawyers had. You're going to hear from Mr. Arbitblit. What involvement he had with the report, how many drug cases Dr. Farquhar has testified in where Dr. Arbitblit -- or Mr. Arbitblit has been the principal lawyer who handles him. Documents refer to Mr. Arbitblit as his handler.

There are questions as to who came up with the specific calculations and analyses, the ideas for those, that are contained in Dr. Farquhar's report. And you'll see later that on a key one it wasn't Dr. Farquhar. It was the lawyers who told him what to do and how to do it.

So we would like very much, if Dr. Farquhar is going to pass Daubert muster, that he be required to present his own opinions and that they not be allowed to take Dr. Farquhar, have him pass Daubert, and then have a bunch of other experts say, well, Dr. Farquhar's report says this and I rely on Dr. Farquhar because he's world renowned and we never get to cross-examine the supposed author of these opinions.

And I should say in this regard, Your Honor, just on a practical note, that in November in the Vioxx litigation they said that, well, Dr. Farquhar recently became sick and he couldn't travel to other trials that were scheduled and so they said they needed an immediate trial preservation deposition and they wanted to take it in the one week I had between two different Vioxx trials. Judge Fallon said okay. We said we'd send one of my partners to do the deposition. Then it was canceled and to my knowledge there's been no effort made to preserve his Vioxx testimony since then.

And, Your Honor, I say that only because if, in

fact, the Court holds that Dr. Farquhar passes Daubert muster, we do not want to be in a position down the road where they say, well, gee whiz, he's too sick to travel to Minnesota, just like he was too sick to travel to New Orleans, and therefore he's not going to be here to defend his own opinions, but luckily for us we've got other experts who will adopt his opinions as their own.

So I don't know what the solution for that problem is, but I wanted it on record that they've announced in another MDL that he is too sick to travel and testify and if he passes muster and if that is still the case, then we don't want to forfeit our right to cross-examine him on these opinions just because other experts have been adopting them.

Let me now turn -- so that's the parroting issue and that's why we feel so strongly about these other experts adopting Dr. Farquhar's analysis as their own without doing the analysis.

I mentioned the adverse event reports. I think Your Honor is pretty familiar with this general subject, so I'm not going to spend a huge amount of time on it, but it is very important.

Here what we have is the plaintiff experts seek to rely on comparative rhabdo adverse event report reporting rates for the opinion that Baycol was more toxic to muscles

than other statins and you heard Mr. Arbitblit say that, well, there's a consensus, he claims, that Baycol is the most toxic of the various statins.

And their reasoning for this, their expert's reasoning, is that because Baycol had a higher rhabdo adverse event report reporting rate that it somehow must also cause more nonrhabdo injuries than other statins. And that runs throughout the reports of Dr. Farquhar. Dr. Austin does the same thing. And then that's parroted by the experts who adopt Dr. Farquhar's analysis.

And we believe this proposed testimony of theirs that's based on adverse event reports is inadmissible as a methodological matter for two reasons:

First, the adverse event reports themselves are inherently unreliable and the FDA itself, which administers the Adverse Event Report System, has said that they cannot be used for the purpose that the Plaintiffs' lawyers and their experts try to use them here and that is to, number one, establish causation and, number two, establish differential safety between different statins with different reporting rates. So the FDA says that that's a misuse of the Adverse Event Report System.

And then secondly, and I hope this doesn't get lost here, and that is, as I mentioned before, these are by and large rhabdo adverse event reports and not myalgia

adverse event reports and therefore it's an extrapolation from data that is itself unreliable without any basis for doing so.

So let me give you some background on the Adverse Event Report System. These adverse event reports are what are called anecdotal reports. When somebody -- it can be a nurse. It can be a doctor. It can be a patient. It can be a plaintiff's lawyer.

When somebody says, gee whiz, here's a person who experienced this event contemporaneously with taking this medicine, they can send that in either directly to the FDA or to the pharmaceutical company, which then passes it onto the FDA, and that's an adverse event report.

So if you're taking Baycol and sprain your ankle, you can get an adverse event report saying that there was an ankle sprain while on Baycol. People are encouraged to gather all this information without making judgments about whether there was causation or not.

And they also report this without regard to whether other medication, for example, is being taken or whether there were other causes that could account for this. Somebody who is taking Lipitor who experiences muscle aches, they may have been taking Lipitor for two years. They experience muscle aches one day and somebody sends in an adverse event report, and on that same day they happen to

for the first time in five years go to the gym and work out and lift weights for a long time, but the adverse event report goes in anyway and that's how the system is devised.

Then the FDA collects this as part of their postmarketing surveillance and what they do, the FDA as well as the pharmaceutical companies, is they use this data to generate signals to say, well, there's a bunch of adverse event reports of this condition along with the drug. There's all sorts of issues about the reliability of it, but there's enough of these that it's a signal that we ought to go out and do a scientific study and then you go out and do, for example, an epidemiological study.

Mr. Lockridge said there aren't going to be massive placebo controlled clinical trials. There actually were some that we're going to report on. But there was an epidemiological study that was done called PacifiCare at our behest based on the signal that was raised by the adverse event reports of rhabdomyolysis along with the use of Baycol.

As I said, the adverse event reports themselves are not verified. They're not even verified to see whether someone is taking the medicine or not, let alone whether there are -- there's no verification whether the adverse event was real or not real. As I said, there's no causation requirement at all.

This is what the FDA says on the absence of causation requirement and the adverse event reports. This is from the CFR. They have a disclaimer at the end where they go on to say, A report or information submitted does not necessarily reflect a conclusion by the applicant or the FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect, and then they go on and elaborate on that.

As I mentioned, the FDA has said itself that there are limitations on how these things can be used and I want to put up an important document on that issue, Your Honor.

What happens with adverse event reports is somebody who wants to see all the adverse event reports from Baycol or Lipitor or Zocor can file a Freedom of Information Act request and then they get this information from the FDA and the FDA sends out a cover memo. You are looking right now at page 1 of the cover memo describing the information that's being turned over.

And then page 2, this is caveats that the FDA itself sends out when they release this information to people who want it. And there they say, number 1, it's only those reactions that have been voluntarily submitted or reported; number 2, the information contained in the reports has not been scientifically or otherwise verified.

And that's very important, Your Honor, because the

information is subjected to lots of different types of bias. One form of that is how recently a drug came on the market. And here's one of their experts, Dr. Austin, acknowledging that.

"The newer the drug, the more likely it is that a healthcare provider will make a voluntary report, correct?

"I believe that is correct.

"Two drugs could have the exact same safety profile, but if one was introduced ten years ago and one was introduced five years ago, you may observe a difference in the rate of voluntary reports, correct?

"You may, and for a number of reasons."

MR. BECK: So how recently a drug came on the market affects how often adverse event reports are sent in. And Baycol was the youngest of all of the statins. That was Dr. Austin acknowledging that.

There's also something called publicity bias, which he also was asked about.

"Have you ever heard of the term 'publicity bias' before?

"Yes.

"What is that, sir?

"My understanding of the term is that more spontaneous reports would occur if, in fact, there was publicity pertaining to that drug and its adverse events and adverse

events thought to be associated with it."

MR. BECK: So that's another reason that the FDA and others recognize the limitation of these adverse event reports. So they haven't been scientifically verified, as paragraph number 2 said.

And paragraph number 3 specifically says, again, that there's no causation requirement. It says, For any given report, there is no certainty that the suspected drug caused the reaction. This is because physicians are encouraged to report suspected reactions. The event may have been related to the underlying disease for which the drug was given, to concurrent drugs being taken, or may have occurred by chance at the same time the suspected drug was taken.

And here we're talking -- ultimately the cases we have left are myalgia cases. These are aches and pains by old folks, so there's a million different reasons that that can take place. Even by not so old folks we occasionally have our aches and pains.

And they go on to say -- because of these limitations, paragraph 4, the FDA says, Accumulated case reports cannot be used to calculate incidence or estimates of drug risk. And that's for a particular drug. They cannot be used for that. And that is exactly what Dr. Farquhar uses them for and exactly what Dr. Austin uses

them for.

And then they go on to say, Numbers of these data must be carefully interpreted as reporting rates and not occurrence rates. True incidence rates cannot be determined from this database. But that's what their experts do.

And then the last paragraph -- or last sentence here is extremely important, Your Honor. They say, Comparison of drugs cannot be made from these data.

So they say, first of all, you can't draw safety conclusions, causation; and secondly, you certainly can't compare one drug to another based on these AERs. But that is precisely what Dr. Farquhar has done, precisely what Dr. Austin has done, and then precisely what all the hangers-on do when they adopt Dr. Farquhar's analysis.

Now, courts -- and the parties have put the cases in front of Your Honor. Courts have routinely excluded expert testimony based on adverse event report data and this is often true when the only question is whether -- is general causation, i.e., is it possible for Baycol, for example, to cause rhabdomyolysis, and courts have excluded adverse event report data or opinions based on it because of the limitation.

But there are courts that have allowed it in for general causation, they say on that issue we'll allow it in, but the courts have consistently excluded it where people

have tried to do what the Plaintiffs' experts have done here, which is to say not only can I draw a causation conclusion, but then I'm going to compare the adverse event report rates for Baycol with the adverse event report rates for different drugs and I'm going to make a judgment as to which one is more likely to cause this, which one has a greater risk. And that kind of attempted testimony has been consistently excluded.

But here what they've done is they've gone a step further and they say, okay, we're going to use adverse event report data to establish causation, even though the FDA says we should not, and we're going to use comparative adverse event report data to say that Baycol is more likely to cause rhabdo than other statins, even though the FDA says we cannot.

And then we're going to do a third thing. We're going to stop talking about rhabdo, as Mr. Arbitblit did, and start talking about toxicity and we're going to take the rhabdo adverse event reports and then we're going to change the language that we use and we're going to talk about muscle toxicity. And then once we've generalized it to muscle toxicity, we'll pretend that it applies to aches and pains and myalgia.

So we think that that is way over the top, beyond any legitimate use of adverse event report data on

rhabdo, to then make a drug comparison on a different condition.

And that's very important here, Your Honor, because, as Mr. Ismail is going to get into in more detail when his green light is on this afternoon, they really have a theory here, their doctors do, that there's a different mechanism at work with rhabdo and myalgia or these other aches and pains.

But rhabdo involves, as Your Honor has heard so many times, the destruction of muscle cells. And when muscle cells are destroyed, a couple of things happen. One is the cells destroy and these CK enzymes leak out into the system and so you can measure and get these highly elevated CK levels. And another thing that happens is myoglobin ends up in the urine. And so we have destruction of muscle cells as evidenced by these two things. Meanwhile -- and so we've been settling all those cases.

And then there are a bunch of people who say that their arm hurts, but that's not the same -- assuming that a statin can cause that, it's not the same mechanism because by definition they don't have the highly elevated CK levels that come with destruction of muscle and they don't have the myoglobin in the urine. If they did, we would have settled their case because they would have had a different injury. Instead we have a different condition which presumably,

according to their experts, results from a different mechanism.

And so to say that we're going to stretch and stretch and stretch and use adverse event reports in a way that the FDA says we should not as to rhabdo and then from that we're going to extrapolate to a different condition that has a different mechanism we think is a completely inappropriate methodology and doesn't pass the Daubert standards.

So let me now turn more specifically to Dr. Farquhar, and there's really two issues that we have with Dr. Farquhar.

One is what he calls a meta-analysis of the adverse event report data. Meta-analysis in this context, Your Honor, means that he's taken not just the FDA database, but a couple of -- you know, a worldwide database, an Australian database, put them all together, and had somebody else analyze it is what he did. So that's point number one.

And then point number two is what he's done with the PacifiCare results where instead of just criticizing and taking issue with the conclusions, he's manipulated the data in a methodologically nonsensical way to try to come up with a result-driven conclusion that fits the Plaintiffs' lawyers theories.

First on his AER meta-analysis, as I said, he

combined data from several different databases. They all have the same limitations that we have up on the screen and very importantly, Your Honor, in none of these was the principal focus myalgia or aches and pains. He's looking at rhabdo information.

Now, maybe, in fairness, it was back when he thought there were going to be or the Plaintiffs' lawyers thought there were going to be a lot of rhabdo cases, but there aren't anymore.

And so he's looking at adverse event reports from different databases concerning rhabdo and then extrapolating backwards somehow to myalgia and we have that same issue that I just talked about, how that's inappropriate, and I am not going to go through that again.

But in addition to that flaw, to the basic flaw of using adverse event reports to compare medicines even if you had the right injury, he's got other methodological flaws that I want to talk about.

The biggest one is that whatever his credentials are, in this case what he did was the antithesis of science. In this case what he did was he concluded and accepted the conclusion that Baycol is more toxic to the muscles than other statins based on what other people had said and then he turned around and analyzed the AER data as well as the PacifiCare data in order -- in an effort to support that

conclusion. And the Eighth Circuit has said in the Sorensen case that when you do that, which is clearly what he did here, you stood science on its head.

Instead of testing a hypothesis and trying to prove that the hypothesis is false, which is the scientific method, instead what he did is he said here's the conclusion that I'm supposed to reach and let me see if I can manipulate the data in a way that supports the conclusion that I'm supposed to reach; and that is the antithesis of the scientific method.

Here's one place in his report, paragraph 43, where he says basically what Mr. Arbitblit was arguing and that is he claims the scientific community has reached a consensus that Baycol is substantially more toxic than other drugs in the same class.

And then -- and so then what he does, having started with what he claims is this consensus, is he then sets about in an effort to prove that that's true by manipulating the data from the adverse event report databases.

And so he uses the adverse event reports in a way that the FDA says you cannot do, compare one drug to another. Even as to rhabdo they say you can't do it, but that's exactly what he does.

And he admits, meanwhile, that he doesn't have any

real experience with adverse event reports and how to analyze them and what their limitations are prior to his being hired to give testimony in this litigation.

I'm going to go through some of what he says about his prior lack of experience with anything having to do with adverse event reports.

"You've never had responsibility for collecting spontaneous postmarketing adverse event reports on behalf of any regulatory agency or any pharmaceutical manufacturer?

"No, I have not.

"You have not had any responsibility in any professional capacity for coding spontaneous postmarketing adverse event reports either for a pharmaceutical company or a regulatory agency; is that correct?

"That is correct.

"You've not had responsibility in any professional capacity for analyzing spontaneous postmarketing adverse event reports on behalf of any regulatory agency or any pharmaceutical company; is that right?

"That's correct, until being involved in this case where the analysis of the AERS data and others was --

"Right.

" -- under my supervision.

"Right, I understand -- that's what I'm -- and let's make sure we're clear. I'm talking about -- I'm not

including this case as answering that question. I'm talking about prior to your involvement in this case you've not had any responsibility in a professional capacity for analyzing spontaneous postmarketing adverse event reports; is that right?

"Correct.

"Have you ever conducted any study of two or more drugs in the same class based on spontaneous postmarketing adverse event reports prior to your involvement in this case, whether the results were published or not?

"No.

"Had you ever before your involvement in this litigation used the FDA's Adverse Event Reporting System database to obtain numbers of adverse events for different drugs?

"No, I have not prior to this done research on drug toxicity and comparisons among drugs using the Adverse Event Reporting System.

"Do you know -- do you understand the way data are coded in the FDA's adverse event database?

"Well, I really don't. You know, this was under Dr. Ahn's -- he was directed to do the search.

"Okay.

"And I didn't look to see what the ingredients were within the database in the sense that you're asking.

"Outside of the context of litigation, have you ever

done a meta-analysis of this type?

"On drugs?

"Yes.

"No."

MR. BECK: Then the last clip in this sequence I'm going to show, Your Honor, has to do with his proportional reporting rate analysis. This is one of the calculations that he does and that he claims to rely on. And here's where he's asked whose idea was this.

"Did Mr. Arbitblit suggest to you to do a proportional reporting rate analysis?

"The idea of proportional reporting rates was given to me in a telephone call by Mr. Black, and I don't remember when.

"Okay. Had you ever personally done a proportional reporting rate analysis prior to this date?

"I don't know that I had done it at this date, but -- no, I certainly have not.

"Is the first -- is it fair to say that the first time you learned about proportional reporting rates was in connection with your services as an expert in this case?

"That is correct."

MR. BECK: So, Your Honor, we have this threshold question about whether it's appropriate to use adverse event reports as they've been used here. We think it's not. But

if it could be used, if they could be used that way, Dr. Farquhar is not the man to do it.

He has no acquaintance with the Adverse Event Report System whatsoever. He didn't do the work himself. There's some other person he said, Dr. Ahn I think his name was, his assistant, he just turned the job over to him. He doesn't know how the data is coded. He doesn't know how the data was analyzed. He's never done the kind of calculation that the lawyers told him to do and put in his report in this case.

And so he's not the man who ought to be manipulating the adverse event report data this way, if anybody in the world could be allowed to do it.

One of the big problems with his manipulation of the data is that, again, coming back to the scientific method, the scientific method involves establishing a protocol in advance for how data is going to be collected and analyzed.

And it's very important to follow that. Otherwise you can make it up as you go along in order to jigger the results to come out the way that the people who hired you would like them to come out.

And so it's important to have a written protocol in science that lays out the steps in advance that are going to be followed. It, number one, minimizes the chance that

you're going to manipulate the data as you go and, number two, a written protocol allows other scientists to test your thesis.

And that repeatability is also, of course, a hallmark of the scientific method, where people should be able to go to the same data and use your methods which you've laid out and replicate the analysis and see whether you are right or wrong.

And that can be a very important issue in admissibility under Daubert and, in fact, that was one of the factors that was emphasized by the Supreme Court in Daubert.

Here's what Dr. Farquhar had to say on this key question of whether there was a written protocol that he used when he compared the adverse event report rates from one drug to another.

"Well, the studies, right, the studies that you did that are -- the results that are set forth in 8a and 8b, did you have a written protocol for conducting that study?

"No, I didn't have a written protocol. I had a mental protocol. I knew what search terms I was going to ask be used.

"Okay. Well, that's my next question. What were -- so there is no written protocol anywhere, just so I'm clear on that?

"No, no written protocol. Dr. Ahn and the data and then there's also a data tape. Okay?"

MR. BECK: So there's no way for us to tell whether and how he changed the analysis along the way because he never set forth his protocol. He just claimed to have it in his head. But meanwhile he's not even the one who did the searches, it was somebody else who did that. And so we can't test his analysis, which you're supposed to be able to do under the scientific method.

There's other problems with his analysis. For example, because he uses these different databases, there's overlapping data and there's double counting and he made no effort to try to correct for that.

"Now, did you -- one of the databases on which you did a meta-analysis was the FDA's U.S. adverse event reporting database, right?

"Right.

"Another of the databases on which you did the analysis was the FDA's worldwide reporting analysis?

"Right.

"Did you determine that there was -- did you attempt to learn whether there was any overlap of cases between those databases?

"There is overlap."

MR. BECK: So he knows there's overlap.

"Did you take steps to avoid duplication of individual cases in your meta-analysis?

"There was -- no, I did not. There was no way to do that with the information that we had available. We were taking the data as given to us. Of course, when we went to the -- what we have in Table 8, that was something where we did the entire extracting of the cases and relating it to the denominators, as we have discussed earlier."

MR. BECK: Your Honor, one of the problems with the Adverse Event Report System, one of the reasons why you cannot compare one drug to another is that different pharmaceutical companies may take different approaches in terms of how they report information.

A lot of these adverse event reports come from doctors or nurses. They're sent to Bayer or Pfizer and then Bayer or Pfizer makes a judgment on is this -- does this fall, go in the rhabdo bucket, does it go in the myalgia bucket, does it go in the myopathy bucket.

And there are no consistent standards used from one pharmaceutical company to another. So you could have exactly the same -- you could have 50 situations that are exactly the same, all reported as rhabdo by one company and reported as something else by another company.

So that's a known limitation of the system and, again, Dr. Farquhar knew that that was a limitation, but

made no effort to account for it.

"Well, what I would like to say at this point is that when I have used rhabdomyolysis or myopathy or myositis or toxic myopathy or myalgia from the AERS data, I have to take those terms at face value as they were used."

MR. BECK: And, Your Honor, it may be that there is nothing that he could do to account for that, but that's precisely one of the reasons why you can't use adverse event report information to make comparative safety conclusions, because there is no way to correct for that.

And the FDA recognizes that and uses the word "cannot," that the information cannot be used for this purpose, partly for that reason. And then he says, well, there's no way that I can correct for it, so I used it anyway for exactly the purpose the FDA says that I cannot.

I think I have already touched on the new drug phenomenon. When a drug comes onto the market and it's the new boy in the neighborhood, people are paying more attention and more likely to report adverse events than they are with drugs that they've been -- that have been on the market for a long time. That, again, is an inherent limitation and he did not properly take account of that either.

As I said before, Baycol was the youngest of the statins, so that effect was going to be felt most strongly

by Baycol. And what he did was he said, well, I looked at it with Lipitor, which was around the same age, just a little bit older than Baycol, and there was a difference between Baycol and Lipitor, so I don't see that the new drug phenomenon was much of a big deal.

And in doing that, that again is a flawed methodology because you can't just compare it to one drug, especially if you're going to say it is the most toxic of all of the statins.

If you're looking to see whether there's -- you know, the reporting rates in the first couple of years, you have to look at all of the drugs, which is what the FDA did and which he ignores.

This is an FDA table and if you can see up here on the highlighted part, it's talking about cases of rhabdo in the first two years of marketing and then it lists for statin or fibrate as used as monotherapy. So they're trying to take out gemfibrozil.

And then they have where my arrow is crude reporting rate, which is basically the ratios that he relies on. Cerivastatin, that's Baycol. There you have, you know, 5.96 and it's higher than the next two, but it's lower than simvastatin. It's lower also than lovastatin. So it basically ends up right in the mid range in terms of the reporting rates for the first two years that it's on the

marketplace.

And yet Dr. Farquhar when dismissing the phenomenon of the new drug effect chooses to just look at one of the other drugs, of course one of the drugs that had a lower rate, and he says when I look at that there's a big difference and so these higher rates can't be due to a new drug effect and he ignores all the other statins during their first two years on the market. Again, it's a methodological flaw that goes to admissibility rather than to quibble with his conclusions.

Another --

THE COURT: Before you move on, you said something earlier that caught my attention dealing with the adverse event reports. You said that the reports came -- are different depending on how the -- can't be compared between drug companies because they report them differently and put them in different categories.

Now, you made a big deal about adverse reports coming into the FDA if someone took Baycol or took aspirin and sprained their ankle, that an adverse report would come in.

But does -- is there a screening process that we have here that would take that kind of case out of the realm of possibility because Bayer would get the category and get the report and take a look at it and say, well, it doesn't

fit rhabdo --

MR. BECK: No, Your Honor, there's --

THE COURT: -- it doesn't fit --

MR. BECK: No. It would go in under sprained ankle. So every adverse event report -- there are some, and my understanding is it's a pretty small minority, that get sent straight in to the FDA by people. The vast majority get sent by doctors, healthcare workers.

THE COURT: So there is a screening process that Bayer went through by taking a look at --

MR. BECK: There's a categorization process, but there's not a process where Bayer says we got this adverse event report, but we don't think it makes any sense because it's a sprained ankle, so we're not going to send that on to the FDA. That would be against the law. All the adverse event reports that come in get sent to the FDA. What Bayer would do is Bayer has, you know, established --

THE COURT: They would put them in categories.

MR. BECK: Would put them in categories, right, and Bayer -- and there are no criteria imposed from on high by the FDA to say, for example, here is the definition we want you to use for rhabdo and if it meets these criteria put it in the rhabdo pile. And so -- and what has happened over time is definitions of "rhabdo" have changed and evolved and different companies have used different

definitions.

And rhabdo is just one adverse event report out of a large universe of possible adverse events and many others have the same problem that rhabdo does, and that is there is no precise, generally accepted definition that all pharmaceutical companies adhere to and therefore there are -- and it's not that anybody is doing anything wrong or fudging.

THE COURT: I understand that.

MR. BECK: They just have different criteria. And so because they have different criteria -- and yet they're all doing their best to apply those criteria consistently.

So therefore you can get cases that are on the margin of whether they would qualify as rhabdo or not and depending on the approach to the criteria that a company takes, they might all get swept into rhabdo, they might all get excluded from rhabdo. And everybody is acting aboveboard and being honest and doing their best. They may not even know what one another's criteria are.

But that reality in life is one of the reasons that the FDA says you cannot use these to compare drug safety between one drug and another. So it's not -- no one is doing anything wrong. It's just the realities of the system mean that you can't -- it's point number 5, the last sentence of the caveats, that it cannot be used for this

purpose. And yet, as I said, that's precisely the purpose that they try to use it for here.

Another flaw in the methodology, Your Honor, is the denominator. We've been talking about the numerator, which is the number on top of the fraction 1/3, and then there's the denominator, the number on the bottom, the 3.

And so you're looking at how many cases of rhabdo, however the particular company defines that, are being reported and that is as a function of some other number, you know, how many people are taking the medicine, and then you come up with a reporting rate of whatever it is. So you have to have a good idea of how many people are taking the medicine in order to come up with that percentage or that fraction.

The problem here, Your Honor, is that this -- this is another reason why you can't compare one to another, particularly with Baycol because it was the newest of the statins and was trying to get a foothold in the marketplace, lots and lots of samples were given out. And, in fact, when they sued us in the rhabdo cases, they complained that we overpromoted and gave so many samples away.

But the problem is that the reporting rates that they use don't take account of the samples. It's based on prescriptions that are filled by pharmacies rather than samples that are given out by reps to the doctors and then

by the doctors to the patients.

And this is no small matter. I'm putting up here Dr. Farquhar's report, paragraph 118. He says here apparently Bayer's marketing of Baycol included distribution of a very large absolute number and a percentage of free samples in comparison to prescription purchases.

So the denominator is all fouled up because what happens is if you have, you know, 5 cases of rhabdo and 100 prescriptions, then the way that Dr. Farquhar has done the analysis, the rate is 5 percent.

But if you had 5 cases of rhabdo and 100 prescriptions and you also had 50 samples, those samples are not included in his analysis. He's made no effort to include those in the denominator.

And so the rate would go from 5 percent to something less than 5 percent, which I can't figure out, but it would get cut down because there's a larger universe that it's being compared against. And he had to acknowledge that that would affect the validity of his analysis.

"If there were a lot of people who should have been in the denominator for analysis purposes who weren't in the denominator because they received samples rather than prescriptions, that would cause the reporting -- the adverse event reporting rate for rhabdo for Baycol users overall to be artificially higher; is that correct?

"It would be higher assuming that the reporting rate is unaffected by samples versus prescriptions."

MR. BECK: So he acknowledges that it's going to affect the reporting rate if, in fact, there are lots of samples. And in his report he says that there's a large number of samples both in absolute terms and as a percentage. So that's still another methodological flaw in his use of the adverse event reports.

And as I said, Your Honor, then once he does all of that, he gets reporting rates basically for rhabdo, he improperly compares reporting rates that are driven by rhabdo for different medicines and then he says those must apply to a different condition that has a different physical mechanism from rhabdo.

So all of those are hopelessly flawed methodological problems.

In terms of his PacifiCare approach, the background here is that we're getting these adverse event reports, "we" being Bayer, and Bayer sees that there is this large number of adverse event reports and we use them the way the FDA says you're supposed to use them and that is we commission an HMO, you know, who has a big database showing people who use different statins over time and what problems they encountered, we commission them, PacifiCare, to do an epidemiological study, a controlled scientific study. And

PacifiCare compared the rates of myopathy across statin users in this large HMO. This is the basic finding of importance from the PacifiCare study.

And, Your Honor, I don't know -- I think you'll probably remember that we had big issues in the rhabdo world where people were taking our medicine along with gemfibrozil when we told them not to and we couldn't get them to stop. And also people were starting on .8 when we told them not to start on .8 and we couldn't get them to stop that either.

And so one thing we were interested in is what if there is monotherapy, no gemfibrozil, at .4, which is supposed to be the starting dose, what do the data show there?

And this is what PacifiCare concluded doing an epidemiological study, that there was no increase in the risk of myopathy for Baycol monotherapy compared with other monotherapy statins and hospitalization rates for myopathy was not elevated for Baycol compared with other statins except when gemfibrozil was used concomitantly.

So those are the key conclusions that came out of a real-life epidemiological study that was done looking at the health records of thousands and thousands of people. Dr. Farquhar agrees that that's the conclusions that the authors reached, but he says that there were flaws in the PacifiCare study.

And, Your Honor, I want to say that we have no quarrel with him criticizing the PacifiCare study if that's what he is called to do, but what he has done is not simply criticized the PacifiCare study and say here are some important limitations and its conclusions cannot be taken at face value. He's changed the results of the PacifiCare result study and he has done so through arbitrary means that are not -- again, don't follow scientifically proper methodology.

Again, he worked backwards from his conclusion. His conclusion, which he set forth, is that Baycol is more toxic to the muscles than others and therefore let me see how I can massage the PacifiCare data to come up with that result.

And so he points out supposed flaws in the PacifiCare data. One of them he says is, well, there's a healthy person effect and he says that Baycol numbers may not show the true extent of rhabdo because people who took Baycol by and large were being switched from other statins and therefore they must have been tolerant of statins already. So we have statin tolerant people who are taking Baycol.

That's an interesting hypothesis, but he didn't test it in a scientific way and he just -- what he did is he said there's a possibility for why it is that Baycol doesn't

look worse and because that's a theoretical possibility I'm going to assign a number, 30 percent, and make an adjustment with no basis at all for the number that he used to make the adjustment.

And meanwhile the people who actually did the PacifiCare study looked to see whether there was a healthy person effect. And this is from the PacifiCare study. Excuse me. I'm on the wrong page. There we go.

So he's saying, well, those who were on Baycol, they switched, more of them switched to Baycol than switched to other statins and switchers are going to be healthier than nonswitchers, so Baycol got the benefit of that.

Well, the folks who did the PacifiCare study looked at switchers regardless of which statin they were started on and switched to and what they found, you'll see over here, is ever switching HMG, being a statin. No and the rate was .385. Yes and the rate was .359.

So they were basically indistinguishable in real life and yet he assigns arbitrarily, with no scientific basis, his own plug number to make an adjustment to make the numbers come out his way. Again, that's a methodology issue, not just disagreeing with his conclusion.

Similarly, he says, well, there may have been misclassification of cases where people, you know -- PacifiCare, they probably made some mistakes in putting them

in the rhabdo category or the myopathy category or the myalgia category.

So he says they probably made some mistakes and if I assume that 10 percent was their error rate and they all went in favor of Baycol, then the numbers come out against Baycol.

So he says they probably made some classification mistakes and without any effort to see whether those somehow benefitted Baycol versus other statins, he just assigns a plug number that drives the PacifiCare numbers in his direction.

So what we've got -- and here's how he does this, Judge. I'm scared because my yellow light is on and it takes a few minutes to explain it.

THE COURT: You've got 19 minutes.

MR. BECK: Oh, okay. Well, then I'm starting to get relaxed. I think I can do it in 19 minutes.

What he does is this is hopelessly circular and bootstrapping. He says, well, Baycol is coming out just like the other statins in the real-life epidemiological study and I've already concluded that Baycol is worse, so my theory is that there's a misclassification of results.

So how do I decide on what percentage correction I'm going to make? Well, I'll go back to the adverse event reports and I'll see that there's a difference in the

adverse event reports of a certain magnitude, so I will take that differential and apply it as a correction to the actual epidemiological study.

So he's taking these pieces of data and these analyses and he is completing standing them on their head. The function of the adverse event reports is to raise a signal to do an epidemiological study to find out what the real story is and the function of the adverse event reports is not to make drug safety comparisons between two medicines.

And so Bayer sees the adverse event reports, doesn't know what it's from, is it from monotherapy, is it from gemfibrozil, is it from .8, is it from some combination. Let's do an epidemiological study and see. So someone does an epidemiological study.

Dr. Farquhar is being paid by lawyers who don't like the way it comes out, so he goes back to the AER in order to come up with an adjustment to the epidemiological study. And it's just not good science. There's no way that that is proper scientific methodology.

The proper use of the adverse event reports is to prompt somebody to do an epidemiological study. It is not to change the results of an epidemiological study so that it comes out the way that the people who hired you wished that it came out.

So much of what I said about Dr. Farquhar applies also to Dr. Austin. He is another epidemiologist and biostatistician. He's got the same issues with misuse of adverse event reports and making comparative drug safety conclusions when the FDA says you cannot do that because of the inherent limitations in the data.

He also goes into PacifiCare and instead of simply criticizing it and saying you can't take it at face value, he tries to change the results through a series of flawed computations as well.

He did a couple of calculations. In fact, we saw one of them already, the proportional reporting ratio. I mean, here we have an epidemiologist who is coming in and doing a proportional reporting ratio. This is when he's using the adverse event report data and he's never heard of this before.

Mr. Black, one of the lawyers for the Plaintiffs, told him to do it. It wasn't -- he didn't sit down and say what's the proper way to analyze the data. Mr. Black called him up and said, I want you to analyze the data this way.

He had never done that in his life, he had never analyzed data like that in his life, and he did it because the lawyers told him to because the lawyers knew that if you do that particular computation, it comes out their way.

So he's never done this computation in his life

and he does it only because a lawyer tells him to do it and then he puts it in his report and that's the basis for his conclusion that the adverse event reports can be used to show difference in drug safety.

And on that one, Your Honor, there's a real irony here that I want to touch on, if I don't get to cover the other matters with him, on this witness. If you look closely at this proportional reporting ratio, it's this formula (indicating) and he has it in his report. But here's the funny thing is it's rhabdo over all other adverse events and then you compare that for Baycol on the top of the formula, for one of the other statins on the bottom of the formula. So rhabdo as a function of all other adverse events.

And the core assumption in the formula that Mr. Black came up with is that all other adverse events are going to be the same for Baycol as well as for Lipitor. And so that is a core assumption, which he admits is a core assumption, in this formula of Mr. Black's.

Well, the problem is, of course, that then what they do is they say in applying Mr. Black's formula, rhabdo is more common with Baycol than it is with other statins. Okay. If they had a rhabdo case, but they don't. They've got a myalgia case.

And so then they extrapolate from that and they

say we can tell from this formula that because it's more -- it causes more rhabdo, it also must cause more myalgia and more myopathy. But in the formula itself, the assumption is that there is no difference because that's the denominator under each thing.

So it's a crazy formula and, you know, that happens when lawyers come up with the formulas instead of epidemiologists. You come up with a formula that gives you the answer that you want, but it doesn't make any sense scientifically. And so that's a deep flaw in the methodology.

Dr. Austin has got the same problems that Dr. Farquhar does in terms of the new drug effect. He recognizes that it exists, but he hasn't accounted for it. Publicity bias, he recognizes it exists. He didn't account for it. He didn't make any effort to account for any of the biases that can creep in.

And, again, that's inherent limitations in the data. That's why the FDA says don't use it this way. And he uses it that way anyway without any effort to correct for those things.

I went through the weird deal with his formula. Once you get the lawyers writing the formulas you're going to get the results you want, but they don't make any scientific sense. So it's not a surprise that he never used

this formula in real life for any purpose other than writing the report that Mr. Arbitblit and Mr. Black asked him to write.

In terms of the PacifiCare data, while he does slightly different types of computations, it's the same basic methodological problem where he starts with the proposition that Baycol is worse than other statins.

And then instead of simply criticizing PacifiCare, he tries to manipulate PacifiCare data in order to support that conclusion in ways that don't make any sense as a matter of science or epidemiology.

For example, he says that, well, perhaps there are false positives that account for the fact that Baycol .4 monotherapy, there's no difference there in myopathy between Baycol and the other statins. So he assumes that there may be false positives, but without any evidentiary basis for that and without any methodology to establish what they would be.

And similarly he says, well, maybe the reason they come out the same is because of differences in exposure, how long people were exposed. But, again, he doesn't have any scientifically based methodology to make his corrections. They're just plug numbers that he uses in order to change the results.

For example, on the false positives, without any

basis at all he says, I just think I'll assign a 30 percent number. And if I say that there's 30 percent false positives, that changes the results more in line with the way I think the conclusion should be. But there's no basis for the 30 percent.

And then he assumes a correction of two to four times once he does this with false positives. Again, there's no basis for the false positive rates that he's assuming.

Same thing is true for what he calls the misclassification of exposure. He just inflates the Baycol rate by 10 percent and he says I think there may have been misclassification; and if so and if it's 10 percent and if I combine that with my false positive 30 percent, why, voilà, the results come out different and Baycol is worse.

So, Your Honor, for both of those gentlemen, they may be highly credentialed, but that's not the end of the inquiry. The Court, you know, tedious although it may be, is really required to take a close look at the methodology that they followed here.

They start with a fundamentally flawed methodology of using adverse event reports in a way the FDA say they should not be used and they use it not only to show causation, but then to compare Baycol to other statins, which the FDA says you should not do.

And all of that is for rhabdo and then they change the term and call it a muscle toxicity. And by changing the terminology they pretend that myopathy and myalgia must follow the same course even though they're fundamentally different mechanisms, if they result from statins at all.

And then the same kind of result-driven methodology leads them to manipulate the PacifiCare data, not just criticize the study, but to manipulate the data in ways that are methodologically unsupported in an effort to support their own conclusions.

Thank you, Your Honor, for your patience.

THE COURT: Thank you. We'll take a 15-minute break, 15 minutes.

(Recess taken at 11:15 a.m.)

* * * * *

(11:30 a.m.)

IN OPEN COURT

THE COURT: Let's continue.

MR. BLACK: Good morning, Your Honor.

THE COURT: Good morning.

MR. BLACK: My name is Bert Black. I don't believe I have appeared before Your Honor before, but I have been involved in the case from the very beginning and I have at least attended a couple of the earlier hearings.

I've prepared a PowerPoint on the adverse event

reporting issue and I certainly don't intend to go through it slide by slide, but I think there are some slides that will be helpful to the Court in understanding what's really at issue here.

And in order to facilitate Your Honor's following, if I might approach, we have a paper copy of it that we can leave with the Court.

THE COURT: You may.

I'm going to give you the same amount of time I gave Mr. Beck.

MR. BLACK: Which would be an hour and a half, Your Honor?

THE COURT: Yes.

MR. BLACK: I will not be taking up that whole time because Mr. Arbitblit will follow me on Dr. Farquhar and then I will get up again and talk about Dr. Austin and finally Mr. Lockridge will deal with the reliance issue.

THE COURT: We will -- what we'll do, we'll stop at 12:30 for a luncheon break and start up again at 1:30. So you will have an hour to -- I don't know how you want to do that. How long is the PowerPoint going to be?

MR. BLACK: Might I suggest, Your Honor, just in the interest of keeping things together, if we broke for lunch at the end of my presentation on the adverse event reporting, that would probably take us to about 12:00.

THE COURT: That's great.

MR. BLACK: And then Mr. Arbitblit could continue in one piece.

THE COURT: We will break at 12:00 noon, then. We'll break at 12:00 noon, I'm just telling my staff so I can have my lunch available.

All right. Go ahead.

MR. BLACK: Thank you, Your Honor. I want to really start off with trying to explain what the adverse event reporting issue really is, and I'm going to go through this rather quickly.

You have something called relative risk and then we have relative reporting ratio or relative reporting rate; it goes by different terms. But for relative risk you start off with two populations that you're going to study, population A, population B. You expose one to some substance or give them a drug. The other one is unexposed. And then you see what happens in terms of the development of the disease. Here it's the dreaded yellow circle disease.

And if you count up the dots, there are 50 dots or 50 people in each population. In the people that were exposed, there were 8 cases of yellow circle disease. In the other population there were 2. So you get 8/50 divided by 2/50 and you get a relative risk of 4. A relative risk greater than 2 has been held by a number of courts to be

strong evidence of a causal relationship.

And I do want to add a note here that I was dealing just with the number of people in each population. Epidemiologists actually allow for the fact that some people are exposed more than other people. If one person is exposed for six months, that would be considered a half a person-year. One person exposed for two years would be two person-years.

And so they use this concept of person-years in the denominator instead of just the number of people to account for the fact that some people are exposed for different amounts of time than others.

Now, the problem when you're dealing with adverse event reports is, first of all, we don't have all the reports -- excuse me -- all the cases come in. Estimates are that something less than 10 percent of the adverse events that actually occur in a population get reported as adverse event reports.

Not only that, you don't have an idea of what your denominator was either in terms of person-years or people. But you can approximate the denominator by using prescription data. It makes sense that the more people who take a drug, the more prescriptions there are going to be.

I would like to address one of the points raised by Mr. Beck in terms of sampling. That might have been an

issue earlier on with Baycol, but the differences that were seen by the experts who went through the adverse event reports persisted.

And so the sampling might have been there early on when they were trying to develop market share, but the same problem persisted throughout the time the drug was on the market. So I don't think the sampling problem in terms of using prescriptions as a denominator really applies here.

What you do, then, is you take the number of adverse event reports for a given period and you divide by the number of prescriptions for the same period, recognizing that the prescriptions are a reasonable approximation of person-years of use. And what you come up with is something called the reporting rate ratio, the reporting rate for Drug A over the reporting rate for Drug B.

And I've gone through an example here, a numerical example. All the bases for the example are in the PowerPoint, but you can have a reporting rate of 20 reports per 100,000 prescriptions, recognizing that we probably have something like 1/10th or less of all the cases that really occurred. And then if you knew the actual incidence rate, it might be something -- in my example here, 40 cases per 1,000 patient-years. Now, in the example I'm assuming that we know both the reporting rate and that we have the actual incidence rate.

And by the way, another point that Mr. Beck raised, he said that we were using adverse event reports to calculate incidence rates, which you can't do. And obviously you can't because you're only getting 1/10th or less of all the cases. So you're not going to get an accurate incidence rate that way.

No expert for the Plaintiffs in any way ever tried to approximate an incidence rate with adverse event reports. What you can do is divide one reporting rate by another because then the incidence problem goes away. That's what we did.

In any event, that's Drug A. You can have similar data for Drug B and then you can do a comparison of the two. You do a relative risk, A versus B, of 1,000 cases over 25,000 patient-years versus 100 cases over 12,500 patient-years and you come up with a relative risk of 5.

Now, if you do it in terms of the adverse event reports and do a reporting rate ratio, you have 100 adverse events -- that's 1/10th of the 1,000 cases -- per 500,000 prescriptions and Your Honor can follow the math, it comes out to 5 again, lo and behold.

Now, in order for that to happen -- that shows, by the way, that you can use the relative reporting ratio or the reporting rate ratio as an approximation of relative risk. That's what our experts did.

What conditions have to apply for you to be able to do that? Well --

THE COURT: Excuse me for a second. Lori, is this too fast?

COURT REPORTER: No, it's okay.

MR. BLACK: Excuse me?

THE COURT: Just making sure that you weren't talking too fast.

MR. BLACK: I'm sorry, Your Honor. I'm trying to fit a lot into a limited amount of time. Please do slow me down because I do talk fast.

THE COURT: She will.

MR. BLACK: Thank you, Your Honor.

What conditions have to apply? First of all, the percentage of reporting, whatever it may be, 4 percent, 5 percent, 10 percent in my example, has to be roughly the same for both drugs and the ratio of patient-years to prescriptions has to be roughly the same for both drugs.

Important point. The bigger the reporting rate ratio, the less exactly these conditions have to be met for you to make some reasonable conclusions from your analysis.

Just like big bold print is easier to read, if you've got a real big signal coming through in your reporting rate ratio, things don't have to be as precise as

they would be for a smaller signal.

Now, let me go on here. This is a document, it's Exhibit 11 to the Arrowsmith-Lowe deposition, but it's a report -- not a report. It was a study that was done by Bayer. And the point is that they were doing reporting rate ratio. That's what's shown here.

If Your Honor looks, there's a column that says atorvastatin. Let's see if I can point here. I guess I can't do -- yeah, here we go. There's a column that says atorvastatin.

They used patient-years because they do a multiple that -- but it's based on prescriptions. They approximated patient-years with prescriptions and they wound up with .2 cases per 100,000 patient-years.

And for Baycol, cerivastatin, it was 2 cases per 100,000 patient-years. Well, 2 divided by .2 gives you 10. That number right there, Your Honor, is a reporting rate ratio. That's what Bayer did. So it's a method that Bayer itself used to consider what the effects of Baycol might be in terms of myopathies.

And this is just some quotes from the report. I'll bypass that.

Here's Bayer's arguments on adverse event reports and the reporting rate ratio. Especially with regard to Dr. Kapit, they're arguing that adverse event reports aren't

good for anything, can't use them at all.

Dr. Kapit, as I'll explain later this afternoon, was essentially just giving opinions about whether or not there was a signal at certain points in time. He isn't primarily an expert on causation.

So by criticizing his reliance on adverse event reports, I assume that Bayer is saying you can't use them for anything at all. I guess we are just wasting our taxpayers' money collecting them.

Then they say -- and this is what Mr. Beck addressed -- that you cannot use a reporting rate ratio to determine if there's a difference between two drugs in terms of the rate of occurrence of a disease.

And even if maybe you can do that for a disease like rhabdomyolysis, you certainly can't do it for the lesser myopathies.

I think those are the three steps to Bayer's argument. I'm not going to go -- this is just an outline of our response.

What I would like to start with is that numerous courts have recognized the value of adverse event reports, but no court has considered the reporting rate ratio. There's no precedent on that at all. We are going to have to go take a look at the scientific literature.

But to briefly go through some of the cases, a

number of courts have recognized that even considered anecdotally, even just using a single adverse event report or a small group of adverse event reports, not this kind of statistical analysis that we did here, even that limited number of adverse event reports can provide sufficient evidence for an expert to give opinions.

The Neutraceutical Corporation case, it's an administrative law case, but adverse event reports were a big part of the evidence the FDA considered in banning ephedra.

There's a number of other cases here. I won't go through them in any detail. I will say that -- where is it? Here they are -- a number of the cases that Bayer relies upon happen to be cases that arose in the context of litigation over a drug called Parlodel.

And some courts held that testimony based on adverse event reports would be excluded. And this, again, is the anecdotal use. This isn't the reporting rate ratio. And some courts held that such testimony was, in fact, admissible.

The Globetti case from the Northern District of Alabama is one that held that this testimony was admissible and the judge in Globetti cited the Kittleson case from the District of Minnesota.

That's an unpublished decision, but it was another

case in which adverse event reporting data was considered to be admissible as a basis for expert testimony. Again, a limited number of reports. And then there's another case that was also cited there.

The bottom line on adverse event reporting case law, Your Honor, is that no court has yet considered the reporting rate ratio.

And there's two cases that are cited by Bayer and I do have to address them. The Doe case involved claims about -- it's a drug that had a preservative in it called thimerosal, I believe. In any event, the substance was taken out of the drug and then the expert did a comparison of adverse event reports for the drug with the substance in it and without.

First of all, our comparisons of adverse event reports were contemporaneous. This was subsequent. And there's all sorts of methodological problems because of the changes that took place there, some of which involve some of the publicity that Mr. Beck talked about.

But in any event, we're not sure what methodology the expert used in the Doe case. The court in excluding the testimony noted that the Institute of Medicine had criticized the lack of transparency in the statement of the expert's methods. No evidence in that case that there was a reporting rate ratio done.

And then the other case is the Meridia case. The Meridia case didn't involve reporting rate ratio. It involved this proportional reporting rate ratio that Mr. Beck described to you and about which I will talk more in a little bit, but it wasn't RRR.

So what we're left with is we have to consider what the scientific literature says about reporting rate ratio, what the logic of the method is. And I think I've outlined the logic pretty clearly. I hope that I've explained that adequately.

Let's take a look and see what the literature says. There's an article by Pierfitte. The conclusion is the ratio of reporting rates approximates the ratio of actual risks. That's exactly the point we're making. That validates the method.

And there are a number of other examples. There's the letter that Staffa, et al., submitted to *The New England Journal of Medicine* on Baycol, a peer-reviewed publication, and they used the reporting rate ratio.

And from this they concluded that the increased reporting associated with the use of Baycol appears to be more than an artifact related to an increased awareness of statin-associated rhabdomyolysis or to secular trends in reporting.

So that's the method that the FDA used. That's

the method that served as the basis for withdrawing the drug from the market.

Here's an article by Psaty, et al. This is the point that I was trying to make earlier, Your Honor, when you have a reporting rate ratio as high as we've seen here. Given the highly elevated RRRs for Baycol, the usual limitations of AER data were largely overcome.

This article by Pasternak, et al., that's several very prestigious organizations, American College of Cardiology, American Heart Association --

COURT REPORTER: Wait a minute.

MR. BLACK: Too fast?

COURT REPORTER: Too fast. Several very prestigious organizations, start over after --

MR. BLACK: -- American College of Cardiology, American Heart Association, National Heart, Lung, and Blood Institute.

The point here is after Baycol goes off the market there's concern about statins and so these three institutions get together and they want to compare the safety of the other statins.

And they say all the other statins are just about as safe, one is about as safe as the other. What do they base that on? Adverse event reports. So you can use adverse event reports to compare the safety of drugs.

That's exactly what the National Heart, Lung, and Blood Institute did.

There's an article by Bays which indicates that adverse event reporting data is a highly reliable form of data.

An article by Chang, again, from the FDA. This one in -- this is Chang and staff and others in their official capacity.

And Wiholm on spontaneous reporting systems outside the United States, again, verifying the use of the method.

Okay. Mr. Beck relies heavily, Bayer relies heavily on the FDA caveats about adverse event reports. Let's go through the caveats.

The medicine in the AER may have had nothing to do with the reported event. That's true enough, but that's going to be true -- if you are comparing two drugs, that's going to be true for both drugs if you are comparing adverse event reports.

And to the extent that that's a problem, it biases the comparison towards unity in favor of Bayer in the current situation and here's why that would be. If you start out with cases related to the statin for two drugs, you might have 5 with one and 30 for the other. And if you take the unrelated cases, they're going to be about the same

for both. Let's say that there's 25 unrelated cases.

So here for purposes of this example I assumed 200,000 prescriptions for each drug. Then you get a reporting rate ratio of 6 for the related cases and less than 2 because it's biased downward because of the other cases. The point here is, Your Honor, that if that's a problem, it favors Bayer, it doesn't favor us.

Underreporting and biases, again, true enough, but there's no reason to believe that there was any bias in favor of reporting Baycol events; and the articles by Psaty, et al., and Chang make that point.

Publicity bias. Again, the comparison with Lipitor shows both in terms of temporal comparisons -- in terms of publicity bias, you could compare Lipitor to Baycol and show that that problem didn't exist.

Now, if you want to test the hypothesis that there wasn't any problem because of reporting bias or lack of being at the same time, Lipitor is the best comparison because that's a contemporaneous period.

Going back and comparing the first year of the drugs, the first year one may have occurred in 1997 and another occurred in 2000 or whenever it was. That's got a whole set of other problems attached to it.

So verifying the hypothesis about there being no problem with those biases, the best comparison is with

Lipitor alone.

New drug bias. Again, comparing with Lipitor, I've already explained that.

Variability in coding, the point about which Your Honor asked a question, that doesn't make any difference because -- let me try and explain how the system works and the MedWatch form comes in.

And I think we have an example maybe we can put on the screen. My monitor here isn't working. I don't know if we can do that. It's not letting me switch back and forth, so let me just --

THE COURT: You can.

MR. BLACK: Let me just --

THE COURT: You can switch back and forth.

MR. BLACK: The light isn't on to let me do that, Your Honor.

THE COURT: There's another monitor down --

MR. BLACK: Okay. Well, let me just do it this way in the interest of time. There's some MedWatch reports. There's an example. This is the way the system works, Your Honor.

Your Honor will notice that on the left-hand side there's a block number 5, describe the event or problem. It says please refer to the next page in this case. But in any event, what goes there is the problem that comes into the

company. A doctor calls up. The description that the doctor gives has to go virtually verbatim in that block.

Then if Your Honor will look over to the right, there's a block number 4 that says diagnosis. Okay? And then -- in any event, there's a block here and I'm not finding it where -- the classification of the adverse event, there's a block available to do that. The company doesn't have to fill that in at all. That can be left blank.

And the reason is that when these reports go into the FDA, the FDA looks at the coding and then recodes based on the description, the raw data that came into the company. It's got nothing to do with what the company did to the data. It's the raw information that came into the company the FDA recodes, if necessary. So there's uniformity. Everything in the AER system was effectively coded by the FDA.

And lest there be any doubt about that, that's what Dr. Arrowsmith-Lowe says. Who puts the information into the form? Well, the company. It can be modified by the agency? Right, correct. That's what happens.

And, Your Honor, with regard to Baycol, you could look at the Clintrace system, the internal collection of adverse event reports, the way the company coded it, and you can compare that with what's in AERS.

And I'm not sure of the exact number. I think

it's 10 or 12 examples that we found of where Bayer would code something based on the description as muscle pain and then the FDA would recode as rhabdomyolysis.

So in the Bayer system it would -- there's nothing wrong with this, by the way. We're not accusing Bayer of doing anything wrong. They sent the report in. They didn't have to code it at all. But when the FDA saw it, they called it rhabdomyolysis. They actually did some recoding. So for all companies the coding is uniform and that problem just simply does not exist.

Lack of scientific review or verification, to the extent that there's that problem, it again is one of those things that would bias towards unity.

Can't be used to calculate incidence rates, well, we certainly agree on that. I think I covered that right up front. You're only going to have an incidence rate that would be about 10 percent or less of what it should be. But you can when you compare and do the relative reporting rate or reporting rate ratio. That washes out.

Can't be used for drug comparison, well, maybe as a general rule, but certainly not when you're doing RRR. And, in fact, the FDA itself recognizes that comparisons of reporting rates can be valuable, particularly across similar products -- that's what we have here, all statins -- or across different product classes prescribed for the same

indication. That's certainly what we have here.

The leading treatise on pharmacoepidemiology recognizes that with adverse event reports and prescription data, comparisons can be made to approximate relative risk. So this isn't something that we've cooked up. It's something that the FDA recognizes, you can do the drug comparisons.

The RRR is valid and reliable for determining causation of both rhabdomyolysis and lesser myopathies. I've got some slides on this.

Basically what happens is that you have a continuum of injuries and everybody recognizes that these are all essentially the same family of injuries. It's just a question of degree of seriousness, with rhabdomyolysis at the top and other muscle injuries at the bottom.

And rhabdomyolysis -- if you have people taking statins who contract rhabdomyolysis, it almost certainly was from the statin. So your comparison there is very precise. It gets less and less precise because there are, as Mr. Beck pointed out, other causes for some of these lesser muscle injuries.

But what comes out here is that the signal is so strong that despite the fact that you've got those other sources which bias you towards unity, despite all that you still see a signal coming through.

And I want to let -- Mr. Arbitblit is going to address some of these issues, too, in connection with his discussion of Dr. Farquhar. I will discuss the PRR a bit more when I talk about -- the proportional reporting rate ratio -- when I talk about Dr. Austin.

I want to make one thing clear, Your Honor. I didn't cook that up. It comes straight out of Dr. Farquhar's -- Dr. Strom's book. Their expert's book discusses the proportional reporting rate ratio. And as a matter of fact, it's one of the methods for analyzing adverse event reporting data that's recommended by the FDA in its guidance document on pharamcovigilance. And I will talk about that a little bit more when I discuss Dr. Austin. I may have suggested to experts that they look at these sources to see if it might be a method that would be applicable in this case. I sure as the devil didn't cook it up.

And with that I will turn it over to Mr. Arbitblit, who will talk about some of these same issues and others in the context of Dr. Farquhar.

THE COURT: Should we stop here?

MR. BLACK: Yes, I guess at this point we should stop, I having suggested that originally.

THE COURT: Let's stop here and we'll start up again at 1:00.

(Lunch recess taken at 11:55 a.m.)

* * * * *

(1:00 p.m.)

IN OPEN COURT

THE COURT: All right.

MR. BECK: Your Honor, before Mr. Arbitblit assumes the con, I am happy to report --

MR. ARBITBLIT: As in pro and con, you mean?

MR. BECK: That's right.

MR. ARBITBLIT: Thank you.

MR. BECK: I am happy to report that the one case that was mentioned this morning that was a rhabdo case in Phase I and Phase II that was close to being settled has been settled. So that case is now off of the docket.

And also, Your Honor, violating the BlackBerry rule, but I can read, if you would like, a two paragraph explanation about the settlement with the states.

THE COURT: Please.

MR. BECK: This, I understand, comes from -- was adapted from a standby press release. I have to get it at exactly the right distance so that I can read the small type.

Bayer Corporation entered an agreement with attorneys general of 30 United States states and/or commonwealths to resolve concerns regarding the company's

promotional and marketing practices for Baycol. Under the terms of the agreement, Bayer will pay $8 million to be shared among the signatory states and/or commonwealths. Bayer has also agreed to register all nonexploratory Phase 2 and all Phase 3 and 4 Bayer sponsored clinical studies on ClinicalTrials.gov when those studies are initiated and post summaries of clinical study reports from all Phase 2 exploratory and nonexploratory, Phase 3 and Phase 4 trials on ClinicalStudyResults.org for all Bayer products that are approved for marketing in the United States. Bayer will post links to these websites prominently on the Bayer home page. States entering this agreement will terminate their respective investigations regarding these matters.

THE COURT: So that's just not specifically pertaining to Baycol, it's --

MR. BECK: It was -- the investigations pertained to Baycol and as part of the agreement Bayer agreed to do I think what it was already in the process of doing, which is to post all the clinical trials on these government websites so that people can look at the data; and that would be obviously for products other than Baycol.

THE COURT: All right.

MR. ARBITBLIT: May I begin, Your Honor?

THE COURT: You may.

MR. ARBITBLIT: May it please the Court, I also

have a PowerPoint that's quite lengthy and I will try to go through it as quickly as you would like and I will hand one to Mr. Beck.

Your Honor, I will not spend much time on credentials since Mr. Beck essentially said they were qualified, but I do want to point out just a couple of things about Dr. Farquhar since the Court has not had any opportunity to meet with him. It will only take a minute of the time.

Dr. Farquhar is 80 years old. He's been a physician since 1952. He is a distinguished scholar. He has received a series of awards for pioneering achievements in health primarily relating to his work on preventive cardiology, which is the study of how to keep people from getting heart disease in the first place, including awards from the National Cholesterol Education Program for lowering cholesterol, a research achievement award from the American Heart Association, and recently the Fries award for promoting public health.

He has been a fellow of the AHA --

MR. BECK: It's not coming up on the screens.

MR. ARBITBLIT: I'm sorry. Thank you for the courtesy, Phil.

MR. BECK: Sure.

MR. ARBITBLIT: I apologize, Your Honor. I've

been telling people all week that I'm a low tech person. I will try to do better. Is this going to eventually come on or do --

MR. BECK: I've been telling everybody I'm a high tech person. I think you need to do -- I'm a high enough tech person to call up the guy who really knows what he is doing.

MR. ISMAIL: It's the function key.

MR. ARBITBLIT: Thank you very much. I appreciate it.

In any case, Dr. Farquhar has addressed Ninth Circuit judges on issues of cardiovascular health; a member of the World Health Organization continuously since 1984, expert panel on cardiovascular diseases; over 200 publications.

One of his principal works has been the Stanford Five City Project, which helped communities learn how to protect themselves against heart disease by lowering risk factors. And that program has been the model for the Minnesota Heart Health Project, where he is a member of the advisory board for 13 years. That's a sister project.

And as far as his previous testimony, in 50 years he's served as an expert witness in only three cases, which I don't think qualifies him as a hired gun, and in the two prior cases where he's been challenged his opinions were

permitted.

I think that it's fair to say that this is not a person whose character speaks of concocting things for litigation, but instead is a person of distinguished character who has devoted his life to serving the public.

And with that, I'll proceed to the substance of this presentation.

Now, in summary, the methodology that was used was reliable because Dr. Farquhar relied on multiple, consistent sources, not only on the adverse event reports that were discussed this morning.

And I did hear that we were going to get something from Bayer about clinical trials. Maybe that's yet to come, but I haven't heard anything about it yet. But we will present what some of that data shows that's in the reports and the documents.

The literature review showing unanimous conclusion of the scientific community that Baycol is more toxic, we will go through 18 separate sources on that.

Epidemiology studies that have been done since the reports confirm the findings that were made and the reporting ratio study that followed peer-reviewed methods, the same methods applied by Dr. Staffa and her FDA colleagues, who have subsequently published in their official capacity a very similar analysis.

So we have clinical trials, the gold standard for proof of causation. And Bayer's clinical trials showed, in summary, that there was more rhabdomyolysis than other statins, greater CK elevations than other statins, more myalgia than placebo patients.

There were no direct comparisons to other statins, but the import of that is that it's distinct from what appears on the label and then gets into the literature, that there's no difference between Baycol and placebo for myalgia; and we will go through that data.

Dose-responses, one of the hallmarks of causation. If you are exposed to a higher dose and you have more of the disease, it's presumed by scientists that that shows causation; and we will show the data on that.

And statistical significance indicates the reliability of the data, that it was not due to chance.

So another -- some other things that were not shown or discussed by defense counsel that were raised by Dr. Farquhar as additional sources of his opinions:

An epidemiology study from the general practice research database in Great Britain where the medical records were reviewed showing Baycol was more toxic than other statins despite lower doses.

PacifiCare, which has been challenged in terms of what Dr. Farquhar's interpretation was. However, we will

show that his analysis followed exactly the recommendation of Bayer's own head of regulatory affairs, Dr. Posner, and that subsequent studies have used the same methodology in terms of person-years rather than simple percentages in published peer-reviewed articles, validating the methodology that Dr. Farquhar used.

So the reporting rate study itself used the Staffa method and this relative reporting ratio that Mr. Black addressed. That was not litigation driven and her conclusions have been accepted as estimated incidence rates, for example, in the Thompson JAMA article of 2003. That's a quote from what he described in that.

In other words, as Mr. Black was saying, under the circumstances unique to this case, where you have such an excessive risk compared to what you would expect with other drugs or background, there are -- if you're arguing about what's on the margins, you might not want to do what they call a rigorous comparison. If you're talking about 1.5 versus 1 or 2.0 or 3, as the Psaty and Furberg article said, those would be places you wouldn't go on a relative reporting ratio.

But when you're talking about 16 to 80 times, the peer-reviewed literature calls that clearly excessive and accepts the Staffa findings as the equivalent of epidemiology studies; and that's -- I'll show you where that

is in one of the 2006 publications.

So the idea that Dr. Farquhar started from a conclusion is turning science on its head. Dr. Farquhar read the literature, which established a consensus. And that's a good place to start, Your Honor, because a consensus shows that people have already looked at this and come to some decisions. Dr. Farquhar didn't start that process. He read the literature that showed it and what's happened since is that it's been confirmed even further.

Now, Mr. Beck -- I don't want to talk a lot about Vioxx, but I am involved in that litigation and I know Mr. Beck from that litigation. I'll just briefly say that in the Vioxx case there's been a document introduced after Vioxx was off the market which the defense uses to try to show that there's no difference between COX-2 inhibitors in terms of cardiac arrest.

And we dispute what the import of that is, but the point I'm making here is that's been introduced by them because it helps their case, they think, to show that the FDA is not sure which drug is worse out of the COX-2 class.

There's been nothing like that presented here, Your Honor. There is nothing in the published literature that says Baycol is on a par with the other statins. All of the literature, as we'll show, says more toxic, more toxic, more toxic.

Here are the peer-reviewed studies and I will show you that this same analysis was done not just by Dr. Farquhar, but by the defense consultant, Mr. Loutanbach, whom I mentioned earlier, who is a consultant with their testifying expert, Dr. Strom.

And of course they criticize Dr. Farquhar for working with an assistant, but Dr. Strom did the same thing. He didn't do all the work himself. And it is normal to have assistance, just as lawyers and judges depend on clerks to do some of their work. We can't do it all ourselves.

He is 80 years old and he has a history of working with Dr. Ahn as a statistician who helps follow his instructions. And we'll show that that was hands-on, person-to-person, face-to-face, not just handing off the ball through selective deposition cuts.

What we see here is all of the published clinical trials gathered and presented by Bayer to the EMEA, the European regulators. And what you see in this column, the relative risk column, is it's 8.6 at the .4 dose, 8.8 at the .8 dose.

And the P-values are highly significant, showing that for confirmed rhabdomyolysis Baycol was much more toxic and statistically significantly so in clinical trials, the gold standard. And that's in Dr. Farquhar's report. It's not mentioned today.

Now, in fairness, there are data on the same page of some of the EMEA for unconfirmed rhabdomyolysis that are not -- that do not match these, but the EMEA itself concluded that the confirmed rhabdomyolysis cases were more reliable because they had gone through a review process to show that they were real rather than simply unconfirmed reports.

Now, what about myalgia? Now, Mr. Beck is a fine lawyer, excellent representative of his client, but he's not speaking from the published literature when he says that myalgia is a different disease from rhabdomyolysis.

They are on a continuum of mild to severe from the same mechanism. And that's what the defense expert, Dr. Dorfman, said. That's what Plaintiffs' expert, Dr. Richman, said. And that's what the literature says. It's a matter of degree, Your Honor.

Myalgia is muscle pain that corresponds to increases in creatine kinase or CK, which comes from the destruction of the muscle cells that cause the pain.

So sure there are confounding factors, sure people can get aches and pains, but that doesn't mean that it's a different disease when you have a statin-induced myalgia.

When you have a statin-induced myalgia, what you

have is a mild form of the same condition that could progress in some people who can't handle that much of the drug to a more severe condition, such as myopathy or in some categories myositis or in the worst-case scenario rhabdomyolysis. There's no evidence before the Court that those are different diseases. There is simply lawyer talk.

Now, here's the data on myalgia versus -- for Baycol versus placebo that was never published, and it's in the defense exhibit. We didn't get it until after our expert reports were in because it was in his file. He was deposed in March 2004. Our expert reports were all in by February.

So here's -- excuse me. Here's the data. On the label it says 2.5 versus 2.3, pretty much of a wash, so you would think. But what it also says -- and this is in the exhibit that I'll show you in a moment -- is that that only included about one-third of the patients, less than 3,000 of them.

And what was submitted after the drug was off the market to the EMEA was a larger data set with a relative risk of 1.76 and a statistically significant P-value, which is the hallmark of reliability in clinical trials.

A "P" less than .05 means that scientists will presume that in the absence of some other really good explanation, there's likely to be a cause and effect

relationship.

And that was on all the trials that they labeled short-term trials, up to 24 weeks. Now, it may be suggested, well, what about the long-term trials, did they change that? But what you will see from the exhibit is that there wasn't any data collected, that the comparison they did in the long-term trials was against other statins rather than placebo.

So for common doses you'll see it was even higher, which corresponds to the dose relationship, dose-response relationship; and Dr. Farquhar mentioned these tables in response to deposition questions.

Now, the defense consultant analyzed, just as Dr. Farquhar did, the published trials on rhabdomyolysis and also came up with similar numbers. That tends to validate that Dr. Farquhar was on the right track in the first place.

And in terms of the .8 milligram dose, we looked earlier, in fact, I think it's -- here we see that at the .8 milligram dose Dr. Farquhar's relative risk was 8.8. Now, if we go on to Dr. Strom's consultant, what we have is on slide 19 you'll see that for the .8 milligram dose the analysis by the defense consultant was almost identical, 8.68. So, again, that speaks to a good methodology being verified by the other side's expert but not talked about this morning.

Now, on the .4 milligram dose Dr. Farquhar's relative risk was higher, it was 8.6, but you'll see under the column Pr, pravastatin, that there were 18,000 people there with no cases. So that's going to raise the relative risk because Baycol had cases and the other drug didn't.

And you'll see that in the analysis by the defense consultant for whatever reasons that pravastatin was not included at the .4 milligram dose and so the relative risk came out here at 3.42, still elevated, but not to the same degree because some of the data was not included.

So this is a graph made from the data in Bayer's report, the CIOMS report, to the EMEA showing a dose-response relationship between the Baycol dose and confirmed rhabdomyolysis. Well, that's proof of a cause and effect relationship.

And going on to the -- here's the data on myalgia, Your Honor. This is from the Exhibit 11 that's been submitted to the Court from the Strom deposition and identified by Dr. Strom as having been prepared by his assistant, Mr. Loutanbach.

And here's what he finds, that for the short-term analysis the -- instead of 2.5 versus 2.3, it's actually 2.5 versus 1.4. And I would like to make sure that I find the actual slide where that statistical significance finding appears.

Here it is. This is the analysis by the same gentleman, Mr. Loutanbach, where the myalgia is shown as 1.76 relative risk, the 95 percent confidence interval is higher than 1, and the P-value is under .05. That means it's statistically significant.

This was data that was never published, never available to the public. The Defense has relied upon the 2.5 versus 2.3 in the Thompson article which says that it's from the PDR, which is the equivalent of the label. The Physicians' Desk Reference is the equivalent of what's on the package insert. So this data was not out there.

Is there some other analysis? Is it fair to use only the U.S. data? The label says that over 5,000 were tested worldwide, but when they report the myalgia they're only reporting U.S. trials and it's only 3,000 people instead of close to 9,000.

So Dr. Farquhar didn't make this up. He didn't concoct anything. The defense expert did these calculations.

And what you'll also see in terms of the continuum and the relationship between these conditions is that myalgia is elevated, CPK is elevated for Baycol versus placebo at a relative risk of 4.73, and you see that each level of CPK is in a diminishing percentage of people, but always higher for Baycol than placebo.

So what you're seeing is exactly the continuum of injury that's talked about in the literature and that for tactical reasons the Defense would like to say it's a different disease. But it's not a different disease. It's a different severity of the same disease.

And so we have the Thompson Table 1 that's mentioned in the briefs of the Defense. It comes from the PDR. It's incomplete data. Thompson couldn't have seen it.

Now, these clinical trial results, it's important to say that even though they are higher, they are not as high as they would be in the real world. And the reason for that is, as stated in Dr. Farquhar's report, clinical trials involve typically younger people, average age in the 50s; whereas, for example, in the HMO studies the average age of Baycol users was 67.

They exclude people who are most susceptible, like diabetics who don't have good renal clearance. And 18 percent in the PacifiCare, for example, were diabetics. And they used lower doses in the mix. The .1 and .2 milligram doses are in the table that we just reviewed.

And so those are part of the data that's used to calculate these rates while excluding some of the people most at risk and also excluding the most dangerous use, which is the combination with gemfibrozil, which is

described in the Insull study of Baycol as a protocol violation.

So you would expect -- and Bayer's own scientists say this when they're looking at the adverse event data, well, why is it higher than we saw on clinical trials. Because the clinical trial populations are healthier, they're younger, it's a narrow population where you don't get as much data.

So here's another dose-response relationship between Baycol and an abnormal CK from Bayer's data, and you see that with dose the abnormal CK goes up.

Same thing for the -- there's a missing blue line to connect the two dots at the end, but the point is that the incidence from the clinical trials is higher in Baycol, especially at the higher doses. There is some variation at the lower doses, but as you move up the chain of doses, you see it's substantially higher for Baycol than placebo.

Similarly with the myalgia data, there's the percentage going up with dose.

Now, moving on to the consensus. And I apologize if I am going quickly, Your Honor. I am trying to cover a lot of material. If I go too fast, please stop me.

So the consensus -- now, I want to talk just a moment about McClain vs. Metabolife. The McClain case distinguishes between cases where there's a consensus of

causation and cases where there is not and it says that the court needn't concern itself extensively with the Daubert analysis of general causation when there is a consensus and the examples they give are tobacco and asbestos, tobacco and cancer, asbestos and mesothelioma. And I am sure Your Honor is familiar with the case.

Now, that case comes up again in Leathers vs. Pfizer and it's distinguished in Leathers vs. Pfizer and I think that the Defense has raised it, and I want to talk a little bit about Leathers vs. Pfizer because it's not this case for a lot of different reasons.

Number one, in Leathers vs. Pfizer the plaintiff did not make the record with any of this data for the particular drug that there was a cause and effect relationship based on clinical trials.

As the court reviewed -- importantly, in Leathers vs. Pfizer the plaintiff was trying to make a case that we are not trying to make. That plaintiff was trying to show a permanent myopathy with a CK that had never been elevated, never. And there's no -- we are not making that claim, Your Honor.

We do say, our experts have relied on articles saying that if your CK is not elevated, you can have a mild myopathy that stops when you stop the drug. That's a reasonable position. It's supported by literature. Some

people might disagree with it, but it's got support in the literature.

THE COURT: Do you have another set of this for my law clerk?

MR. ZIMMERMAN: We can get you one.

MR. ARBITBLIT: Yes, I believe we do, Your Honor.

MR. HOPPER: We do, Your Honor.

MR. ARBITBLIT: The point of it is that the difference is the principle in McClain vs. Metabolife is viable here because there is proof of a consensus that Baycol causes the injury and that it's more toxic.

In the Leathers case that involved Lipitor, there is no such consensus that it's more toxic nor is there a consensus that it causes permanent injury with no elevation of CK.

And, in fact, some of the case reports that are cited by the judge as proof against the plaintiff in Leathers would be proof consistent with the position that we've taken here, which is that there is a variability in the mild to moderate range of from weeks to months to possibly over a year in recovery time.

And some of the case reports cited in Leathers vs. Pfizer include statements that the patient recovered in three months or five months. That's similar to what our experts are saying and that's what the literature says as

well.

So I just want to quickly go through some of these statements on Baycol being more toxic, and these articles have been submitted to the Court.

MR. HOPPER: May I approach?

THE COURT: (Nodding.)

MR. ARBITBLIT: In 2006 the Jacobson article mentions not only the higher rate of rhabdomyolysis than was observed with other statins, but also the incidence of myopathy increases dramatically to 1.5 percent in the new drug application and that's higher than for any marketed statin, suggesting threshold dose, again speaking to the dose-response.

This is authoritative in one of the leading cardiology journals where doctors go to read about drug safety and they want to know, they want to know are we going to run into another Baycol if we use rosuvastatin or another drug. So it's current events. Even though it is past history as far as Baycol, it's very current for doctors to be wondering are these drugs safe.

And so there are comparisons to rosuvastatin and Baycol in the literature. And here's what you see, higher than for any marketed statin. That's a recent statement.

And that's -- here's what Jacobson says about it. The now obvious conclusion from the cerivastatin experience

is that as the statin dose or more likely serum concentration increases, the risk of CK elevation increases to the point where a threshold level is reached. Above this level, myotoxicity begins to accelerate to levels beyond acceptable risk/benefit ratios. From the NDA data and additional postmarketing FDA data, the cerivastatin threshold dose appears to be at the 0.4 milligram dose.

And you will see that they have incorporated both the clinical trials and the postmarketing data in the same analysis, same support for the concept that Baycol is more toxic.

And for statins currently on the market, the threshold concentrations appear to be above currently approved doses except in certain populations that don't metabolize it right or have drug-drug interactions.

But only Baycol, according to this article, reached toxic concentrations in monotherapy at standard doses. And that's the consensus position in 2006 and 2007.

Here are some of the articles that Dr. Farquhar relied on that were saying the same thing four and five years ago when he was first involved in looking at this project:

The Staffa article, again, it's criticized by the Defense. Initially they tried to claim it wasn't peer

reviewed. Well, they had to back off of that because *The New England Journal* submitted an affidavit saying that it was peer reviewed. Even though it's a letter to the editor, it was a serious issue and they peer reviewed it externally.

And this is what it showed. It showed that there was this relative reporting ratio that was 10 to 50 times higher in monotherapy, 16 to 80 times higher in combination therapy with gemfibrozil.

And the statement was made that a comparison to Lipitor was more than an artifact. Well, what can that mean? If it's more than an artifact, it's real. Those are the two options. If it's an artifact, it's not real. If it's more than an artifact, it's a real excess risk and that's how it's been interpreted.

So then you see early articles like Farmer and Hamilton-Craig that rely on Staffa and say we think this shows it's higher, that cerivastatin is an exception to the favorable risk/benefit ratio, that Baycol is at least 10 times the risk of other statins.

Thompson says that Baycol is the statin with the greatest risk of muscle injury alone or with gemfibrozil in *The Journal of the American Medical Association*.

Thompson states, citing Staffa, that these are considered estimated incidence rates showing Baycol the most

toxic. They're not -- Bayer would like to call them a signal. Well, they are a signal, but they are more than that. They are estimated incidence rates for the reasons explained by Mr. Black during the AER analysis, which is that where you have drugs that are marketed at the same time for the same population and you don't have any -- a priori reason to expect vast differences in the reporting rate, these types of numbers are not otherwise explainable.

And here's the American College of Cardiology consensus statement, again interpreting Staffa as an FDA report that it's more frequent. They're not pulling any punches. They're not saying careful, these are adverse event data. They're saying this is how we interpret it. And they are the leading cardiology groups, including National Heart, Lung, and Blood Institute, which is part of the United States government, so that's a very authoritative interpretation.

Clinical trial data supports postmarketing data, demonstrating higher incidence. Dr. Farquhar looked at both, just as Evans did.

And here's a recent statement from the -- this is not quite as recent, but it was when rosuvastatin or Crestor was being marketed, coming to market, and here's what he says in blunt terms. Because the FDA had been burned by the particularly toxic effects of cerivastatin, which

subsequently was withdrawn from the marketplace, rosuvastatin received a particularly careful scrutiny by the FDA before giving its approval. So particularly toxic.

Arora, 2006, extremely rare for all statins save cerivastatin. I'm sure that it could be stated that Dr. Arora, the author, didn't know what was in Bayer's mind, but nevertheless Dr. Arora said that Bayer concluded that cerivastatin monotherapy did substantially increase the risk compared with other statins and in August 2001 it was withdrawn. Now, that's specific to rhabdomyolysis, but as we've discussed, there was data showing higher rates of myalgia as well.

These are two recent studies, the high quality peer-reviewed *American Journal of Cardiology* and an expert opinion on drug safety. Cziraky is the epidemiology study that showed that there was a 6.7-fold increased risk of hospitalization from muscle disorders with Baycol compared to other statins. And the Davidson article says that it's not a class effect, meaning that even though these are part of the same class of statins, that doesn't mean they all act alike, there are differences within the class that can make one more dangerous; and that is what Davidson is saying.

Psaty -- as the Court is perhaps aware, Psaty and Furberg were Plaintiffs' consultants in one of the Baycol actions. Nevertheless, they disclosed that affiliation and

had their paper peer reviewed in a prestigious journal of the American Medical Association.

And as Mr. Black addressed, and I won't go into it, they found that there was no reason to think that there was any explanation for 16 to 86 times higher besides an inference of cause and effect.

Now, Chang, Staffa, these are the same authors that wrote the 2002 article. And in 2004 they enlarged their study. Instead of just fatal rhabdomyolysis, they analyzed all rhabdomyolysis.

And this time they did it in their official capacity and the paper says on the front of it that it's a work of the United States Government and in the public domain; whereas, the 2002 paper said that they were not speaking in their official capacity.

And they do a similar analysis using the same methodology and the same data sources as Dr. Farquhar and they come up with very similar conclusions, that there's a much higher rate of rhabdo with Baycol than any other statins and the risk for reported rhabdomyolysis associated with cerivastatin is evident.

Yes, the caveats are in that article too, Your Honor, but there's no denying that they're saying the risk is evident and compared to all other statins it had higher reporting rates.

In 2006, relying on the Graham study, Neuvonen finds that the study shows 10 to 100 times higher rhabdomyolysis with cerivastatin.

And then this is the Graham study itself that shows incidence of hospitalized rhabdomyolysis and the risk is substantially greater, 10-fold in monotherapy and 1,400-fold with a fibrate such as gemfibrozil, which is given often to people on statins because it lowers triglycerides. So it's a concomitant medication to treat a related problem.

And here we have the -- what I think is a particularly important confirmation of the consensus because it is so recent, 2006, and in an authoritative journal, *American Journal of Cardiology*, and because of what it has to say about the Staffa article that's now had a few years to be considered by the scientific community. The situation surrounding cerivastatin's withdrawal confirms that some statins at marketed doses have shown a greater risk for muscle adverse experiences when compared with other statins at their marketed doses.

And that's very consistent with what was shown in the first article I presented, which was the Jacobson article, which is also in *The American Journal of Cardiology*.

Now, what Bays goes on to do is provide what's

called an evidence grading system and he grades things as Level A, Level B, all the way down through F, where things are -- where there's evidence contrary to what's being asserted by a particular statement.

"A" refers to clinical trials. That's always the gold standard. But the next level down is epidemiology studies, cohort, case control, claims database studies, and, significantly, reports to regulatory agencies of hard safety endpoints, i.e., death, that clearly exceed that of population averages and/or comparator treatments.

Now, that Level B then goes on to a statement in another table about various types of assertions about statins and the assertion some statins are safer than others with regard to potential adverse muscle experience is given a Level B or the equivalent of all these epidemiology studies and the hard endpoint adverse event reports.

And the references that are given for that include the Staffa 2002 article and it's described as a high level of evidence because there was such a clear excess of risk that's not explainable by any of their means.

I'm not going to talk about it much at this point, but there's a mechanism study also cited that was cited by our toxicologist, Dr. Smith, who is subject to a Daubert motion as well.

Very briefly, general practice research database,

it's in Dr. Farquhar's report, but it's not in Bayer's papers. It shows that Baycol was more toxic even at lower equivalent doses than other statins without any adjustment, correction, only taking the data and comparing other statins to Baycol at much lower doses on an equipotent basis than the other statins because in Europe they were using lower doses of Baycol primarily.

Now, the PacifiCare study was done for Bayer and Dr. Posner, who is the head of regulatory affairs for Bayer, recommended the analysis of the PacifiCare data that was done by Dr. Farquhar, but not by the PacifiCare authors.

Specifically, the healthy patient effect is not something that Dr. Farquhar dreamed up. There are multiple sources for what's called the healthy worker or healthy person effect where you have to consider whether a particular population is more tolerant.

And the issue that's raised by that is whether there's selection bias, meaning that the results of the study can be altered if one population is somehow different from the other population.

And people who have tolerated statins are considered in Bayer's own documents to be statin tolerant, not a so-called naive population; and people who have never been on a statin are more of an open book, no one knows what's going to happen.

So what happened here is that Dr. Posner recommended that you do the never switched category. And, in fact, Dr. Farquhar did not do any corrections, adjustments, or fancy footwork. He just took the data in PacifiCare itself, which I will show you in a moment Dr. Strom's consultant, Mr. Loutanbach, also used, and showed that Baycol had a higher relative reporting rate. He just didn't do the overall relative risk, but he looked at the same data and confirmed that this is the right way to do it.

Now, the never switched category was recommended for analysis also by Dr. Faich, Bayer's consultant, because the switchers were more statin tolerant so you're not going to get a fair picture.

So this is data that was in PacifiCare and when you looked at it without any adjustment whatsoever, it showed a statistically significant 1.54 increase risk for Baycol and a highly significant P-value that shows it's not likely due to chance, not likely.

And so here's the same data. Let's go to the chart here, and I think it's probably easier for Your Honor to see it with these little call-outs. What you're looking at here is the relative risk and the top row where it says ever switching HMG, that's a statin, and the answer is no.

So what you're looking at here in the top row is

Bayer's own consultant looking at the same data that Dr. Farquhar looked at and showing that in each case, each comparison to each statin you have a higher relative risk for Baycol. The only thing that he didn't do was the last step and that is put them all together and compare them.

And if you do, this is what you get. If you look at the data on both sides, they both have the same comparison and this is the calculation. And that's what Dr. Farquhar did with raw data from PacifiCare. No funny business. Just took the data and did the analysis.

Now, as far as the adjustment for time, this is a no-brainer, Your Honor. Every published study of Baycol in a claims database -- and now there are two that are recent and not just for Baycol, but let's talk about Vioxx. Patient-years of treatment is the denominator in the Vioxx studies and it's the denominator in the Baycol studies and it's the denominator that should be used because relative risk is an incidence rate in the exposed over an incidence rate in the unexposed.

And an incidence rate, as stated in the Reference Manual, involves the rate of disease and reflecting the number of cases that develop during a specified period of time.

So if you don't look at the amount of time, you are biasing the results in favor of the group that has the

shorter duration because you're cutting out some of their numerator, you're cutting out time when some of those events would occur. And that's what happened with Baycol is because they were switching Baycol into this HMO, they had a shorter duration of use on average.

So this is just an example. This is not from the PacifiCare, but just an example. If you've got 10 events in 100 people and you just -- versus 5 events in 100 people and there's no time adjustment, that's an obvious relative risk of 2.0 because you have twice as many with the same denominator.

Let's assume that the patients in Group A average two years of use while on Drug B they averaged four years of use. Then if you calculate by patient-years, which is the standard method, you see that there were five events in .125 -- you see that the rate is .125 and the rate is .5, so the relative risk is 4 instead of 2. So if you don't take that into account, you wind up with distorted results.

And so Dr. Posner from Bayer's head of regulatory affairs says, "Has there been any adjustment for time in these data?" Well, yes, now that Dr. Farquhar has done it, but not previously. "It would make a difference if patients were on other statins longer than Baycol." Yes, it did. It made a big difference.

So to say that Dr. Farquhar dreamed this up,

concocted it, or manipulated the data is false. It's insulting. What he did was standard epidemiologic methods that were not done by the health economists at PacifiCare who did not have his credentials or his experience to know what the right methodology was.

"Have we looked at the switch versus nonswitch patients? Switch patients will have a lower incidence of adverse events because they previously tolerated another statin." This is exactly what Dr. Farquhar did for the best analysis, which is nonswitch patients adjusted for time, and that's what we have Dr. Farquhar doing.

So as Dr. Farquhar points out, Dr. Posner of Bayer made the same criticisms that he stated and that he did these corrections.

So the correction for time would not be so important if all the events happened quickly. Now, Dr. Strom thinks that they do happen quickly, so you shouldn't adjust for time, but he is looking at the wrong data. The reason he is looking at the wrong data is his basis for that is the rhabdomyolysis events in the MedWatch reports.

The reason that's not appropriate to compare to PacifiCare for this purpose is that rhabdomyolysis in the adverse event reports in MedWatch actually did happen quickly because a lot of those were people with gemfibrozil.

It was fulminate. It was going quickly.

And as Mr. Black said, rhabdomyolysis is almost always going to be attributable to the statin if you're on the statin. In fact, the two epidemiology studies that we looked at already, the Graham and Cziraky, had a period, a run-in period where people were not on any drug and they had zero cases in 300,000 patient-years of exposure when no one was on a statin, zero cases.

So it's statin -- if you're on a statin and you have rhabdomyolysis, it's very clear, not 100 percent clear, but very highly likely that the statin caused it; whereas, in PacifiCare there was a vague description that the FDA criticized harshly for not being limited to cases that could be identified with any certainty. It was called myopathy and it included a bunch of claims, everything from myositis to renal failure to myalgia, and they threw it all together.

And those events are not necessarily linked to Baycol, as Mr. Black -- as Mr. Beck has pointed out. Excuse me, Mr. Beck. They're not necessarily linked, so they're going to be occurring over time.

And, in fact, they did. They occurred -- the average time to event is shown in the PacifiCare actual data and those events were going on -- average time was more than six months. The range was a year or more. So it really did matter that the Baycol duration of use was shorter because

events were cut out of the numerator.

So this is the Posner recommended -- this is what Bayer's head of regulatory affairs recommended, take the never switched folks, adjust for time, and your relative risk is 2.33.

Now, I'm not going to go into there was -- Dr. Farquhar did believe there was a basis to go further than that and adjust on the basis of some data in the adverse event reports, as Mr. Beck pointed out. That's in his report.

But in his supplemental report he said, look, set that aside for the moment. Just do what Dr. Posner said and here's what you get. You get a statistically significant excess of doubling of the risk in spite of all of the failings of PacifiCare.

And then you see Graham, as I was just mentioning. They used person-years of treatment. They did not use number of events over people. They used person-years of treatment so that there was an adjustment for time and then they reported the risk as 10-fold greater based on person-years of treatment.

Same with Cziraky. They used person-years of treatment and calculated their incidence rates to get the relative risk of 6.7.

And this is what Dr. Farquhar showed as the risk

doing the Posner recommended analysis.

THE COURT: Would you go back to the last two. You went so quickly that I --

MR. ARBITBLIT: I'm sorry, Your Honor?

THE COURT: The last two.

MR. ARBITBLIT: Yes, sir. The point here is that, as we've been saying, as Dr. Posner said, as Dr. Farquhar carried out, adjustment for time is the standard way of doing relative risk because you're looking at incidence rates, not mere percentages of people with events. Time is a very essential part of incidence. It's part of the definition of "incidence," that it's a specified period of time.

So these published authors, Graham and I believe it's Chang and Staffa from the original publication in *New England Journal* were on that paper with him, they used person-years of treatment, which is what Dr. Farquhar did when he analyzed PacifiCare. That's not dreamed up. It's standard practice.

And so they didn't even report incidence in terms of a percentage of events over people. They only reported it this way, with a denominator based on an adjustment for time.

Likewise with Cziraky in *The American Journal of Cardiology*. It's the largest published study of a claims

database using the methods espoused by Dr. Strom in his pharmacoepidemiology textbook. You take the database, you record the events, and you calculate an incidence rate based on patient-years of exposure that is adjusted for time. And this is what they found.

And this is new, but it's confirmatory, Your Honor. We believe that this simply confirms that Dr. Farquhar did the right thing and he did what the peer reviewers would have asked if PacifiCare had submitted its article -- an article to a topflight journal instead of presenting an abstract at a conference.

Is that clear enough, Your Honor? Is there anything further you would like me to address?

THE COURT: Go ahead.

MR. ARBITBLIT: Thank you.

I know Mr. Black addressed the FDA caveats. They apply to the data alone. They do not apply to the relative reporting ratio analysis. Mr. Beck showed that slide. It only mentioned AERs. It did not mention using a denominator based on IMS data.

FDA officers have made such comparisons, including the one we just talked about by Chang and Staffa, and they have used it to make those comparisons. Yes, they have had the caveats, but they've also made their conclusions that risk is evident; and they've been cited by the recent

literature as saying that's equivalent to an epidemiology study in terms of the evidentiary value.

And here are those criteria that make it valuable, same class, same indications, similar population, marketed at approximately the same time. And that certainly applies to Lipitor, only a six-month difference in marketing.

And there's the quote from the 2006 article that there's a high level of evidence in circumstances of the Baycol case. That doesn't say that you would always use adverse event reports, Your Honor, but you can't make the generalization that Defendants choose to make here, which is that they are never usable, they are never reliable. That's not how science works. It's not all either/or.

You have to look at the circumstances. You have to look at the totality of the evidence. You have to look at whether there's consistent evidence from clinical trials, which there is. You have to look at consistent evidence from the epidemiology studies, which there is.

And then you see that the relative reporting ratio study is right in line with those and you also see that it meets these criteria and you see that the relative reporting ratios are enormous and not otherwise readily explained.

I have already discussed everything that's on this slide, so I will move along.

The FDA actually did use it to make the

comparisons in August 2001, but I am going to move on past that. I don't need to address it given the interest of time.

This is simply the declaration showing that it was peer reviewed initially.

There's a statement in the Bayer brief that I did want to correct. The underlined text is what was omitted from the brief so that the text actually said, "The reporting rate is a crude measure of the number of reports received by the FDA."

But the actual statement in the Staffa article is with the underlining, "The reporting rate is the number of fatal cases divided by the number of prescriptions dispensed and is a crude measure of the number of reports received by the FDA relative to the extent of the use of an agent in the U.S. population."

Now, sure, there are still caveats about that, but you can't just leave out that last part. You can't leave out the fact that it's relative to use, because that's where you get your denominator. That's what differentiates a relative reporting ratio from raw adverse event reports with no denominators that don't allow any comparisons under any circumstances.

So more than an artifact, that's not mentioned in the briefs.

We've talked about Psaty, we've talked about Bays, and we talked about that (indicating) already.

Now, here's something we haven't talked about yet that I want to hit head on. There's an assertion that Dr. Farquhar failed to take into consideration the higher adverse event reporting rate for new drugs. He did take that into account. He made the same comparison to Lipitor that Dr. Staffa and many others have made.

Now, Mr. Beck introduced an FDA document from 2000 that's never been peer reviewed to suggest that Baycol was in the middle of the pack during the first initial time of marketing, but that's been rejected in the peer-reviewed literature.

The new drug effect and publicity effect on relative reporting rates are negated by an actual analysis of trends, and that's in the FDA Officials Chang and Staffa article "Pharmacoepidemiology and Drug Safety" wherein they say, "Sub-analysis of reporting rates for each statin for the first three years of marketing only and for the 19-month period immediately preceding the withdrawal of cerivastatin revealed the same relative patterns seen in the overall analysis." And that should say, "Emphasis added," Your Honor. I apologize for that oversight.

The point is, though, that they looked at the trends and they saw the same relative patterns. And they

are doing that specifically because they're aware of people's concern is this a new drug reporting effect. And they're saying, no, it's not. The relative patterns were the same.

And why did they look at that 19-month period before Baycol withdrawal? If you follow back to December 1999 from August 2001, what you come to is December 15, 1999 when Bayer first sent out "Dear Doctor" letters saying that there's a problem with co-use with gemfibrozil. So that's when you might start the clock running to see whether adverse publicity might be playing a role.

But what they're saying is we looked at that and it didn't. So what we have from the Defense is speculative. It's saying here's what might happen, you might get bad publicity in some other case affecting the reporting rate. But you didn't get it here. You did not get it here because they looked at it and it didn't change it.

So here's another example of selective quoting of the deposition. Yes, it's true that Dr. Farquhar had not done adverse event report/IMS analysis, but what he said at his deposition is this:

"I really would like to add that, if I may, that the general principles of epidemiology that were set in motion in that analysis are the same as those that I have used in many other circumstances."

Now, as lawyers, as judges, as doctors, we're always faced with slightly different circumstances, but we use our experience and we apply it to the case at hand. This is a gentleman who has been practicing as an epidemiologist and physician for 50 years.

It's not that this is rocket science to take the data from the FDA MedWatch and put it over denominators. All he had to do was tell Dr. Ahn which terms to look for, which he did. So you plug in the terms and it spits it out.

And you'll see in other testimony that this is exactly what had happened. He didn't just hand it off, as Mr. Beck suggested. He testified, "We were going at it together," with Dr. Ahn. That's right out of the transcript.

And then there's an extensive discussion, it goes on for five pages where Dr. Piorkowski was grilling Dr. Farquhar about who is Dr. Ahn and what did you do. He was a trusted in-house biostatistician who's worked with him on past projects. Dr. Farquhar directed and instructed Dr. Ahn as to what terms to search in the database.

Now, there was a highly technical clip that was pulled about what kind of coding. Well, I don't think you need to know what kind of coding is done to know what to tell your biostatistician to search for.

And then you see that actually they did it

together.

"Just imagine that I am standing here and he's there and there's his computer. He and I have worked out the program. And he's the one that presses the button and gets the compilation of data. Okay?"

That's not a handoff. That's a ministerial function of carrying out Dr. Farquhar's directions.

"So you were telling him what terms to look for?

"Right."

Dr. Farquhar did this analysis with someone pushing the button to help him get the data.

Now, there was a challenge to the meta-analysis. Well, it's important to respond to that briefly in two ways. First of all, the meta-analysis was not necessary to show the greater risk because each of the five sets independently showed greater risk; and that's stated in the report.

Yes, there was overlap, but they didn't show Dr. Farquhar saying that they were sufficiently distinct to furnish an adequately different database.

And they didn't mention that there are three analyses that Dr. Farquhar presented, one for rhabdomyolysis, one for myopathy, and a separate one for myalgia alone, that were all based on the single database; no overlap, no meta-analysis, one database.

And what you'll see in that is relative risk for

Baycol versus other statins of 42 for rhabdomyolysis, 19 for myopathy, and 8.0 with a P-value of less than 1 in 10,000 possibility that that result is due to chance when you compare Baycol to Lipitor for myalgia.

Now, whether the disease endpoints are defined the same or not, as Mr. Black pointed out, that comes -- and as Mr. Piorkowski pointed out in the deposition -- that comes out in the statistician's wash.

"It's important to say that as long as the same methods are being used for drugs in the same class, that one presumes that one is coming out with comparable inaccuracies, if you will, for each of them.

"Is there an epidemiological way of saying it all comes out in the wash?

"Well, it all comes out in the statistician's wash."

And Dr. Farquhar was using the same methods here that were peer reviewed and accepted not only in *The New England Journal* letter to the editor, but in the subsequent full publication.

So, yes, there are uncertainties, but do they explain a ratio of 8 to 1, 19 to 1 or 42 to 1? No, they don't explain that. And the P-values confirm that that's reliable.

And another comparison here just based on the single database shows that actually the peer reviewers said

it was even worse for Baycol than Dr. Farquhar. So if you want to analyze whether Dr. Farquhar was biased against Bayer, well, the evidence doesn't support that.

We're using the same reporting ratio method. They both used FDA MedWatch adverse events as the single source of the numerator. They used somewhat different definitions, which led to somewhat disparate numbers of events.

The Chang definition in the published article included not only rhabdomyolysis, but a CPK over 10,000. Dr. Farquhar's search did not have the CPK limiter, it was just for rhabdomyolysis. It's similar, but it's more inclusive.

So the number of events, if you see in the last paragraph, Dr. Farquhar and Dr. Ahn pushing the button to get the number of cases came up with pretty darn similar numbers for Baycol, 495 vs. 479 in the published article.

As to Lipitor, it was more disparate, but it was going in the same direction. 109 according to Dr. Farquhar's definition without the CFK. 51 for -- excuse me. The 109 came from Chang. They found -- no, I'm sorry. 109 came from Farquhar, which favored Baycol because it led to a higher reporting rate for Lipitor.

But on the prescriptions they were both using the IMS data, that's the standard source, and they both came out almost identical, the exact same number for Baycol and

6 million off for Lipitor, over the course of several years of marketing.

So what happens here is that Chang's Table 4 shows that Baycol versus Lipitor is 4.29 over .03, which is a reporting ratio of 143; whereas, Farquhar's reporting ratio is 57.5 and there's a P-value that is significant.

So they used the same methodology. Dr. Farquhar had a slightly different case definition that captured more cases, but there's nothing inconsistent about these results.

If anything, the fact that Dr. Farquhar's ultimate finding of the relative reporting ratio there was lower than what the peer-reviewed article said negates any argument that he concocted this in a biased effort to sink Bayer's ship. It's a single database. It's not a meta-analysis. It's a peer-reviewed methodology.

Likewise on the free samples. Your Honor, that's an interesting point, but the point that again comes out in the statistician's wash is that Lipitor is made by Pfizer. They were giving out free samples too.

During the lunch hour I Googled that and found that they had something like 7.3 million samples in their first year. And I am not going to represent that I have precise data for each year, but the point is that Defense has not introduced any evidence that sampling was

differentially related to Baycol versus Lipitor.

So if the IMS data didn't capture samples, then it didn't capture Lipitor samples either. So, again, it comes out in the wash. If you've got a 16 times or a 50 times reporting ratio for Baycol, there's no way that that's going to be explained by the marginal difference in how many free samples were given out by Pfizer as opposed to Bayer if, in fact, Bayer outdid Pfizer in the free sample department, which there's no evidence of.

So, again, uncertainties affect them in roughly the same manner and there's no reason to throw the analysis out. It's been peer reviewed using identical data sets.

Pierfitte, Bayer says that it shows widely disparate reporting rates, but the authors say that the differences remain low and reinforces the credibility of calculations and comparisons made in this context, in the context of similar drugs, similar class.

Let's see. In the Hamilton-Craig article -- again, supporting from another source -- 88 per million versus 2 per million reporting rates for a European database where the reporting is mandatory, not voluntary. So 44 times higher. Consistent.

FDA officials have written about the use of even individual adverse event reports so much that there's

stronger evidence with denominators. I think I'm going to skip over this.

I do think that it's worth looking at, if Your Honor has any interest in seeing, that there are methods for looking at individual case reports, which we didn't need to do here. But if you have rechallenge evidence, which we do have and we've submitted one, and supportive cases, even from small numbers of individual events causation can be addressed with clusters, that we have clusters of cases.

We have the baseline rate is close to zero, as I was saying earlier, so that if you have a cluster of cases, that becomes more meaningful.

This proportional reporting rate methodology, I'll address it briefly. Dr. Wiholm, who unfortunately passed away a couple of years ago, was a regulator from Europe who came to the United States and was working as the head of the Division of Epidemiology at Merck until he died in 2005 and he authored this chapter in Dr. Strom's textbook.

Dr. Farquhar didn't make up the proportional reporting ratio method and, again, it's not used as a strong foundation by Dr. Farquhar or by Plaintiffs. It's merely another consistent piece of evidence.

The purpose of a proportional reporting rate is that since all the events are reported for each drug in the same time frame, you're not looking at anything that could

be influenced by a publicity effect or a new drug effect.

And so it came out the same and there's a recent peer-reviewed study that we have submitted using the same method. Now it's been peer reviewed for another statin that validates the choice to use that as one part of an overall analysis.

The Meridia case is distinguishable. There was a PRR there, but it was the only adverse event analysis presented, not simply a consistent additional analysis.

The court criticized the failure to submit the raw numbers, which could make the analysis misleading, but here Dr. Farquhar has submitted the raw numbers showing hundreds of cases, thousands of total adverse events in the denominators that make it transparent to the Court and the parties as to what is being compared and still finding that rhabdomyolysis was a much higher percentage of the total of adverse events.

That's what proportional reporting rate does. If you want to see whether one drug has more of that type of event as a percentage of all the adverse events, it's considered by Dr. Wiholm to be acting in a fashion similar to relative risk. Dr. Farquhar followed that methodology to the letter and it's in Dr. Strom's textbook.

So, again, general causation here is based on many admissible elements, including clinical trials that we've

discussed, scientific consensus up through the latest publications, and epidemiology studies, in addition to the reporting ratio studies.

And I would be happy to entertain any questions if you would like, Your Honor. Otherwise, I'm happy to sit down also.

THE COURT: You saw your red light come on.

MR. ARBITBLIT: I should have, but --

THE COURT: It just came on.

MR. ARBITBLIT: Thank you. Sorry, I didn't know. I was blocking it with my computer.

THE COURT: It just came on.

MR. ARBITBLIT: My co-counsel were too polite to tell me. Either that or they liked it. I don't know.

MR. LOCKRIDGE: Could we have ten minutes, Your Honor, for Dr. Austin? I know we've run over a little bit.

MR. ARBITBLIT: I would be happy to waive some of my time on the muscle people if that would make a difference.

MR. BECK: Your Honor, I have no objection if they want to take ten minutes on Dr. Austin. I would like a few minutes to -- just a few minutes to respond.

THE COURT: You will have a few minutes to respond.

MR. BECK: Okay.

THE COURT: You may.

MR. LOCKRIDGE: Thank you, Your Honor. It will be Mr. Black.

MR. BLACK: Your Honor, again I prepared a PowerPoint, but Mr. Arbitblit has anticipated many of the things I was going to address and I think if I could approach and just give you the paper copy and call the Court's attention to --

THE COURT: Do you have a copy for my law clerk too?

MR. BLACK: We will get a copy for your law clerk. In fact, you can take this one. I can do this from memory.

MR. BECK: Can I have one?

MR. BLACK: We do have a third copy.

While we're waiting for that, this is a point that relates to both Dr. Farquhar and Dr. Austin with regard to the coding and interpreting, the coding of the adverse event reporting data and Dr. Farquhar was accused of not understanding how it was coded.

Dr. Strom didn't know how it was coded either. This prominent pharmacoepidemiologist, the editor of the treatise of *Pharmacoepidemiology*, Bayer's expert, didn't know how the data was coded either.

As a matter of fact, he didn't know how to access it at his deposition. He said, oh, it was very difficult to

do that. You have to get all these -- put in a special request and get the disks. That wasn't true. You could buy the data for like a thousand dollars at the time. Now you can download it from the Internet for free.

Dr. Strom didn't know how to do that, didn't know how to access it, didn't know the beginning of how the coding was done. And yet he works with it because he works through assistants, just as Dr. Farquhar did. So I think that's the reddest of herrings.

The proportional reporting ratio, Mr. Beck made a big deal about the fact that Dr. Austin did a proportional reporting ratio analysis. Well, he did, but that wasn't the principal focus of his work and I think Mr. Arbitblit explained how that was some additional analysis we did that -- or had the experts do that corroborates the other work that they did.

The one point that I specifically want to address about Dr. Austin relates to this accusation that he somehow just made up the 30 percent figure to increase the relative risk. He didn't just make it up.

He explained very clearly in his report where the number came from and slide 28 in the PowerPoint that I prepared, which is I think page 14 of the handout because there were two slides per page, explains what he did.

The effect of misclassification of the cases, the

magnitude of that effect depends on what percentage of the cases are misclassified and what the actual relative risk is; and he showed that in a table in his report.

And then based on work that he had already done, correcting for duration -- and Bayer doesn't dispute his correction for duration of use. That's undisputed. He knew already that Baycol was the worst of the statins. The correction for duration, which he had done, which isn't disputed, established that Baycol was the worst of the statins.

And then he had also taken a look at the adverse event reporting data and that gave him some idea for a ballpark estimate of what the actual relative risk would be and he used that to come up with an estimate of 1.26 for the multiplier. So that's 26 percent.

And then he did exactly what Mr. Beck says scientists ought to do. He goes and he says, well, that's my hypothesis. Now how can I corroborate that? How can I check that out?

And he says, you know, in the PacifiCare study -- we're talking PacifiCare now, we're talking about his re-analysis of PacifiCare. He said they went and looked separately at those cases that were diagnosed in a hospital setting where you would think that the diagnosis is going to be more precise and accurate and so -- this was only done

for the rhabdomyolysis cases. This was a limited number of cases.

But he says, you know, if you compare the diagnosis in the hospital where it's going to be accurate, you won't get misdiagnosis and you compare that to the rhabdo cases that came from outside the hospital setting, why then you multiply by a factor of about 16 or 17, 16 or 17, not 1.3.

And then he said, well, given that magnitude of a correction factor, when I go and take a look at the data, it seems very, very conservative to me to use a correction factor of 1.3 or 30 percent.

So he tested his hypothesis. He verified it. He had an explanation for where it came from. It was not something just plucked out of the air.

And I would only add on that that Dr. Farquhar went and made the corrections that Dr. Posner, Bayer's in-house doctor, had suggested making and he came up with a higher correction to the PacifiCare report than Dr. Austin did.

Dr. Austin's corrections were conservatively low and they were well explained and they certainly weren't based on just assuming the result that he wanted and then reaching it, and that was the one point that I wanted to make sure that I hope I've clarified on Dr. Austin.

If the Court has any questions, I'd be happy to entertain them.

THE COURT: No. Thank you.

MR. BLACK: Thank you, Your Honor.

THE COURT: Thank you.

MR. BECK: Your Honor, let me -- I want to show a few things here, but while I'm doing that, just on the topics that Mr. Black just covered, on the coding and the AERs he said that, well, our famous Dr. Strom who wrote the book didn't know the codings for the AER system.

But, of course, our expert, Dr. Strom, wasn't trying to re-analyze the AERs and wasn't trying to do a meta-analysis and use the AERs for purposes that they should not be used. And so he had no occasion to try to get in and figure out what all the coding was about, unlike somebody who does purport to re-analyze the AERs.

And on this adjustment, the 30 percent adjustment that Mr. Black was just talking about where he said it wasn't just made up, it was interesting to listen to his description of the methodology, if he wants to call it that, used by their witness.

He said, well, he starts with the knowledge that Baycol is the most toxic and he also can look at the AERs and see a relationship there. So he's taken the AERs to adjust data in an epidemiological study.

And then he says, well, he went to the hospitalization data and he used this factor of 16 or 17 times. It so happens that that comes from gemfibrozil. So he's using data that comes from the situation where Baycol is used along with gemfibrozil.

And then he says I kind of put all that together and I put it on my forehead and I say 30 percent is conservative and that was the scientific methodology. It was not a computation of any sort. It was someone who, according to their lawyer, started with a presupposition and then set out to prove it and came up with a plug number that sure enough proved it.

Now, Your Honor, I have a few things I do want to cover.

On the AERs, none of the things that they showed you says that you can use AER data to make reliable comparative risk determinations from one drug to another. None of them said that and that's what they've used it for.

I want to look at a couple of the things that they showed you. This is from the FDA. They say this is, you know, the recent guidance from the FDA. In yellow is what Mr. Black -- I'm sorry. I think it was Mr. Arbitblit. I got lost. Whichever one -- it was Mr. -- whoever was talking about the AERs. And I apologize. They both covered some of the same stuff. Mr. Black.

Yellow is what he said is real important and he read, "Comparisons of reporting rates" -- and this comes from his slide 62 -- "Comparisons of reporting rates, particularly across similar products or across product classes prescribed for the same indication." So that's what he quoted. And then -- so he said the FDA blesses the use of this.

And then the FDA goes on in the green, which he left off his slide, to say, "However, such comparisons are subject to substantial limitations in interpretation because of the inherent uncertainties in the numerator and denominator used. As a result, FDA suggests that a comparison of two or more reporting rates be viewed with extreme caution and generally considered exploratory or hypothesis generating. Reporting rates can by no means be considered incidence rates for either absolute or comparative purposes."

And that's exactly what they've done by coming up with these relative reporting rates is they've used it the way that the FDA has said, again, you should not use it.

Then, Your Honor, they also showed you the Staffa letter to the editor several times and here this is -- I just did this a second ago, but the yellow is the sentence that this time it was Mr. Arbitblit reading.

And he said that when we quoted the yellow sentence we left out some of the phrases in our brief and he wanted you to look at the whole yellow sentence, which says, "The reporting rate is the number of fatal cases divided by the number of prescriptions dispensed and is a crude measure of the number of reports received by the FDA relative to the extent of the use of an agent in the U.S. population."

He said it's so important to put that last part in about the U.S. population and then he stops. And then the rest of the note in green says, "Rigorous comparisons between drugs that are based on these data are not recommended 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 incidence rates."

So, again, the Staffa letter has the same cautionary note about the use of AERs. And I should say, Your Honor, that Staffa, as with everything else they did, has to do with rhabdo, not with myalgia.

They referred to Psaty. That's an article written by experts being paid by the Plaintiffs' lawyers and they repeated the Plaintiffs' lawyers arguments. Again, it had to do with rhabdo, not myalgia.

They showed you a document that came from our files, somebody named Mr. Niemcryk. Let's see here. I'm

messing this up. They showed a table from Mr. Niemcryk and let me see if I can find what they showed. Here it is. They showed you this table and said, well, the folks inside Bayer did exactly the same thing that Dr. Farquhar did.

What they didn't show you, though, is what Mr. Niemcryk said about this kind of data, that they look at it to see whether there's a signal or not to see whether it should lead us to go out and do an epidemiological study.

And he cautions when he uses the data in the appropriate way. He says the interpretation of these data is not straightforward. Data from adverse event reporting can be heuristic, identifying potential relationships that should require further exploration. However, estimates of disproportionate risk cannot directly be generated by these reporting systems.

So of course what Mr. Niemcryk does is he acknowledges the limitations that the FDA keeps repeating, exactly the opposite of what their expert did.

Mr. Arbitblit mentioned that I said, gee, there are clinical trial data and then I forgot to talk about it in my opening remarks. Myalgia is what we're left with now and there is clinical trial data on myalgia.

All of the statin manufacturers reported the incidence of myalgia that occurred during the clinical trials that led to the approval of their statins. And what

happened was that -- and it's all in the labels for all of the different statins.

And in terms of absolute terms, how many people got myalgia per, you know, thousand patient-years or whatever, Baycol was the second lowest of all the statins. And in terms of comparing it to placebo, Baycol versus placebo was the second lowest of all of the statins when it came to myalgia.

And that's very important because the myalgia data -- almost everything that was shown to you has to do with rhabdo and then there was one little part where Mr. Arbitblit showed some data that had to do with myalgia.

All of that data was Baycol versus placebo. None of it, not one speck of the data that he showed you was Baycol versus other statins. Not one speck of data that he showed you or that's been identified by their experts says that there's any difference in terms of the reported myalgia from Baycol versus other statins.

And there's no study saying that there's a statistically significant difference between Baycol and other statins when it comes to what we're concerned about with the remaining 1,700 cases, not rhabdo, but myalgia.

And he had slide 21, Mr. Arbitblit, talking about myalgia and the language that he kind of glossed over that was on his slide said, quote, no data on the long-term group

with regard to myalgia is noted. So once again we get back to rhabdo, not myalgia, and again true in every single article that they showed you.

Mr. Ismail will discuss later this afternoon the mechanism question about whether this is all part of one continuum and how the argument they're making this morning contrasts with what they're saying in connection with some of their other experts.

Lastly, Your Honor, on PacifiCare, there was no -- they say the Posner recommended analysis. Dr. Posner of Bayer did not recommend the analyses that were done by their paid experts here years later. He did not suggest those calculations.

But what was interesting to me was they then segue from the PacifiCare to Graham and Cziraky and a whole series of other publications. And again, Your Honor, every single one of those had to do with rhabdo. None of them had to do with myalgia, which, as I said, was true for all of their articles.

Thank you for your indulgence here, Your Honor.

MR. ARBITBLIT: May I have one moment, Your Honor?

THE COURT: I'll give you one minute.

MR. ARBITBLIT: Can I just use this? Is that possible?

THE COURT: Yes.

MR. ARBITBLIT: Do I have to plug something in or do I have to push a button or call someone that knows?

MR. BECK: This counts against his time, right?

THE COURT: It does.

MR. ARBITBLIT: Phil, do you know how to do it?

MR. BECK: Yeah, I do. Dennis.

MR. ARBITBLIT: I just wanted to point out, Your Honor, that something I mentioned but didn't have time to show during the presentation was, in fact, myalgia in Dr. Farquhar's analysis. These are the adverse event data, but what he did was look at -- let me make sure I have got that --

THE COURT: You can touch the screen. It's a John Madden screen. No, not that screen, but the monitor.

MR. ARBITBLIT: Thank you. I wanted to make sure that the heading is correctly shown here. This is for myalgia alone using the same methodology with the caveats, and I think I was careful to say that the caveats do apply, but that the rates are so much higher that other explanations are not likely.

And what you see is that for every statin, including Lipitor, the one marketed closest in time, the IMS data relative reporting ratio for myalgia was statistically significantly greater at rates of 8, 7 times, 27 times, 9 times, 10.7 times, and a total of 8.5 for all statins the

myalgia rate was higher. I did mention that, but I didn't have a chance to show this document that's attached as Exhibit 9 -- Exhibit 8-B to Dr. Farquhar's supplemental rebuttal report.

Yes, over time it became apparent that myalgia was going to be a focus and so he said, well, since Dr. Strom mentions myalgia, I will go look at the data and see. Let the chips fall where they may. I will just use that term, I will tell Dr. Ahn on the same study using myalgia, and that's what it showed.

And as far as the clinical trial data, I didn't gloss over anything. They just didn't add anything to the data from those long-term studies, Your Honor. So the short-term studies give everything they have.

Thank you, Your Honor. I appreciate it.

THE COURT: All right. What's up next?

MR. ISMAIL: Your Honor, we have a collection of arguments based on five experts all geared to the muscle injury. We would like to take a break now. These are experts Boult, Mayer, Richman, Zizic, and Carlson that I would like to address for efficiency purposes in one argument.

THE COURT: Mr. Ismail, you're talking about, what, an hour?

MR. ISMAIL: Yes.

THE COURT: And response on that is going to be what?

MR. HOPPER: Your Honor, as Mr. Beck talked about or at least we did with Katie earlier, I have to leave here to catch a plane at 5:00. Mr. Arbitblit was going to go first on Dr. Richman after Tarek finishes and then if I can go again, if that's fine with you.

MR. ISMAIL: Sure.

MR. HOPPER: If that's acceptable to the Court.

THE COURT: How much time?

MR. HOPPER: I need about 20 minutes for each of those at the most.

MR. LOCKRIDGE: We would like about an hour and a half, I think, if we can, to respond to all of their experts -- all of their motions on the muscles, if we may, Your Honor.

MR. BECK: Your Honor, we have a few other motions. If they take more time than we do, I don't know if we are going to get through all the other ones today.

MR. LOCKRIDGE: My expert just told me an hour is fine anyway, Your Honor. So I guess we can live with an hour, Phil.

MR. HOPPER: You are taking an hour and a half?

MR. ISMAIL: I am taking one hour for five motions.

MR. HOPPER: We'll take one hour, Your Honor.

THE COURT: Do we need to break now?

COURT REPORTER: Yes.

THE COURT: The boss says yes. We'll take a 15-minute break.

(Recess taken at 2:35 p.m.)

* * * * *

(2:50 p.m.)

IN OPEN COURT

THE COURT: First off, congratulations, Counsel, for being named in the top 40 under 40.

MR. ISMAIL: Thank you, Your Honor. That's all I wanted to address today. Thank you.

Good afternoon, Your Honor. As I indicated before the break, I did want to take as a group the five experts and our related motions relating to muscle issues. As you saw from the briefing, there's considerable overlap both in the argument and the scientific data relied upon in support. So rather than repeat it five times, I thought we could do it all at once. And the experts again are Drs. Mayer, Richman, Boult, Carlson, and Zizic.

And what I want to address collectively is their opinion, which each give as their own opinion, that Baycol is the most toxic statin but not repeating the discussion we've had today, their opinions as to a statin myopathy that

is permanent that does not resolve upon discontinuation of the medicine, and lastly their opinions regarding the appropriate methodology by which you can diagnose a statin myopathy.

And if I have time at the end, I may -- there's a couple of straggler issues as to unique experts, and if I can get to those I will. Otherwise I'm happy to rest on the papers for those issues.

As I indicated, each of the experts that I just mentioned opine as their own opinion that Baycol was the most toxic statin. And whatever the Court resolves with regard to the appropriateness or not of adverse event data for that comparison, none of these experts by their own qualifications and experience pass Daubert muster to give that opinion in their own right.

And Mr. Arbitblit and Mr. Black to some extent gave a lengthy presentation of their view of the evidence on the comparative safety issue. None of that, other than the adverse event data, is relied upon by these five muscle experts.

And I'm going to play, Your Honor, just straight through some deposition testimony from Dr. Richman, Boult, and Carlson which shows the limited basis upon which these experts rely to give their opinion on Baycol.

"Are you aware of any data supporting the conclusion

that Baycol had a higher risk of myotoxicity other than spontaneous adverse event data?"

MR. ISMAIL: This is Dr. Richman, Your Honor.

"No, I'm not.

"Your opinion regarding the comparative muscle toxicity of Baycol versus the other statins is based entirely upon reporting rates of adverse events, correct, postmarket?

"Yes."

MR. ISMAIL: Dr. Carlson.

"Other than the medical articles that you cite in paragraph 8 and paragraph 46, do you have any other basis for the opinions that you set forth concerning the relative toxicity of Baycol versus other statins?

"Let me see which -- these are representative of the papers that I would have read that indicate a higher incidence of myopathology in Baycol treated patients.

"Okay. Do you know that many of these -- well, do you understand that all of these references in paragraph 8 and paragraph 46 are all based on analyses of spontaneous postmarketing adverse event reports?

"Yes, I am.

"You do understand that?

"Yes."

MR. ISMAIL: So what we have, Your Honor, is a group of experts that relied not upon the data that you

heard today presented by the attorneys, but rather solely on or in substantial part upon the spontaneous adverse event data.

I don't want to repeat our position on the unreliability of that data, but a threshold question under Daubert is one of qualifications and experience. An expert must pass that hurdle before questions of reliability and relevance get addressed.

And here none of these experts have in their professional or academic experience the qualifications that would allow them to utilize this data to give a comparative safety opinion.

Dr. Zizic is a rheumatologist. Dr. Mayer is a physical rehabilitation medicine specialist. Dr. Richman is a neurologist. Dr. Boult is a geriatrician. Dr. Carlson is a doctor specializing in physiology.

None have done any research on statins. None have ever written or studied or published in the area of comparative drug safety. None are epidemiologists or biostatisticians. And each have a lack of professional expertise utilizing this data.

First this is Dr. Mayer, one of the experts subject to our motion, and this is his testimony as to his experience.

"Have you ever made any analysis into spontaneous

adverse event reports associated with prescription drugs?

"That's a role of the FDA to do. That's not -- I'm not an FDA officer, obviously.

"Is the answer to my question, no, you have not?

"No, I have not."

MR. ISMAIL: Again Dr. Mayer.

"Would you agree that there are a number of potential biases that impact the relative reporting rates of spontaneous adverse events?

"Yes.

"Have you made any effort to assess the relative reporting rate of spontaneous adverse events with statins by controlling for biases that are part of the data?

"No.

"Have you in any context for any drug made any investigation into biases that affect adverse event reporting?

"No.

"Have you done a literature review, either in this case or for any other exercise, to determine what others have said about biases in spontaneous adverse event reporting?

"I have read commentaries and editorials, et cetera, about cerivastatin, but in terms of doing a formal review, no.

"Are you aware of any guidelines the FDA has put out

regarding whether spontaneous adverse event data can be used to show the relative safety profile of drugs?

"I'm not aware of that.

"Prior to your expert report in this case, have you ever written a safety assessment of a drug based on its spontaneous adverse event rate?

"No."

MR. ISMAIL: Your Honor, we went through the caveats document and the Plaintiffs reference some guidelines of the FDA and the proper use of this data, and we have debated today whether those guidelines and caveats preclude or not the use of the data.

But here we have an expert who bases his opinion on that data and is not even aware of the guidelines put forth by the FDA or the debate that we have already had today regarding the FDA's commentaries about how to use its own data.

Dr. Richman has similar gaps in his professional experience. This is his testimony.

"My question was: You are not an expert in how to use the FDA's adverse event database to compare the safety of drugs in a class, correct?

"I think I'm a reasonable expert for this.

"You've never done it before, have you, Doctor?

"No."

MR. ISMAIL: So here we have a doctor who has never done the analysis that he did in this litigation and he considers himself expert enough to do the analysis.

And the case law has commented on this question of qualifications, that the court need not accept an expert's say-so that he is qualified to do an analysis for the purposes of litigation and instead the case law requires the court and the parties to go further and see whether, in fact, the expert does have a background that is relevant.

And the cases talk about does an expert -- is his opinion in litigation a natural progression or outgrowth of the work that he or she has done outside the litigation, is he doing outside the courtroom what he purports to be an expert in inside the courtroom.

And Dr. Richman wants the Court to accept him as an expert in epidemiology and comparative safety analyses, but by his own admission he's never done it before being retained as an expert in this case.

One more clip from Dr. Richman on the same point, Your Honor.

"How did Dr. Staffa calculate the number of cases of fatal rhabdomyolysis?

"From the adverse event reporting mechanism.

"Do you know what the general scientifically accepted methodology is for using the FDA's spontaneous database to

make comparisons between drugs in a class?

"This would seem to be a very good one.

"Is that the first one you've read?

"Yes.

"Have you ever read a text on pharmacoepidemiology?

"No, I haven't."

MR. ISMAIL: Again, Your Honor, we have an expert who wants to rely for his opinion on Dr. Staffa's letter and he wants to give the opinion that it's a good analysis for the purposes of comparative safety determinations and yet, as you just saw, that's the first one he's ever read before.

He does not have the qualifications to enable him, just as the other muscle experts do not have the professional experience that enable them, to make comparisons between Baycol and the rest of the statin class.

And the Plaintiffs' response to this -- and let me show, Your Honor, the opposition on Dr. Carlson's motion. So this is the Plaintiffs' memorandum in opposition to our motion on Dr. Carlson.

And on this question of Dr. Carlson's lack of expertise they write, No one can be an expert in all areas. Such a rule would ignore the modern realities of medical specialization, quoting from cases that have been cited by both parties in this case.

And continuing on to the next paragraph, they go

on to describe how, gee, in medical science doctors and scientists often collaborate to reach a sort of joint effort with respect to conclusions that they're coming to in their research.

And we agree that witnesses cannot be expected to be experts in everything, but the consequence of that is not to excuse their lack of experience on the question of qualifications.

The Steering Committee wants to take Dr. Carlson's and Dr. Mayer's and Dr. Richman's lack of expertise as an excuse for their lack of qualifications under Daubert. The cases that they're citing here excluded the testimony of the experts because they were not qualified.

So to say that, gee whiz, you can't expect everyone to be an expert in everything, that is true, but the consequence is not that therefore we don't examine their qualifications. The consequence is that the opinions and the experts are excluded as to those issues in which they're not qualified to render opinions.

And that is the fundamental disagreement here as to these experts who admittedly do not bring to this courtroom their professional and academic expertise on the question of comparative drug safety, but instead want to do it here for the first time.

And just briefly, Your Honor, Drs. Mayer and

Zizic, two other experts on this comparative safety, in addition to relying upon the adverse event data purported to give an opinion on pharmacology.

And just to refer the Court here to testimony that we cited in our brief, this is Dr. Mayer's deposition and -- Dr. Mayer in his deposition and I believe in his report, if you look there, beginning at line 15.

"You pointed me to, for example, bioavailability as support for the testimony that Baycol was more dangerous, correct?

"Yes.

"You're not aware of any study making that connection, correct?"

He goes on to say, "I said I couldn't cite a specific study making that connection because that's not my area of expertise that I focused on in my review for this report."

And then continuing on, we get to the nub of it with Dr. Mayer at page 263, line 10.

"Is it fair to say, Dr. Mayer, that you are not qualified to give statements about comparative safety based upon a drug's bioavailability?

"That is fair to say."

So here we have a witness who by his own admission is not qualified on his own expertise to give an opinion about comparative safety based on pharmacology grounds, just

as he is not qualified on adverse event grounds to give comparative safety opinions.

Dr. Zizic, and I won't take the time here to show the testimony, but there's a lengthy passage which we cite in our papers in which he disclaims prior experience as a pharmacologist, prior research or publications on statin pharmacology.

And, again, he doesn't come here as an expert in pharmacology. He's a rheumatologist. And he cannot bootstrap his opinion on comparative drug safety by for the first time in this court becoming an expert in pharmacology and rendering opinions that he say support his fundamental opinion that Baycol is the most toxic statin.

Now, Your Honor, I wanted to turn to the second topic, unless the Court had areas you wanted me to address there --

THE COURT: Go ahead.

MR. ISMAIL: -- and that is this question of permanent injury.

And I'm sort of in an odd situation here because Mr. Arbitblit about an hour ago stood here and said we're not claiming in this litigation that a patient can have -- a patient who does not have a demonstrated increase in CK can have a permanent muscle related injury.

And that is contrary to a vigorous debate in the

papers that had been submitted to this Court under the Daubert analysis and what their own experts have said in their depositions and reports themselves.

And so the question is: Is there a permanent myopathy in which a patient can have muscle symptoms persist after discontinuation of the statin even in the absence of an elevated CK?

And on that question, Your Honor, here we are through Phase -- or in the middle of Phase III and IV in discovery where we're getting case-specific expert reports. We have patients today in this MDL claiming that they've never had rhabdomyolysis, they don't have an elevated CK, and they're claiming in 2006 and 2007 a permanent injury. And so -- Baycol has been off the market for five years.

And so what we have is a concession, so to speak, from the Plaintiffs that we're not claiming that those injuries exist and yet we have experts in this case, including the experts the PSC has brought, claiming that there is this permanent class of myopathy for patients who do not have an elevated CK.

So I don't want to convince the Plaintiffs that they're advancing a position that they're really not and I'm not trying to create an opinion that they're disclaiming here before the Court, but we're here on an MDL-wide Daubert analysis and we're mindful of the fact that these cases may

be remanded for trial and we have expert reports and expert depositions from these five individuals who are describing a permanent injury even in the absence of an elevated CK.

And so what we think is appropriate to address here, notwithstanding the comment this morning or this afternoon, is to show the Court that there is no basis in science for an opinion that there's this permanent injury absent an elevated CK.

And just to go to the point that I was making, Your Honor, their own experts comment -- this is Dr. Richman.

"If a patient presents to you with normal CK and complaints of muscle pain and weakness and they're also taking a statin, okay, and you remove the statin and the pain and weakness do not go away, does that tell you anything about the likelihood that the statin is causing the patient's muscle problems?"

Dr. Richman says, "No."

And there's other examples in reports and in the briefing here that the Plaintiffs have submitted that they're holding out hope that there's this type of disease that's a statin myopathy that does not involve an elevation of CK that can be permanent after discontinuation of the statin. And that's what we're attacking here on Daubert grounds. It is that opinion that we're seeking to exclude

as unreliable and not recognized in medical science.

And I have other examples I was just jotting down while Plaintiffs were finishing their discussion of Dr. Farquhar. It's in their opposition to Drs. Boult, Mayer, Dr. Richman where they have briefed before this Court that there is a permanent statin myopathy, not a permanent rhabdomyolysis. They specifically want this Court to accept that there's a permanent statin myopathy, and that is what we're attacking here.

And I would like to begin, Your Honor, with a discussion of the Leathers case, which is what was briefly mentioned this afternoon by counsel. Your Honor, we have -- this is a case that came up out of the Northern District of Georgia in 2006. It is a claim by a former Lipitor patient for a permanent myopathy in the absence of elevated CK.

So it's the same class of drugs, it's the same alleged injury, and it's the same motion that we have brought here and that opinion was challenged under Daubert grounds by the manufacturer of Lipitor in that case.

And the Plaintiffs have tried to distinguish the Leathers case under various grounds and this is their opposition to Dr. Zizic -- excuse me -- their opposition to our motion on Dr. Zizic.

And I'm going to go through each of these purported areas to distinguish the Leathers case, but none

of them is what counsel said this afternoon is the principal distinguishing feature and that is somehow the plaintiff in Leathers was alleging an injury that they're not alleging here. That's not what they told the Court in their papers.

So I'll be addressing what they actually submitted here and what their experts have said to make sure that in this MDL-wide Daubert proceeding we do get what we believe is the focus on this statin -- permanent statin injury that they've alleged up until today.

And what they alleged here to distinguish the Leathers case, first of all, they say the court in Leathers found the expert was not qualified. That's one of their points to distinguish the Leathers case.

And to the contrary, the court in Leathers found -- although the court had reservations about the plaintiff's expert there, the court specifically found the expert at issue in the Leathers case was qualified on the area of myopathy and permanent injury.

So the first point to distinguish Leathers is not true, that the Leathers court did accept that expert as qualified.

The second ground that they've raised to distinguish Leathers is that the plaintiff there did not address general causation, and that also is not true. The court found that the expert submitted articles and argument

in support of his specific causation opinion and the court took that reasoning as their support for general causation. So the court specifically addressed general causation in the context of a proffered opinion, which is exactly what we're seeking to have this Court do here.

Now, the third ground that they have brought or have alleged to distinguish Leathers is that the manufacturer of Lipitor has not challenged -- has challenged general causation; whereas, Bayer has not. And that also is not true.

And in the Leathers case the court noted defendants freely admit that physicians have long been aware of certain muscle related adverse events that have been associated with statin drugs, quoting from the defendant's submissions to that court.

So there is no difference because it has long been the case, as Bayer has long recognized and warned of, that certain muscle related adverse events have been reported and are associated with all statins, including Baycol.

There's no point of disagreement or distinction between what Bayer has conceded, if you want to use that term, and what the manufacturer of Lipitor did in the Leathers case.

And the last point that they made to distinguish Leathers is that, well, that drug -- that case involved

Lipitor, this case involves Baycol, and you should disregard the Leathers opinion because of that simple distinction.

Your Honor, that's also a false distinction and the reason is this. Each of these experts that I'll be talking about relies on non-Baycol statin literature in support of their permanent myopathy opinion.

There's the Phillips article. I'll be getting to each of these articles in detail, but they are in every one of the briefs. Your Honor has seen them. Phillips, Hildebrand, Argov, all these literature that they say support their Baycol opinion is based in whole or in part on other statin research.

And their clinical experience that they keep talking about in support of their motions, very few of them and some of them had no experience with Baycol-induced rhabdomyolysis, but they had experience with other statin-induced rhabdomyolysis.

So the PSC cannot have it both ways. They cannot cite to this Court non-Baycol statin literature in support of the permanency opinion and at the same time say this Court should ignore Leathers because it involved a non-Baycol statin. Either the research is supportive because the opinion is the same or it's not.

And so they bring to this Court these non-Baycol medical articles but want this Court to ignore the

non-Baycol case law, and we believe that is just an illogical and unsupported position to take.

So now that I have gone through the areas that I found that they have tried to distinguish Leathers, the holding which the court reached in the Leathers case is aptly stated in this called-out section of the opinion:

The 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.

That is the holding of this court after it went through the purported scientific support for the plaintiff's general causation and specific causation opinion in the Leathers case.

We understand that the Leathers case is a district court holding not binding here, but I will go through, Your Honor, why we believe that opinion is correct and the similarities between the evidence presented here and that which was at issue in the Leathers court.

Baycol, Your Honor, was a medicine that was used by some 6 million patients worldwide. The Plaintiffs have not cited to this Court a single report of a permanent muscle injury from a patient who did not have an elevated CK or other objective indicia of serious muscle disease, none,

not a report in a clinical trial, not a report of a patient in an epidemiological study, not one of these adverse event reports that they have relied upon to such great extent in this litigation.

Nor have they cited any such report for any of the other statins either, and that's -- those are a class of medicines that have been used by greatly in excess of 6 million patients worldwide and yet there is no report of such a patient in the medical literature.

And it's not just our say-so, Your Honor. This is what their own experts have admitted. First is Dr. Carlson.

"Are you aware of any case reports that document a muscle function impairment more than six months after the acute statin-induced injury has resolved?

"Most of them have been more short term in terms of the frame of reference. And, again, I don't know whether these reports would indicate that complete resolution has occurred or if they just didn't go any further.

"Okay. So are you aware of any studies that document impairment of muscle function after statin-associated injury greater than six months after discontinuation?

"No, if you use the six months, I'm not aware of any."

MR. ISMAIL: Dr. Richman.

"Are you aware, sir, of a single article describing a

patient having normal CK and have muscle symptoms persist following discontinuation of the statin?

"Not that I can come up with right now, but it doesn't seem as an impossibility.

"Are you aware of a single article describing the possibility that a patient with normal CK can have muscle pain or weakness persist following discontinuation of the statin?

"No, I'm not aware of any article that does that --

"Have you --

" -- that states that. But in terms of my own opinion, I could conceive of circumstances where it would be a very significant possibility.

"Have you ever treated a patient in your clinical practice who had normal CK and had muscle symptoms persist following discontinuation of the statin?

"I actually want to go back just one second. I mean, it relates to sort of the very first things we talked about in my testimony, that the CK level depends on the timing, of course, and that's always the proviso that I, you know, would want to put in there. But in terms of a patient that I've taken care of that was taking statins, had muscle symptoms, normal CK, and then the statin was discontinued and the symptoms continued, no, I haven't treated a patient like that."

MR. ISMAIL: Dr. Mayer.

"Are you aware of any medical literature that would support the notion that in patients with normal CK during the statin use, that muscle symptoms can persist following discontinuation of the statin?

"I'm not aware of any literature that states that."

"Now, Dr. Mayer, are you aware of any medical research that would support the notion that a patient with normal CK can have muscle symptoms persist after the discontinuation of a statin?

"I don't know that anybody has studied that at this point.

"So you're not aware of any such research?

"That's correct."

MR. ISMAIL: I want to show now, Your Honor, to show the juxtapose, what was at issue in Leathers to what the Plaintiffs' own experts have testified here.

So this is Dr. Mayer's testimony that I just showed you the video clip of, Your Honor, and the question was aware of any medical research that would support the notion that normal CK -- a patient with normal CK can have muscle symptoms persist. And the question had to do with statins in general, that there's no statin related research, let alone Baycol specific research, on this point. And he acknowledges that there is no such medical research out

there.

If I can manage to do this, Your Honor, I want to put to that side Dr. Mayer -- and you saw similar citations from the other experts I just showed you -- with the opinion in Leathers.

So this is the district court's opinion in the Leathers case and the district court is citing Dr. Firth, the expert who was at issue in that case and giving the same opinion that we're seeking to exclude in this litigation. And what was significant to the Leathers court is remarkably similar testimony to what Dr. Mayer and Dr. Richman and Dr. Carlson just gave.

"Are you aware of any peer review studies or reports that would show with any kind of statistical reliance that people who take Lipitor who have no CPK elevations and have muscle pain and weakness have a continuing disability --

"No.

"-- for myopathy after, you know, months or years?

"I've seen no studies that address that."

This is the basis for the district court's exclusion of this opinion in Leathers. And, of course, Dr. Mayer gave remarkably similar testimony here, as did the testimony of the other experts I just showed you.

So we have as a basic proposition the Plaintiffs' own experts acknowledging an absence of medical research or

literature in support of this myopathy permanent injury opinion.

So each expert has gone out and has pulled up medical articles that they say are support for the permanent injury hypothesis and each of the articles -- experts rely on an article by Dr. Phillips, who at one time was a Plaintiffs' expert in this litigation and was dropped before his deposition. But for the purposes of this permanency opinion, they talked about this article as support for this idea of a permanent injury.

And what Dr. Phillips actually says -- back up one second. This is a case study of four patients, only one of whom had ever taken Baycol. So then going back to my comment about it's a false distinction with the Leathers case to say that, gee, that involved Lipitor and here we're talking about Baycol, they're relying on the Phillips article even though most of the patients there were not taking Baycol.

But in any event, so we had four case reports, case studies in the Phillips article and there was no elevation of CK. And Dr. Phillips said, well, these patients had subjective reports of pain and weakness and I biopsied them and I found some objective evidence of myopathy.

But as to this question of permanency,

Dr. Phillips noted these patients -- these symptoms normalized when the patients received a placebo and the pathologic abnormality, so the biopsy study, reversed upon discontinuation of statin therapy.

So here we have one of the articles they're relying upon where in point of fact every one of the patients had their symptoms resolve upon discontinuation of the statin.

The Hildebrand article, which at first was an abstract when we deposed all these individuals a couple of years ago and has since been published as an article, the Court has been provided by both sides the actual final article.

Hildebrand was a study of 45 patients, again, the majority of whom never took Baycol but other statins, but nevertheless they rely upon it for their permanency opinion in this case.

In Hildebrand, of the 45 patients studied, patients with statin-associated myopathy experienced full resolution of muscle pain on cessation of statin therapy.

And Dr. Zizic, one of the experts of the Plaintiffs here, admitted as much in his deposition. That (indicating) is not Dr. Zizic's deposition, but that (indicating) is.

So down here he is asked, "So, again" -- and this is after some questioning where Dr. Zizic identifies the Hildebrand study as support for the permanent myopathy theory.

"So, again, Hildebrand, because we do not know, provides no evidence that you can have prolonged statin therapy leading to permanent muscle damage or progressive myopathy in patients with normal creatine kinase levels?"

I apologize, Your Honor, I lost -- oh, there it is.

"THE WITNESS: Correct."

So there's the answer to the question I just showed. Dr. Zizic acknowledges that the Hildebrand study does not support the permanent myopathy theory for patients who do not have a demonstrated elevation in CK.

The England study, which is another piece of literature each of their experts relies upon, it's, as you can see from the title, the study of Zocor and Pravachol, again non-Baycol statins -- and these are 15 patients -- a study of their claims of muscle pain and weakness.

And as to these patients, all symptoms and signs resolved on cessation of the drugs and then reoccurred in patients who were rechallenged, which means the symptoms came back when they were again given the statin.

And this is the material that they cite in their

reports and their depositions in support of the permanent myopathy theory and what I want to show, Your Honor -- so we have seen three examples of literature that they are relying upon in which, contrary to the assertions of the Plaintiffs and their experts, every single patient had a resolution of symptoms after they were removed from the medicine.

And so going back to the Leathers case, so here is the court's analysis in Leathers. So the court is now analyzing the medical articles submitted in support of the permanent myopathy theory and the court notes, well, in the very articles that you're submitting here in support of your opinions we see things like symptoms resolve completely upon statin discontinuation or repeated muscle biopsy performed three months after discontinuation of statin therapy revealed complete resolution.

And interestingly here, Your Honor, the court is talking about the Phillips article. You can see that by actually going to Phillips itself. So here the court is saying in the very articles you're citing here, all the patients resolved.

And if you look at the quotes, interestingly, the court is talking about Dr. Phillips' observation of his own patients. So here we have the patient's muscle symptoms and hip weakness improved three months after she discontinued statin therapy, repeated muscle biopsy performed three

months after discontinuation of statin therapy revealed complete resolution of the abnormal lipid stores.

Each of these patients studied in the Phillips report had complete resolution of the statin myopathy, the very same observations the Leathers court found in support of its opinion to preclude the opinion.

And the PSC's response to all of this is, well, gee, the Phillips article and the Hildebrand article and all the other citations that we have in support of our theory, even though all the patients resolved, had their symptoms resolve, it's actually not inconsistent with our theory for various reasons.

And so here (indicating) this is I believe Dr. Boult's opposition and he is talking about the Hildebrand article, which we just showed. There's nothing in this report to contradict Dr. Boult's opinion.

The PSC has -- the burden here is upside down. They've cited these articles in support of the permanent myopathy opinion and none of them, not one, did the patients have a permanent myopathy.

And they say, well, we can distinguish our own articles and say that it's not fatal to our opinion, but that's beside the point because they have the burden to support their theory here.

And the fact that every single patient in these

articles who had normal CK had a resolution of the symptoms is fatal to their claim that there's a reliable basis in medical science in support of a permanent myopathy theory, the same way the Leathers court found similar admissions in the articles there to be supportive of the preclusion of the opinion.

Since the depositions were taken, Your Honor, additional articles have come out. The PSC has described them in their briefs. I'll note that none of their experts submitted supplemental declarations relying upon these articles.

And if these new articles really were the saving grace for their opinions here, one might expect that we would see a supplemental expert report relying on these medical articles.

And the reason why we don't is because they're just like all the others with respect to this permanent myopathy and, in fact, none of them support the theory that's advanced.

In the interest of time I will just show a couple of them. One of them is this article called -- written by a Dr. Dobkin. This is an article that apparently came out after their experts were deposed and submitted reports. And this is a study of 18 patients. None were taking Baycol. And each of their -- and, again, these are articles they

identify as support for their permanent myopathy opinion.

By three months off statin all -- they're talking about all 18 patients -- recovered 5/5, which is the measurement of strength there in that case. By three months off statin all recovered 5/5 proximal strength, again noting that each of the patients in that study fully recovered from the statin -- the alleged statin myopathy.

And I'm not going to go now, Your Honor, to each of these articles. We've distinguished them in our papers. Actually not even distinguished them. We embrace them in our papers because the patients there did not suffer permanent myopathy, those who had normal CK or other -- absent other indicia, objective indicia, of a muscle injury.

So here we don't have any clinical data in support. The very research they cite to this Court demonstrates the opposite of the conclusion they want the Court to reach. And their experts have admitted that they haven't found such a patient in the medical literature that they're advancing as a theory in this case.

And for all those reasons we believe the Leathers court got it right and for reasons that are remarkably similar to the way the record has developed in this case.

Your Honor, I wanted to turn to the third topic, which was the question of diagnosis, absent any issues you

wanted to me to address on --

THE COURT: Go ahead.

MR. ISMAIL: -- the permanency.

Several of the Plaintiffs' experts have given opinions in the context of general causation on what it would take to diagnose a statin-induced myopathy, and I want to take these together because I believe they suffer from the same methodological flaws amongst them.

And I'm talking now about Dr. Richman's retrospective diagnosis opinion, Dr. Boult's clinical criteria that he outlined in his expert report for how to diagnose a myopathy.

And it applies to the other experts as well to the extent Dr. Carlson and Dr. Zizic, they hint at a diagnostic criteria, although they don't spell it out in their reports like the others do, but the opinion, whether shared by all of them or not, is what we're seeking to exclude here under Daubert.

All the studies that they have talked about, the Phillips, the Hildebrand, the Dobkin, begin as their starting point an affirmative diagnosis of myopathy. All those studies begin with some contemporaneous objective indicia of myopathy, not vague reports of aches and pains analyzed months later. We're talking CPK elevations, EMGs, electromyograms, muscle biopsy, quantitative strength

testing, objective criteria to diagnose a myopathy.

And that's what the medical profession has identified as the only reliable basis upon which to diagnose a statin-induced myopathy. A couple of the experts have come up with alternatives.

This is Dr. Boult, his expert report. So up here in his expert report he acknowledges that typically there's objective indicia of myopathy, CK increase or EMG, the electromyogram, or abnormal biopsy results.

But then he goes on in his report to say even without these objective findings, the presence of moderate cerivastatin-induced myopathy can be deduced in persons meeting three clinical criteria.

So we are now deducing a myopathy after the fact absent objective evidence that a myopathy actually exists and we're talking about subjective reports of pain or weakness, a temporal association. And this third point is interesting in light of counsel's comment this afternoon.

So the predicate here, we have patients who have no objective evidence of a myopathy and Dr. Boult is saying, well, you can still diagnose a statin myopathy if you can show these three factors.

The third one is the symptoms either diminish or persist. So we have patients who don't have a demonstrated elevation of CK and Dr. Boult is saying you can still

diagnose a myopathy even if the symptoms persist, which is not what I heard from counsel this afternoon as to what they're claiming in this MDL, but instead is what Dr. Boult is asserting is a diagnostic criteria.

So Dr. Boult is asked in his deposition, now that he has staked out this opinion, Can you show me where your criteria are used in the medical literature to deduce a statin-induced myopathy? He answers, No.

Then he's asked, and I am going to show this longer passage from his deposition, why it is that this clinical criteria that he's advancing in this litigation does not appear in the medical literature.

"What was the purpose of you coming up with your three criteria?

"Yeah, just very briefly, to create some guidance for clinicians in being able to determine whether a person has moderate to severe statin-induced myopathy.

"Have you communicated your criteria to any other treating physician?

"No. It's all stayed within this context here.

"Well, how is it going to be useful to other physicians if you don't communicate it?

"It's a process, you know, it's -- in the future it may be useful to other clinicians. Right now I haven't submitted it for publication and I wouldn't because I

haven't gone through the rigorous process that I mentioned to you. This is a first step, you write it down, you put together the evidence as best that the evidence seems to indicate, and then you get perspectives from other people. And once you've debated it all out, then you submit it for publication. This is too preliminary."

MR. ISMAIL: So Dr. Boult states that the clinical criteria in his expert report is too preliminary to be subject to publication in a medical journal, which, of course, is one of the questions, again, under Daubert, has the clinical -- has the opinion been accepted, generally accepted, has it been subject to peer review. He doesn't think it's even firm enough to be put through a peer review, let alone pass peer review.

And there's a comment from Judge Posner, I believe, that the law should not lead science. Instead it should lag it. And that passage has been cited in this circuit and others as one of the things to consider under Daubert.

And here we have an expert who wants to give his opinion a test run here. It's too preliminary for other doctors and for publication, but he thinks it's good enough to bring here because he wants to air it out and get some views from others.

That's the opposite of what should happen under

the Daubert analysis. The opinion must reach general acceptance before it's submitted to a jury to give a basis for a verdict, not the opposite. You don't put it through a test run here, see how it does, and then go publish it in an article later.

Now, Dr. Richman -- I'm not exactly really sure where Dr. Richman ended up with his diagnosis opinion. We describe in length in our motion that he talked about in his deposition this concept of retrospective diagnosis of rhabdomyolysis, and the Plaintiffs respond that Dr. Richman did not mean for his testimony to be so interpreted.

This is their opposition on Dr. Richman where he is talking about retrospective diagnosis of rhabdomyolysis even in the absence of an elevation of CK and acknowledging that he did testify to that at his deposition in response to questioning.

But then they say here that Dr. Richman intended his, I guess, future testimony to be interpreted that in the absence of a timely CK level measurement, a retrospective diagnosis could be made on the basis of some combination of the factors in the constellation of symptoms he described.

Whether it's exclusively upon one factor or on a constellation of factors, we've cited to the Court where Dr. Richman has admitted this concept of retrospective diagnosis of rhabdomyolysis he's never seen before in the

literature, he's never seen that phrase before, he's never written about that concept before his expert report in this case.

So whether it's on one factor or on three factors, the point of the matter is this is something that he has come up with for the first time in this litigation rather than something that has been put through and accepted by the scientific community.

I'll point out as well, Your Honor, that this -- well, I guess in the interest of time I will move on rather than show the clip, but we have shown the Court other examples from Plaintiffs' own experts.

THE COURT: Let's see the clip.

MR. ISMAIL: This is Dr. Mayer, Your Honor. We are talking again about this question of diagnosis and Dr. Mayer has given an opinion -- I'm going to show you Dr. Mayer talking about what it takes to diagnose muscle cell destruction, myopathy, in a patient.

"In terms of being able to affirmatively diagnose muscle cell destruction in a patient, you need to do one of four things, either test for elevated CK, do a biopsy, do an EMG, or do a quantitative strength test; is that correct?

"Those are probably the four primary ways we could diagnose it, yes.

"Is there another way?

"I think those are probably the four best ways of diagnosing muscle disease, yes.

"Is there another way?

"Not that I can think of off the top of my head."

MR. ISMAIL: So this is Plaintiffs' proffered expert on muscle diseases stating as his opinion there are only four generally accepted ways to diagnose a myopathy and they're all contemporaneous objective criteria, not retrospective diagnoses, not can we deduce it from the presence of three clinical factors, none of which have been accepted in the medical literature.

And to the extent that Dr. Richman and Dr. Boult and others are suggesting a different criteria for diagnosing a statin myopathy, it is inconsistent with the generally accepted view in medical science.

Your Honor, on the question of mechanism, which I will turn to next, there's this question of -- first of all, the Plaintiffs have stated that, gee, none of their experts have postulated different mechanisms that work for statin injuries.

And this is Dr. Richman's deposition and he's asked, Do statins cause a muscle injury that -- sorry that the photocopy is faded here -- that does not involve muscle cell death? As the Court is aware, the hallmark of rhabdomyolysis is death of skeletal muscle and the spilling

of its contents in the blood. And he's asked, Do statins cause a muscle injury that does not involve muscle cell death? And he says, Yes, without question.

And Dr. Zizic similarly is asked in his deposition, It is your opinion that you can have myalgia in the absence of cell death, muscle cell death? And he says, Certainly.

So getting -- not to again repeat much of the discussion this morning, but you have this syndrome of rhabdomyolysis, which as its definition is muscle cell death, and then you have experts saying, well, you can have a statin-induced injury that is not muscle cell death.

And so the question of whether you can use analyses of rhabdomyolysis to give the opinion of the lesser injury of myalgia, pain and weakness, their own experts are saying we believe that there's this syndrome out there that does not involve death of skeletal muscle.

And they can call it a continuum in terms of severity, but by their own admission there's no generally accepted view on how statins cause myopathy or rhabdomyolysis. They acknowledge that there's not a generally accepted view on mechanism.

So how can they say that there is a single mechanism that would account for muscle cell death injuries and nonmuscle cell death injuries when they don't know what

mechanism is causing either of them?

But the point of the matter is it is a different endpoint, one that is not indicated by a death of skeletal muscle. And that's the point that we've made in our comparative safety challenge.

And I know Mr. Beck put as a placeholder that I would comment here on this question of what's the mechanism for myopathy. They acknowledge that there is no generally accepted mechanism of myopathy, but they also acknowledge and it's their position in this litigation that there is a syndrome of muscle disease that is indicated by death of skeletal muscle and they believe there's a syndrome of myopathy in which there's no death of skeletal muscle. And that's the point that we've been making.

And, Your Honor, as to mechanism, Dr. Richman in his report and his deposition stated that he believes that Baycol is more likely to enter the cell membrane. There's a long discussion of that in the papers. Dr. Richman has expressed that opinion. Dr. Zizic has expressed that opinion, I believe.

And I just wanted to point out on this question of mechanism what it is that we're talking about. Dr. Richman says -- what he says in his report -- excuse me. I meant to show the Plaintiffs' opposition here.

So this is their own papers on Dr. Richman. It

says, Dr. Richman discussed in detail his opinion that Baycol affects cell membranes differently from other statins and the basis for that opinion.

Question: By whatever mechanism statins injure muscle is true for all statins, correct?

And he says, I can't agree with that statement.

And then he says, At the very simplest level, the ability of statins to get into the muscle cells differ and Baycol being the most effective in getting into the muscle.

So he is now coming up with this pharmacology opinion on mechanism. Well, the Plaintiffs promised that he would explain in detail his opinion and all he did was say -- point to an article by Dr. Davidson and the sole basis for Dr. Richman's opinion is the statement the myotoxic potential of statins may not be a class effect and he takes that one clause and he shoves it into a mechanism opinion.

And he's asked at his deposition to confirm that, contrary to his supposition. Can we agree that Dr. Davidson does not describe a muscle injury unique to Baycol? First he goes back and reviews the article again. Yes, I would agree with that, he says, but I think you still have to keep in consideration the fact that muscle cell death is an endpoint which you can get through different pathways.

So he has come up with a mechanism opinion in

this case, Dr. Richman, on the basis of an article in which there's absolutely no discussion of that point.

And we get back to what is at work here on Dr. Richman's opinion and others, and that's the classic exclusion of the say-so of an expert. The analytical *ipse dixit* of the expert is not a sufficient basis to admit the opinion as a reliable and accepted opinion in the published medical research or really a permissible leap from the existing theories that are out there.

Your Honor, my light has flashed and I will stop here.

THE COURT: How much more do you have?

MR. ISMAIL: Well, I was going to point out and just direct the Court to some other issues and that is we --

THE COURT: Because this is a very important area, I want both sides to cover this area thoroughly.

MR. ISMAIL: I have finished my discussion of the muscle issues. But as to these experts, and I won't take the time to argue it, we've pointed out that some of these experts give ethics, state of mind opinions. And I'm happy to address that case law in connection with Dr. Raskin and others --

THE COURT: All right.

MR. ISMAIL: -- but I wanted to make sure that's pointed out.

And we also point out that Dr. Boult has come up with a labeling opinion in his deposition and we point out where he disclaims any professional expertise on labeling to enable him to give such an opinion.

Those are not common across the five and I don't intend to take up more time today, but wanted to point them out. Thank you, Your Honor.

THE COURT: Can we just take a stretch break?

(Recess taken at 3:55 p.m.)

* * * * *

(4:00 p.m.)

IN OPEN COURT

THE COURT: Let's continue.

MR. ARBITBLIT: Your Honor, with your permission, since Mr. Hopper has to travel and I'm going to be doing some lengthy presentation as part of the response to Mr. Ismail, with the Court's permission I would like to take just about five minutes to quickly respond to some of the points and try to narrow whatever issues the Court needs to address on a global basis for the experts and then allow Mr. Hopper to address his specifically and then come back to Dr. Richman, for whom I'm principally responsible. It's a little confusing and I would rather not do it that way, and we won't if you think it's too confusing.

THE COURT: Let's have Mr. Hopper go.

MR. ARBITBLIT: Thank you, Your Honor.

THE COURT: And then you will have a chance to respond.

MR. ARBITBLIT: Thank you.

MR. HOPPER: Good afternoon, Your Honor. I realize it's getting late in the day. Not to take anything away from my brother, his accolades and his accomplishments, it would be just tremendous just to note --

THE COURT: You are always a star in my --

MR. HOPPER: To get some congratulations for making it to 50, Your Honor, would just be wonderful --

THE COURT: Congratulations.

MR. HOPPER: -- after all this.

And also in the interest of time, Your Honor --

THE COURT: So you'll know how I feel later on this year when I make it to 60.

MR. HOPPER: And I have great respect.

And in the interest of time, Your Honor -- I appreciate you working with the PSC on the schedule -- I'm not going to use the PowerPoints, but I would like to hand them up and you can look at them now or later.

As Your Honor knows, I'll be defending against Bayer's challenge to Dr. Chad Boult to exclude his testimony as an expert witness for the PSC. Your Honor, Dr. Boult's testimony comes squarely within the ambit of

Rule 702 and more than satisfies the standards set forth in Daubert.

Briefly, Your Honor, since Mr. Lockridge has already effectively covered Daubert and Rule 702 this morning, I don't want to belabor that, but for the record, Dr. Boult and as to his testimony, I only want to touch on a few key points raised by Mr. Lockridge.

As Dick mentioned, the rules and the case law are very clear that this Court is given wide latitude when applying Daubert in the context of expert testimony. As Your Honor knows, in its role as a gatekeeper the district court exercises its authority by ensuring that an expert's testimony rests on a reliable foundation and is relevant to the task at hand.

In short, Your Honor, as I said that I would be brief here and I'm going to continue to do that, a trial judge in applying Daubert and the standards of 702 and 104(a) must make a preliminary assessment of whether the expert's testimony and underlying reasoning or methodology is scientifically valid and can properly be applied to the facts of the case.

If the testimony is found to be scientifically valid and is proper for the facts of the case, the testimony is deemed admissible and to meet the Daubert standards as codified in 702, reliability and relevance.

Without equivocation, Your Honor, we'll show with the remaining presentations on the various muscle experts that each of these experts and in specific Dr. Boult's testimony meets the Daubert and 702 standards with a plumb.

Your Honor, I listened carefully -- before I get into Defendants' arguments, I want to point out one thing very specifically. I listened very carefully to what Mr. Ismail had to say and quite honestly, to my utter amazement, he miscited the law. He miscited the law, Your Honor.

In the holding in Daubert the holding states, and I'm pointing to pages 2792 through 99, The Federal Rules of Evidence, not Frye, provide the standards for admitting expert scientific testimony in a federal trial. Mr. Ismail cited to Frye. There's no general accepted standard.

Listen, if Your Honor would, to what the court wrote. Frye's general acceptance test was superseded by the Rules' adoption. The Rules occupy the field. Nothing in the Rules as a whole or in the text and drafting history of Rule 702, which specifically governs expert testimony, gives any indication that general acceptance is necessary or is a necessary precondition to the admissibility of scientific evidence. Moreover, such a rigid standard would be at odds with the Rules' liberal thrust and their general approach of relaxing the traditional barriers to opinion testimony.

There's no general acceptance standard here any longer. That's long gone. What we're looking at now and what this Court is entrusted to do by the Supreme Court in Daubert is to play the gatekeeping role and to examine the methodologies and the underlying reasoning of the experts who are proffering their opinions.

Defendants have attempted two rather weak arguments, I would add, to disqualify Dr. Boult in particular. First they claim that Dr. Boult's clinical criteria as the basis for his opinion lacks scientific foundation, and second they claim that Dr. Boult's opinions regarding persistent myopathy are not supported by the scientific literature and that further he has no background or expertise qualifying him to make these opinions.

Mr. Ismail focused a great deal of attention on a few things and I want to take those one by one. In particular he focused on the AERs and he put up there for the Court to see various deposition clips and cuts that they sort of cherry-picked out of all of the depositions.

And they did that, Your Honor, because they want to pin this entire validity of our experts -- apparently they do -- on the AERs. They have a few other touchstones too, but in particular the AERs.

And if that's all it was about, Your Honor, I suppose we could probably pack our bags and go home because

that's why doctors do consults with each other, that's why we have all of this collection of experts. That's consistent with the practice of medicine. That's why doctors share information with each other. That's why they have grand rounds in the hospital, so they can collaborate with one another.

That's the importance in why we have assembled these world-renowned experts from Harvard and Stanford and Johns Hopkins, Ph.D.'s, M.D.'s, 29 years experience, clinical experience, for Dr. Boult.

If you think about it, it just makes common sense -- if you're going to market a drug in the way that Bayer did, largely to a population of elderly people, wouldn't it make sense to have a geriatrician's opinion included in the mix? Of course it would.

And wouldn't it make sense if the effects of that drug, the side effects of that drug, in fact, were going to affect the human muscular system, that you would want to have the opinion of a physical medicine rehabilitation expert? Of course, in Dr. Mayer.

Dr. Boult actually has impeccable credentials and he is well qualified to testify. They didn't want to spend any time on the credentials. I heard what Mr. Beck said earlier this morning, but it is interesting to note that they didn't.

And I think perhaps they didn't because these experts stand very, very firmly on their credentials and their opinions emanate from considerable experience, knowledge, training, and recognition in their field.

Dr. Boult, for example, in addition to his M.D., he also has an M.P.H. in epidemiology. He knows what he's talking about when he looks at these studies. He did a residency in geriatrics at Brown University and he has an M.B.A. as well.

He has 29 years, as I've said, of clinical experience in the field of geriatrics as a geriatrician working with the elderly, a high percentage of the Baycol market, as I mentioned.

He has conducted significant research at the prestigious Johns Hopkins School of Public Health, which has been his researching clinical base for many years. He's received and conducted NIH grants that span 17 years with his most recent grant application receiving a peer-reviewed score placing it as one of the top 1 percent of research grant applications in the country.

Defendants say Dr. Boult is not qualified to render his opinions because he has no experience with statins. Well, he has no experience -- he was honest. I mean, all of our experts have been honest and candid with the Court on these depositions.

When asked about the AERs he said, I don't hold myself out as an FDA expert. We have an FDA expert. We have a neurologist. We have muscle experts. We have a geriatrician. We have a geriatrician for important reasons and as I move on, Your Honor, I know the Court will see that the methodologies and the foundations for his opinions are rock solid.

Dr. Boult's credentials as a researcher and practitioner in geriatrics makes his testimony highly relevant to the Baycol litigation and precisely for that reason -- I have already stated Baycol was prescribed to an elderly population -- you want to have Dr. Boult's opinions into the mix.

The objective is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field. That's directly from Kumho Tire, Your Honor.

To be admissible the opinion must be reasonably based on good science. The analogies, inferences, and extrapolations connecting the science to the testimony must be of a kind that a reasonable scientist or physician would make in a context outside of litigation. And that's -- as Your Honor knows and is familiar with in the progeny of

cases, that's from Joiner.

Daubert nor 702 requires an expert to do specific research. He doesn't have to be an expert in statins or do standalone research on statins in order for his opinion and his clinical experience to weigh in on his opinion.

Dr. Boult, however, does prescribe statins. 25 percent of his patients take them. He's examined and evaluated patients with muscle complaints, many of whom he has taken off statins and many of whom are recovering from muscle disorders and neurological complaints. That's what a geriatrician does. As Dr. Boult testifies in his deposition, he teaches and instructs residents and medical students on muscle disorders and diseases.

Dr. Boult would be prohibited ethically and probably legally, in fact, as well from conducting any research on patients taking Baycol because of the removal of the drug from the market. How could we possibly expect him to reach some gold standard that Defendants argue must be met by putting Baycol to a test? He wouldn't even be allowed to do that.

But that doesn't mean under the current case law, Your Honor, or even under the practice of medicine as we know it and as doctors practice it that he cannot extrapolate.

It was pointed out that all the various articles

and all the various studies that were relied upon, it was pointed out by Defendants and even Dr. Boult said it, it is preliminary.

Well, that's the iterative process, Your Honor, that scientists and doctors do and what they undertake, thesis, antithesis, hypothesis. And it's valid, it's solid, it's rock solid, and it's been the bedrock of the scientific method. A clinician adheres to that. A clinician like Dr. Boult follows that process. He knows that it's evolving.

And he's not going to say something that's not true, but he knows that he can extrapolate. He knows he can take those arguments and the inferences from those studies that my colleagues have cited and you'll hear more about and extrapolate from those to his opinions. And that's what Daubert requires, Your Honor, and that's the scientific method at its best articulation, I believe.

Dr. Boult's practice and experience as a clinician qualifies him as an expert because his opinions and the clinical criteria he set forth are based upon scientifically valid reasoning and methodologies, as I've stated.

Dr. Boult is not basing his opinions on speculation and conjecture. Dr. Boult's development of clinical criteria are based upon sound clinical reasoning and judgment and diagnostic protocols taught to and

practiced by medical doctors.

I made a note when Mr. Beck was talking because he actually pointed out an important element of the scientific process when he said that the scientific method involves having a written protocol that lays out in advance the data one will be following.

Dr. Boult has been trained as a medical doctor to follow those kind of protocols and here they are, Your Honor, here are the kind of protocols that doctors follow. They include patient history, symptomology, environmental and occupational history, they like to look at that, past and present patient medical records, the physical examination, diagnostic tests.

These are precisely the protocols that Dr. Boult has used to develop the clinical criteria in his report. Dr. Boult is not speculating at all. He's following a scientifically valid professional rigor that a clinician would be expected to follow.

Defendants have actually misrepresented Dr. Boult's opinions with regard to the development of clinical criteria. Dr. Boult testified that these criteria need to be viewed within the big picture. These criteria do not exist in a vacuum.

These are the points that he makes in his report, Your Honor, which we submitted with our papers. They need

to be used in connection with a history and a physical exam to perform a differential diagnosis.

As the Court knows, Your Honor, this has already been discussed. An order that this very Court issued requiring Plaintiffs to submit a case-specific expert report that includes a differential diagnosis has already been undertaken in this court.

We're not in disagreement with that. It's precisely what Dr. Boult has testified to already. The criteria he set forth in his report are for that purpose and for all practical purposes that's a nonissue.

The rigor and the methodology that Dr. Boult used in the development of these criteria, Your Honor, is well settled within the annals of medicine and meets without equivocation the reliability prong of Rule 702, as required to substantiate an expert's opinion.

Dr. Boult's testimony further meets the standards set forth in Daubert and codified in Rule 702 because they're well-grounded in scientific methodology and procedure.

Daubert vs. Merrell enunciated in dicta, Your Honor, an important principle for a district court's Daubert/702 inquiry when the court wrote, and I think this is in a footnote, number 12, The inquiry we envision by 702 is a flexible one. Its overarching subject is scientific

validity and thus the evidentiary relevance and reliability of the principles that underlie a proposed submission. The focus must be on the principles and methodology, not on the conclusions they generate.

Dr. Boult not only extrapolated from his clinical experience, but he extrapolated from peer-reviewed literature. And this practice is exceedingly well-founded and the Court will find authority for this practice, of course, in Joiner, one of the seminal cases in the Daubert progeny, as Your Honor knows.

Dr. Boult based his opinions for general causation on medical and scientific literature. He based it on epidemiological data. He's an epidemiologist. He's trained in that. He's based at one of the most prestigious public health schools in the world. He's more than qualified to examine epidemiological information.

He looked at toxicological data, he looked at case reports, and he relied on his training and his clinical experience as a doctor. It's not just about the AER, Your Honor, as Defendants claim.

These same factors have been described amply and the Court will find further instruction in the Reference Guide, which I know Your Honor is familiar with, on Scientific Evidence. There's ample authority for the way that Dr. Boult approached his opinion.

I don't want to take any more of the Court's time to review again all the various studies cited. The lawyers on both sides have presented those. But for the record, Dr. Boult reviewed the Phillips article, the Hildebrand article, Argov, England, Hansen, and Soininen. These articles supported the opinions offered by Dr. Boult at the time he wrote his report and provided his deposition testimony.

And I think in addition my colleague, Mr. Arbitblit, has previously detailed why we don't believe that the Leathers case is instructive. I'm not going to, also in the brevity of time, go over that as well.

But I do, however, Your Honor, want to focus for just a few moments on this methodology and on the reasoning underlying Dr. Boult's opinions since that's the focus and the subject of the Daubert inquiry and that's what this Court will be looking at.

The Supreme Court's decision in Daubert, Your Honor, references several *amici curiae* submitted to the court at the time of Daubert. Importantly, those *amici*, in the court's own words, express a view that science is not absolute when it said, Of course it would be unreasonable to conclude that the subject of a scientific testimony must be known to a certainty. Arguably, there are no certainties in science.

And in quoting from an *amici* that the court wrote, Indeed, scientists do not assert that they know what is immutably true. They're committed to searching for new, temporary theories to explain as best they can phenomena.

That's exactly what Dr. Boult set up in his deposition. That's exactly the candor that he used in answering I believe Mr. Ismail's question when he was examining. He's taking it up to the door. He's using the scientific method to get to the next step. And that's exactly what Dr. Boult has done to formulate his opinions, Your Honor.

In particular he structured his opinion that Baycol causes persistent myopathies in some people, not in everyone and perhaps even not in most, Your Honor, but that doesn't exclude certain people. And as a practitioner and as a clinician and someone who looks at this day in and day out, he knows that it's not the entire population, there are exceptions even after CK declines to normal.

It's consistent with the scientific literature we submitted to the Court, consistent with our experts, consistent with Defendants' experts, Mr. Dorfman, who Mr. Arbitblit is going to address, and consistent with the scientific methodology underlying the etiology of disease.

Etiology, as Your Honor knows, refers to the various levels of underlying abnormality that have led

substantially to the next higher level of abnormality, of disease, or of diagnosis. This chain or this web of causation is considered what in science is well-settled as the pathogenesis or the pathophysiology of a disease.

While the annals of medicine are replete with a discussion on this topic, for most medical doctors this underlying process for diagnosis and causation is often intuitive. They're trained in it. They know it. They understand what they're looking at.

As a clinician they're well-grounded in the art and the science of clinical reasoning, which I previously discussed and which have been more than adequately substantiated as being scientifically valid.

Since we began this case many years ago now, Your Honor -- and I know you know I've been involved in the expert discovery phase significantly -- I've been scratching my head over Mr. Beck's bright-line distinction between rhabdo and nothing else.

And quite honestly, not as a medical doctor, not as a scientist, but even as lawyer, that makes no sense to me because in fact, Your Honor, it doesn't square with pathogenesis, it doesn't square with pathophysiology, and with that web or that continuum that our experts have referred to so carefully and so adroitly.

That's what makes sense. That's what makes sense

to doctors. It's why they do consults. It's why it forms the basis of the scientific method, because they know that it's not a bright-line distinction that it's just simply Baycol -- excuse me -- that it's just simply rhabdo or nothing at all.

With respect to muscle disorders, Dr. Boult's testimony is well-founded on this scientific principle when he discussed a continuum that I referred to or a severity or a progression of disorders ranging from myalgia or, as Mr. Beck has called them, the aches and pains. He likes to refer to them as that.

But it doesn't just start there and then leap to rhabdo. That doesn't square with medical science and it doesn't square with reality. There's myositis and myopathy it progresses to over various stages to rhabdo.

This pathophysiology of muscle disorders is scientifically valid, it's well-settled methodology within the practice of medicine, and it's referred to. And I can give the Court cites to that, if the Court wishes, now or submit them later in an effort to save time, but the same authors of the medical literature we cited relied upon this same type of method as the basis of their opinion.

It also lays the scientific foundation for Dr. Boult's opinion that persistent myopathies may occur in some patients at levels of disorder lower than rhabdo after

taking and stopping Baycol.

Conversely, however, Defendants' argument that Baycol causes mild toxicity only at the level of rhabdomyolysis is not scientifically valid and should be considered for purposes of Daubert and Rule 702 treatment, Your Honor.

If one examines the medical literature carefully of this bright-line distinction, I would say if anything is junk science, Your Honor, not to use that term casually or flippantly, if anything is junk science, saying it's rhabdo or nothing is. That just doesn't square with reality, Your Honor.

But there are many other examples in addition to the science of myopathology that I can point the Court to that follows this same pattern of etiology. For instance, a heart attack may be due to a sudden block, a sudden blockage of a coronary artery, but that heart attack may be due to genetics or diet or lifestyle, a sedentary lifestyle, and smoking. These factors may contribute to the buildup of plaque in the artery, which in turn may slowly build up or break loose to cause the heart attack.

It's not just bad lifestyle and then all of a sudden heart attack. There's a progression. There's stages. There's steps in between. The doctors know that. The literature supports that.

Why would myopathology, why would someone looking at muscle disorders follow any different regimen or any other different professional rigor? They don't and they wouldn't. And our experts have opined to that over and over again.

But we've had to listen to this mantra from Mr. Beck that this bright-line distinction is simply the order of the day and that everything revolves around CK. That's not the only factor, Your Honor. That's not what doctors would conclude.

And you've heard not only our experts testify, but it squares with the practice of medicine that's not the only way to diagnose here in a myopathy situation. There's a web of causation here of all types of indicia.

They want to try to peg us down into CK. They want us to realize and take something that is dynamic and make it static. But that doesn't square with reality, Your Honor, and our doctors have testified to that because they know it's true.

THE COURT: Mr. Hopper, I love to hear you speak, but I got an eye from Mr. Beck that he knows that you're going to be able to catch your plane and I suspect that Mr. Beck wants to get on his plane.

MR. HOPPER: All right, Your Honor.

MR. BECK: I'm staying until tomorrow, Your Honor.

I hope that he keeps going, especially about these heart attacks, because I'm --

MR. HOPPER: You've had your chance. I'm happy to wrap up, Your Honor.

THE COURT: No, no. I'm just telling you --

MR. HOPPER: Dr. Boult's opinions and testimony should be --

THE COURT: You've been going for a half hour.

MR. HOPPER: I'm happy to wrap up. Dr. Boult's opinions and testimony should be admitted. They should be because they meet the requirements set forth in Rule 702 and they meet the test of Daubert and its progeny.

I thank you for your time today.

THE COURT: Thank you.

MR. ISMAIL: Your Honor, in light of Mr. Hopper potentially having to leave, would you like me to respond to that while he is here?

THE COURT: Yes, you may.

MR. ISMAIL: Just a few minutes, Your Honor.

MR. LOCKRIDGE: Well, Your Honor, if I can interrupt here. We have a couple of more people for our hour that would like to still respond.

THE COURT: I'm getting going. I've got my second wind.

MR. HOPPER: I would like to think I helped that

along, Your Honor.

THE COURT: So we can go until 9:00, 10:00 tonight.

MR. LOCKRIDGE: That's fine, Your Honor. My point is I think we get a full hour, so we would like to --

THE COURT: Don't worry about your time.

MR. LOCKRIDGE: All right.

MR. ISMAIL: Briefly.

On the question of the standard under Daubert, I don't think Mr. Hopper's characterization of our position is a fair one. Under Daubert the court must determine whether the expert's opinion is reliable.

And the Supreme Court identified general acceptance as a factor, not dispositive, one of the factors to consider. We certainly address that in connection with some of their experts' opinions.

Some of the other factors include whether it has been subject to peer review. Dr. Boult's opinion was pointedly not submitted to peer review and he said it couldn't be submitted to peer review. So he fails that standard as well as the general acceptance standard.

The other two of the four nonexclusive factors identified in the Daubert case law by the Supreme Court itself in Daubert:

Whether the theory has been tested. And certainly

there's a lot of research in this area and they haven't come up with any that identify Dr. Boult's clinical criteria as being correct.

And whether there's a known error rate associated with it. And of course inasmuch as there's no research on this standard that he's come up with in the litigation, of course there's no error rate that has fallen out of that clinical criteria.

So analyzing these four factors together or in isolation, the opinion is not reliable.

And I know Mr. Hopper did a lot of talking about what experts are allowed to do, they're allowed to extrapolate, they're allowed to rely, they're allowed to even make certain leaps of logic, but he didn't identify any research that supports Dr. Boult's opinion on permanency or diagnosis. He said he looked at case reports, he looked at peer-reviewed articles, but he didn't identify any that actually say what he says in this case.

And there's an analytical gap here, Your Honor, that is simply too great. You have a set of case reports that talk about resolved muscle symptoms and then you have experts who say there's a permanent condition that we're advancing in this litigation. That is not a reliable opinion for the purposes of Daubert.

And with respect to -- and I guess we have heard

the nub of the disagreement on comparative safety opinions from Dr. Boult and others.

As Mr. Hopper indicated, the whole point that doctors frequently get consults for opinions upon which they're not expert in and doctors collaborate, the consequence of that is not to excuse the Daubert standard on qualifications, but to exclude the opinion.

If they're admittedly not expert in the area and they would have to go get a consult to give in their professional capacity, then they can't give the opinion here and that can be left for another expert who does have the qualifications. And so it's not an excuse to circumvent Daubert. It is a basis to exclude them under Daubert.

And with that, I will await Mr. Arbitblit's discussion, I suspect, of the medical literature and hold my comments until he's done.

THE COURT: Thank you.

MR. ARBITBLIT: Your Honor, I just need a moment to set up and I would like to pass the PowerPoint hard copy forward with the Court's permission.

THE COURT: I'm sorry?

MR. ARBITBLIT: I would like to provide the hard copy of the PowerPoint --

THE COURT: Oh, please.

MR. ARBITBLIT: -- to the Court and defense

counsel.

THE COURT: How much time will you need for this?

MR. ARBITBLIT: Your Honor, I'm at your disposal. If you were serious about a second wind, I can tell you as much as you would like to hear about muscle -- I have certainly been studying it and trying to make it as clear as possible.

I can try to go through it quickly if you prefer, but I certainly would appreciate your indulgence in terms of trying to get at some of the subtle issues. So it's entirely at your pleasure. If you wanted me to say a time, I would say half an hour.

THE COURT: Thirty minutes.

MR. BECK: Turn on his yellow light.

MR. ARBITBLIT: Mr. Beck, what was that?

MR. BECK: I said turn on his yellow light, please, Your Honor.

MR. ARBITBLIT: Will someone please tell me if it's --

THE COURT: The yellow light will come on with ten minutes to go. Mr. Zimmerman is in charge of telling you when the yellow light comes on.

MR. ARBITBLIT: Have I started?

THE COURT: It will reflect on the back of his --

MR. BECK: Here, I'll do this for you.

THE COURT: And your 30 minutes does not include setup time.

MR. ARBITBLIT: Thank you, Your Honor. In my case that's a real benefit.

THE COURT: If I can suggest something. You know your topic extremely well and one thing I do not like about PowerPoints is when someone puts something up and I'm looking at it and it flips through -- you've given me this to digest once I leave the bench. Let's hit the highlights. Whether or not you need the PowerPoint or not, I don't think -- I prefer to listen to you just like I listened to Mr. Hopper and Mr. Ismail. It's easier for me to do that. But when you flip the PowerPoint up, my eyes at this ancient age do not adjust quickly to what's on the screen and I'm a slow reader and so I end up getting a migraine headache.

MR. ARBITBLIT: I'll try to certainly avoid that, Your Honor, and only use the PowerPoint if there is some special reason to do so.

THE COURT: I appreciate that.

MR. ARBITBLIT: Okay. So with that, Your Honor, briefly, Dr. Richman is a professor of neurology and a former department chair at the University of California-Davis with a specialization in muscle disease, particularly a disease called myasthenia gravis.

He is familiar with and qualified to interpret the

scientific literature. He's been a principal investigator in numerous clinical trials, as shown in his CV. His methodology was reliable and included over 180 articles that he reviewed, including those as to the consensus we described earlier and which we won't go into any great detail other than to say what he said about it when we come to it, and his experience in treating muscle disease, medical records review.

And I would like to just try to, again, not repeat what I did this morning, but to refocus on what I think has been to some degree ships passing in the night between what the Plaintiffs' experts are saying and what the defense counsel are hearing.

At times I see the defense counsel asking questions trying to elicit opinions and then in the course of the exchange it's not clear what the expert meant, and sometimes what I see happening is that opinions are being challenged that were not in the reports and I'll give you an example of that.

Dr. Richman's report, which -- I'm very familiar with it because he is the expert that I worked most closely with out of the muscle experts. I'm familiar with what he said at his deposition and his report and what's in our papers in opposition to the motion.

He never said that a myopathy that has always had

a normal CK can be permanent. He said just the opposite. He said that a normal CK myopathy is at the mild end of a spectrum of injury and that it stops and it reverses when you go off a statin.

It's been asserted that he's part of a group of people who are saying that there can be a permanent myopathy where there's never been an elevation of CK and no breach of the muscle cells. He never said that. It's not in his report. His report at paragraph 16 says the opposite. It says that it reverses.

So it's very important that we not attack a straw man, that we try to focus on what the expert's real opinions are and whether the literature supports those opinions, not those that are attributed to them.

And I would say that to some degree that may be true with Dr. Boult, but I'm not as familiar with his report. I did not work with him personally and so I'll mostly be focusing on Dr. Richman, but in that context I'll try to make comments that I think are generalizable.

Now, there was a point that was made by Mr. Ismail which is valid, that there are many individual cases that the Court is concerned about that remain in this MDL and that there are case-specific reports coming up.

And so what is the interplay between what happens here and those people? Well, obviously there is an

interplay. That's why we have MDLs. But that doesn't mean that this group speaks for all of those lawyers. It means that our experts and I speak for myself in working with Dr. Richman and knowing his opinions.

And I speak for co-counsel with whom I have met and discussed this do not feel that the literature supports a permanent myopathy where the CK has never been elevated and we do not take that position.

To the extent that it may have been stated in a deposition, it may well be that some of our experts feel that could be the case. They may have testified to that in their deposition because someone asked them their opinion.

But is there scientific literature that passes Daubert to support it? I don't think so. And so in my opinion and Dr. Richman's opinion, more importantly, he never said that. He said that it reverses.

So that's the mild end of the continuum, but there's no doubt that there's a continuum. Dr. Dorfman on the other side -- and I'll read his quote to you when we get there -- said that there's a continuum of injury. In his own report he meant to refer to that and said it quite specifically.

So when we talk about a no elevation CK injury, we have to be very careful what we mean by that. Do we mean a case where the CK was tested and found normal? If so,

that's an easy case. There's no scientific literature supporting that there could be a persistent myopathy off statins. It's reversible. That's what the literature says.

On the other hand, the easier case on the more extreme end is where the CK is tested and it's found abnormal and there it's crystal clear that there's a continuum of increased CK that is consistent with physical damage.

The CK is not the disease. It's the marker. When the muscle cells die due to exposure, the cell walls are gone and the contents go into the bloodstream. When the exposure stops, the muscle cell deaths stop and the body does its normal job of clearing out what isn't supposed to be there.

Ten days to 14 days later, in most cases, the CK is gone. And so does that mean that the patient has recovered? Not necessarily because the marker is not the disease.

Now, there was a lengthy exchange between Mr. Ismail and Mr. Richman where I believe Dr. Richman was trying to explain his opinions about that and I don't think that they were -- I think they were ships passing in the night because I have great respect for Mr. Ismail and his intellect and I just can't imagine that he believes that Dr. Richman was saying one thing when he had said the

opposite in his report.

He never said if -- so the distinction is on the low end CK is tested and it's normal. No claim for permanency or persistence. When you stop the statins, it's gone. That's what our experts say.

Is someone else out in the MDL going to say something different? Probably, but I can't stop that. I can't -- I won't be putting forth an expert to Your Honor who would support that statement, but I don't know what all the experts are saying in all the cases nor what the basis is. I just know what I know from reviewing the literature and working with these experts.

So then you have CK elevated; and when you have CK elevated, you have people defining rhabdomyolysis in different ways. Some people will say it's ten times normal with symptoms. Some people will say it's five times normal with symptoms. Everyone agrees that rhabdomyolysis is the severe end of the spectrum.

And we have testimony from Dr. Dorfman, the defense neurologist, that basically agrees with Dr. Richman that in a small minority of cases people who have severe rhabdomyolysis can have a permanent injury because the extent -- two factors that influence the time of recovery, the extent of injury and the ability to regenerate. Because the injury, again, is not the CK elevation. The injury is

the muscle destruction.

So what happens when a muscle is destroyed is that it has to regenerate and there are many factors that affect the ability of an individual to regenerate muscle tissue, primarily age; secondarily, concomitant disease conditions and specifically those that affect the blood supply to the regenerating muscle or the nerves that are connected to the muscles at synapses and without which the muscles cannot regenerate as effectively.

Now, I do -- when we get to that I do want to show you what Dr. Dorfman said about that because it's very clear that individual host factors completely preclude a blanket definition of when CK myopathy ends when you've got an elevation.

If it's really bad and a very severe injury, you can get fibrosis, you can get scarring. Those are the things that Dr. Richman testified to. Those are the things that Dr. Dorfman testified to.

And those unlucky few that get that, they have permanency or they have a substantial risk of permanency and in some cases it is permanent. That's in the literature. It's in the Woodrow article, which is cited in Dr. Richman's report, which I read that particular sentence to Dr. Dorfman and he agreed with it. He said, yes, in those very severe cases it can be permanent.

Well, how does that happen? It happens because the ability of the muscle to regenerate is exceeded. So some of the regeneration happens through fibrous tissue and scar tissue that create permanent disability.

And so that's the very extreme and it's only in a few cases. And given what's been said earlier, probably there aren't cases like that left, but there are some rhabdomyolysis of varying severity that are still left in the MDL.

So what's in the middle? In the middle there are cases with elevated CK, and probably the best source of information on that is the Hansen article that's been submitted by both sides, which at the time of Dr. Richman's deposition was only in abstract form and involved a smaller population. This is at the University of Wisconsin where they went through medical records.

And of interest in the Hansen study, the authors said that what they were doing was a retrospective study. So the idea that a retrospective diagnosis of whether someone had a statin-associated myopathy, the idea that that's crazy or concocted is just not accurate.

When any expert in litigation is attempting to diagnose what happened to a person, there's an element of looking through the retrospectascope. That wasn't the treating doctor who was there examining the person at the

time. You're doing the best you can with the records you have.

And your differential diagnosis, as Hansen points out, and I'll go through the list of what they did, but very important to Hansen is that -- and with all due respect to Mr. Ismail, he said that all of the literature involved an objective measure of the underlying statin myopathy. That's not true.

The Hansen article specifically said that in 8 of the 45 patients that they looked at, they had normal or unknown CK. And what was the reason for that? They -- here's what they say, and this is submitted to Your Honor with our materials.

THE COURT: Are you on one your slides?

MR. ARBITBLIT: Okay. I can do that, yes, sir.

THE COURT: Just tell me what page.

MR. ARBITBLIT: It's at slide 38. There's a series -- as long as we are talking about Hansen, perhaps I could go through a little bit of what the Hansen article was.

Starting at 37, 45 patients -- actually what they did was they went through about 400 records. They looked through a large database of people who had diagnoses that are listed in a dictionary of diagnoses and from that they identified people who might have a statin-associated

myopathy. And so they looked at everything available to determine whether they probably did.

And from that larger group they selected 45 and those are the 45 who became the subjects of the study. And for those 45 they state that it provides a spectrum of observations, a spectrum. That's another word that's interchangeable with "continuum" in the literature. Some people say "spectrum," others "continuum." Dr. Dorfman said both. The study provides a spectrum of observations ranging from mild muscle pain to acute rhabdomyolysis. That's at 2675. So it's a peer-reviewed study.

And what they said was that 57 percent resolved in one month, 34 percent resolved between one and six months and they don't get more specific than that, and 7 percent resolved by 14 months after stopping statin use. This is the largest study I'm aware of that gives you the spectrum not only of the condition, but of the recovery time. And it's not one size fits all. It's affected by who the person is, how fast can they regenerate.

Clearly their CK went back to normal in 10 to 14 days. Maybe a little bit longer or a little bit shorter in some cases. But that's what CK is, it's a marker. So if someone is out at six months or the 7 percent who resolved somewhere between six and 14 months, those people long ago had normal CK. But did they have a persistent myopathy?

Yes, they did, according to the peer-reviewed literature.

Now, Dr. Richman relied on the abstract of this at his deposition, which had just been published and had similar findings but different numbers because it was a smaller study.

And I believe he said at the time that 24 percent had not resolved by nine months and 76 percent had. I think those were the numbers as of the time of the abstract that preceded the full publication. But the idea is the same. Not everybody is the same. People are different, their ability to regenerate is different; and that's what this article shows.

Now, of interest in the Hansen study is that these -- while they do provide a spectrum of observations, the spectrum is on the low end, which is probably because the distribution of injuries is more mild cases than severe cases. That's typically what you would expect.

But if you look at slide 39, you'll see that the category that -- they used what they called the American College of Cardiology statin clinical advisory --

THE COURT: Let's go back.

MR. ARBITBLIT: Yes, sir.

THE COURT: Your second PowerPoint -- second bullet point -- no, your third bullet point on page 37, peer-reviewed study supports Dr. Richman's opinion that the

statin myopathy can persist after CK returns to normal.

MR. ARBITBLIT: Yes. And is there a particular question about that? The point being that the CK is back to normal in 10 to 14 days, but the muscle pain does not resolve for up to 14 months. So the CK is normal, but the condition continued.

And what I want to make clear by persistent is that it doesn't mean permanent. No one is suggesting in Dr. Richman's opinions or any that I know of and I'm not suggesting that persistent is the same as permanent. It means that it persists after CK returns to normal for some period that the literature describes as, in this range of cases in severity, resolved by 14 months.

But in that small window of the most severe cases that Dr. Dorfman and Dr. Richman both agree do take place you can have a permanent injury, but only with this very severe rhabdomyolysis.

THE COURT: Okay.

MR. ARBITBLIT: So if you -- let's go through 38 where we first started, please, Your Honor, and what's important here is that the authors performed a retrospective study and that passed peer review.

They used medical records to ascertain these cases. They did what they called focused medical record review of the outpatient and hospitalized patients with

muscle related diagnoses.

And then here's the sentence that led me to this slide is they included patients with a normal or unknown CK level because recent evidence supports the entity of statin-associated myopathy with CK levels within the reference range.

The reference range meaning normal, which for this laboratory I believe they said that it was about 170 something for women, who have less muscle mass so they have less normally dying muscle cells to contribute to their upper limit of normal, and somewhere in the low 200s, I believe, for men who have more muscle mass.

But the point is in this article what they did was looked at medical records of patients with normal or unknown CK. And so that means that these people are supportive of the idea that you can diagnose a statin-associated myopathy without having a CK test, either because you can have it while you're in the normal range or that you can have it without knowing what it is by using the other available information to make that determination.

So we'll get to those diagnostic criteria in a moment -- they're at slide 40 -- from the Hansen article, but going on to 39, I wanted to point out that this was the milder end by and large, that they had 37 patients for whom CK was tested and the median CK was only 328 and the low was

36.

So even the median, the most common value where there's half above it and half below it, was not that far above normal and yet it was sufficient for them to be diagnosing that these folks had statin-associated myopathy that could continue after their CK returned to the normal range.

And for 8 they didn't have that information, but they made their diagnosis on other bases. And importantly, they didn't just do that on their own. They made reference to a consensus statement of one of the leading medical bodies in the country.

The American College of Cardiology statin clinical advisory document terms are referenced in the Hansen article as a source for a categorization of statin myopathy from rhabdomyolysis to a myopathy and finally -- a myopathy with three times normal or greater -- and then finally Category 3, myopathy with muscle pain and weakness or an unknown normal or mildly elevated CK level at less than three times the upper limit of normal.

So that's the bottom end of the continuum and that's where 34 of the 45 cases were that were nevertheless persistent for these time periods of one month, six months, fourteen months for 7 percent of them.

And so 13 of the 45, that's about a quarter of

them, were within the reference range, they were normal, and yet they had statin-associated myopathy. So what does that do? It supports the idea that there is an entity of normal CK myopathy.

Does that mean it's a different mechanism? I think that's a leap. I don't think that it's implausible to believe that damaged cells precede dead cells, that whatever the mechanism is that's happening -- and I think the mechanism does not have to be known with certainty. We know this is happening. The mechanism should be plausible.

And there are plausible mechanisms, two or three of them, in the literature that involve interference with the cholesterol or the ubiquinone or the apoptosis. Whatever -- there are only three that are talked about and they all have some supporters and some detractors and they are all considered plausible.

We do not know it with certainty, but that doesn't mean that it's a different mechanism causing damage to cells from the mechanism that's causing death to cells.

And the continuum of damage that you see in some of the clinical trial data with elevated CK going up with dose with Baycol, as we saw this morning, supports the idea that there's a continuum of damage.

Now, people who have less than three times the

upper limit of normal have dead muscle cells. If it's above normal, that's because there are dead muscle cells. They have fewer dead muscle cells than the people above three times the upper limit of normal and all else being equal they'll probably recover sooner. But all else isn't necessarily equal, as we'll see in Dr. Dorfman's and Dr. Richman's testimony.

Going to Your Honor's questions about diagnostic criteria and how to -- I know that's an issue of concern and it's an issue that Mr. Ismail addressed, but these are the things that the Hansen authors looked at, at slide 40:

Onset, duration, location, and severity of muscle pain. That's part of a clinical history.

Inciting drug with dose and duration of therapy before the onset of symptoms for the person taking the statin.

The presence of muscle weakness, and that is considered by both experts on both sides to be a matter for objective testing. It's not just subjective, I don't feel well. It's something that trained doctors test all the time and don't consider to have much uncertainty. If it's just someone saying, oh, I hurt, well, that's different than if you have somebody who you know they are on a statin and you do strength testing.

These are if they were available. Peak CV values

where available, recent thyrotropin test results to see if thyroid condition might be causing muscle symptoms, what therapeutic interventions were done, number of months to resolution of muscle pain and they use the term "months," and the response to other statins.

Then they define "recovery." The time from cessation of the implicated statin to the resolution of muscle pain.

So that's a list of the types of things that might be available in particular cases and a doctor trying to figure out what caused a disease is going to look at as many of them as are available. And in different cases that might be enough and in different cases it might not, but it's not a black and white issue where one size fits all.

So Dr. Richman's methodology to diagnose statin myopathy is similar to Hansen, at slide 41, and this is from his report and this sets aside all the debating at his deposition, clinical history, lab results, CK tests where available, strength testing to detect muscle weakness, biopsy or EMG may be done but are uncommon and not necessary. They're not commonly done.

Biopsy in particular is invasive and painful, and Dr. Dorfman I believe testified that he only did it when he couldn't confirm that it was a statin that caused it and wanted to see if there was some other serious cause.

Dr. Dorfman, his testimony at page 89 on slide 42 on the differential diagnosis. The most important question, according to Dr. Dorfman, is whether you are taking a statin when your symptoms begin and then the treating doctor suspicion that it might be the statin can lead to stopping the drug and then you form what he called a working diagnosis. And if the enzymes normalize and the symptoms resolve, at that point you have a higher level of confidence that the diagnosis was correct.

Now, as far as when that resolves, he testified that he agreed with the idea that it was -- it could be a period of days or it could be months or it could be over a year, and we'll get to that.

So Dr. Dorfman similarly testified to similar criteria at a slightly later point. I won't read them. They're too similar to spend the time on.

Strength testing, is that objective? Yes, both doctors agree. Dr. Dorfman says:

"Can you describe what you're referring to when you say objective evidence of muscle disease?

"Answer: I mean primarily weakness of the type that neurologists are trained to evaluate and assess.

"And how does that assessment figure in your diagnosis of statin-related myopathy?

"Answer: For me to think of the degree of

statin-related myopathy as being more than just a minimal degree of severity, I would like to assure myself that the individual, in fact, is manifesting true weakness of the affected muscles and that the limitation is not merely on account of pain."

So that is -- he's referring to testing for muscle weakness in addition to pain as an objective criterion that neurologists are trained to carry out.

He used the same differential diagnosis for mild conditions with his own patients, mild muscle symptoms, mild elevations, CK and symptoms resolved promptly and did not recur, no other apparent cause, did a clinical exam and did strength testing. So that's one way of doing it.

And he did the same thing for the Defense in litigated cases, as he described, in reviewing records to tell them whether he thought those were more likely than not caused by Baycol, which he did determine in two out of three.

And he looked at -- this is an interesting quote at slide 46. In coming to those opinions he relied on the totality of the medical evidence that he had available to him concerning these individuals, including their past medical histories, the existence or nonexistence of other disorders that might have played a role in causing their symptoms, and adding an additional laboratory test to rule

out alternate diagnostic possibilities.

That's a classic diagnostic differential diagnosis description. It's quite similar to the criteria that the Hansen authors used and it's quite similar to what Dr. Richman said.

So on the issue of recovery, here are some citations that support what I was saying earlier, Your Honor. There's that the recovery depends on the extent and severity and the variable capacity to regenerate. More severe conditions take longer to resolve all else being equal and regenerative capacity is adversely affected by age, disease states.

So then we go to the Woodrow article. Muscle damage from rhabdomyolysis may result in prolonged rehabilitation and permanent disability in a minority of patients, and Dr. Dorfman agreed at page 85 to 86 of his transcript.

He agreed -- and here at page 76 to 77 he says why that would happen. Persistent muscle symptoms, the reason for that is the muscles "have been so badly damaged that the regenerative capacity of the muscle has been exceeded and the muscles are compelled to heal not only by regeneration, but also to some degree by scarring or fibrosis and that the scarring of the muscles is a source of persistent symptoms and disability for these people."

It's in complete harmony with Dr. Richman's opinion. No dispute. If you've got a severe case, it can be permanent. That's what the experts say. Not necessarily what the briefs say on both sides, but that's what the experts on both sides say.

So here are some of the things he testifies to and why that would affect the rate of recovery. And they're very important in this case, Your Honor, because old age is probably the most significant factor in delaying recovery and this is an elderly population of users.

It's partly because of age itself and its effect on regenerative power of muscle tissue, but it's also because of the concomitant issues that go with old age and in particular the conditions that go with people who have high cholesterol, for which Baycol would be prescribed.

An awful lot of people in that condition would have atherosclerosis. And as we'll see here, Dr. Dorfman says that reduces the blood supply by narrowing the vessels and so you have less blood and oxygenation and slower regeneration.

So the elderly are at particular risk of delayed recovery and that's a factor that is case specific, but has to be in the mix of the differential diagnosis of causation and duration.

So here's what he says. Satellite cells are

needed to regenerate muscle and they're significantly reduced in elderly patients. He agrees with Dr. Richman's report.

And that's important due to the advanced age. For example, in the HMO study, PacifiCare, the 19,000 Baycol patients' average age was 67. So -- and that's an average, so many were older than that.

"What is your opinion as to the range of times of recovery from statin-related myopathy for [sic] rhabdomyolysis that is less than the full-blown fulminating paralysis renal type failure that you've described a few moments ago?" And that was the kind he said could be permanent.

And here's his answer. "I think most people will recover over the course of several months, a few perhaps more quickly and a few somewhat longer, but I think the period of recovery can be measured in months to perhaps a year or longer than that." That's his testimony. That's very consistent with Dr. Richman's report as well and with the Hansen article.

Slower recovery for patients with diabetes or atherosclerosis. I asked him whether individual host factors, the condition of the patient affect recovery. And he answered, "Without question" -- that was the first thing he said, "Without question" and then he went on to list some

of them. Host factors affect the ability to recover from statin-related myopathy. General health has a large influence on the rate of recovery. Preexisting conditions, diabetic complications, severe atherosclerosis, "which is why the statin medication was prescribed in the first place, if they have other kinds of co-existing disorders, those will tend to slow down the rate of recovery, I think." That's his opinion.

And specifically to the diabetics -- and, again, 18 percent of the PacifiCare patients were diabetic, 18 percent, and Dr. Dorfman is saying those people are particularly at risk of a slow recovery.

Why? Because narrowed blood vessels slow muscle regeneration and nerve damage also slows recovery because "the intimate relationship between nerves and the muscles is important for regenerating muscles as well as healthy muscles, so that may play a role also." Atherosclerosis lowers the blood supply, "and if the blood supply is limited to a muscle or a region of the body, I would predict that the recovery from injury would be slower."

So these people already had their CK go back to normal within 10 to 14 days, but Dr. Dorfman is explaining why some of them won't get better that quickly. And that's not the same and needs to be clearly distinguished from people who didn't have an elevated CK in the first place.

These are people who had elevation and we're talking about how long does it take to get better. It's not 10 to 14 days. It's some longer period in some cases.

Next, why the elderly have such trouble with recovery. "Any and all disorders, if they are sufficiently severe so as to demand a certain proportion of the body's energies, will restrict energies that are available for regenerating muscles."

And so he then said that it's likely that increasing age slows recovery from statin-related myopathy in part because of the increased prevalence of other health conditions and in part because of reduced ability to regenerate muscle tissue due to the loss, significant loss, of satellite cells that are responsible for the regeneration.

So there's an example here and it's probably the most severe case I know of, and I wanted to show Your Honor this case as an example of someone out in the real world who took statins with gemfibrozil.

In fact, this poor gentleman was an Italian-American and he had a communication breakdown with his doctor and he was on Lipitor and he didn't get off Lipitor when his doctor prescribed Baycol. So he was -- admittedly, this is not your typical case, but the mechanism is the same and it stands for some of the same principles.

This is the -- I bring this to the Court's attention as an example to point out that permanent injury from statin exposure can occur with rhabdomyolysis where you can see in his chart the CPK, which is the other term for CK, you can see it going down in the course of a month while he's paralyzed for several months of these records.

So if you look at the summary, he started Baycol June 29th of 2001 while on Lipitor and gemfibrozil. On July 28th his CK was 137,000 and it peaked at 346,000 a couple of days later on August 1st. By August 27th, a month later, it was 59. His CK had gone down into the normal range. A few days later it was even further down to 37.

And those data are blown up at slide 58. You can see when he first got to the hospital 137,000 and then up to 346,000 and then down, down, down because he's off the drug.

And so he -- after he got off the drug it continued to rise while the drug was in his system killing muscle cells and then the drug cleared from his system and no longer was killing muscle cells. And so the CK slowly cleared over the course of -- there's some missing dates where they didn't test apparently, but the bottom line is 37 within a month.

But look what the records say. Just go to page 7, please, Your Honor, if you want to or I'll just read it if

you would prefer, but -- well, first at page 5, four months later he's got an objective pathology report of a biopsy that says there's evidence of muscle fiber injury.

On January 25, 2002, six months after his CK has been at its peak and gone down back to normal, he's stiff in both lower extremities, he can't bend them, he's got contractures that keep his body from bending. They have to pick this poor guy up and move him like a board and put him on his bed because he can't bend anything. He's got a history of rhabdomyolysis.

And then at page 63 you see he was given Baycol for hyperlipidemia and he has quadriparesis, all four limbs won't go, secondary to rhabdomyolysis.

So that's the injury that this person suffered. He is stiff like a board at page 8. His CK is normal, but six months later he is stiff like a board. That's just an example to bring to the Court's attention in a graphic way that a person can have a normal CK that has nothing to do with recovery of injury.

Now, I don't want to leave the Court with the impression that all people are like that, because they're not. And out of 200 clients that my law firm represented who had claims arising from Baycol, he was the worst one.

And did most of them get better? Yes, they did. And did they have a variable course of recovery? Yes, they

did. And did some of them get better quickly? Yes. Did some of them have high CK? Yes. Did some have low CK? Yes. Did some of them not have a test? That's true too. Do they have differing levels of ability to prove causation in a differential diagnosis? Probably so.

But that's the methodology that Your Honor has, I believe, appropriately endorsed for this litigation and the elements of it are not too far apart between the parties.

And I do want to address one issue on qualifications, Your Honor, if I may, and that has to do with Dr. Richman as someone who is able to rely on the literature.

Now, the question is does a person have to be an expert in adverse event reports or epidemiology to read *The New England Journal of Medicine*, and the answer is no. *The New England Journal of Medicine* is a journal for general circulation to about 200,000 doctors who are not epidemiologists, card-carrying or otherwise. They're not FDA specialists, card-carrying or otherwise. They are doctors who read that journal to learn information that's relevant to their practice and that's why the Staffa article was published.

If you look at what Dr. Richman actually says about that article -- I'm a little out of order, but I do

want to try to find that -- he says that there's a consensus by far of the medical community that accepts the Staffa study as being indicative of a higher risk. And that's what we discussed this morning with the recent articles, in particular the Bays article that calls it a high level of evidence for precisely that point.

You don't have to be an expert to read *The New England Journal* and know what it means. A doctor reads that and knows that's why it's in there is to tell you that there's this extraordinary phenomenon out there where one drug that's now off the market is 16 to 80 times worse and, hey everybody, you better pay attention to that. It's a significant finding.

Beyond that, it's important that Dr. Richman -- I believe his credentials in the area of evaluating drug safety and epidemiologic studies were not fully stated in the defense papers and possibly not in our response.

But it should be pointed out that he's published articles that he testified to in his deposition about myasthenia gravis, which is the muscle disorder within his specialization, comparing the safety of drugs based on case series of myasthenia gravis treatment.

So this is a person who has got some experience with comparing drug safety based on case series, so he knows what that's about. And he testified -- that's at page 132

to 133 of his deposition. And also at 133 he said that he reviewed articles about the adverse event reports.

And Dr. Dorfman, the defense expert, stated at his deposition that he does not claim expertise in the field of epidemiology, but that did not prevent defense counsel from eliciting testimony, after the discovery portion of the deposition was over, eliciting testimony from Dr. Dorfman as to the doctor's opinions on the limitations of adverse event reporting databases as well as their advantages and whether such data can be used to generate estimates of disproportionate risk without claiming any expertise in epidemiology.

And I believe that it would be appropriate for the Plaintiffs' expert, who does have experience with drug safety comparisons, to at least offer the opposing perspective based on having reviewed the literature and having done drug safety comparisons himself.

And I believe I'm done subject to any questions that Your Honor may have.

THE COURT: Thank you.

MR. ARBITBLIT: Thank you, Your Honor. I appreciate your time and patience.

MR. ISMAIL: Is there any further argument from the Plaintiffs on this?

MR. ARBITBLIT: Your Honor, I would just

incorporate the same arguments as to Drs. Zizic and Carlson, that they're professional doctors, they're capable of interpreting something in *The New England Journal of Medicine* and the consensus that arose around it.

The consensus that we talked about earlier today has simply confirmed that they were right when they read those articles, that Staffa was right, that no one has questioned it, and that the drug Baycol is off the market for a reason and the reason is it's more toxic.

THE COURT: So incorporated. Thank you.

MR. ARBITBLIT: Thank you, Your Honor.

MR. ISMAIL: May I respond, Your Honor?

THE COURT: You may.

MR. ISMAIL: Thank you.

MR. LOCKRIDGE: Your Honor, while we're setting up, can I pass up Dr. Mayers' documents from --

THE COURT: You may.

MR. ISMAIL: While that's getting straightened out, Your Honor, I will just begin without the reference to some of the documents.

Starting at the end of counsel's comments as to this expertise question, I think the question is fairly well staked out. Dr. Richman is the fellow whose deposition I showed earlier where he said he had never used this data to do comparative safety assessments. Dr. Staffa's letter is

the first safety assessment he's ever seen using this data. And so that's the lack of expertise that we're focusing on here. And he's further one of the witnesses who said it's the only data upon which he's basing his conclusion.

And counsel stated that, well, gee, Dr. Staffa's letter was in *The New England Journal* and it's a general circulation publication and any doctor can read it. Well, the cases that we've cited both in this district and elsewhere have stated the idea that any doctor can comment on any medical issue, to the extent that ever was valid, has been debunked after Daubert and the specialization that has evolved.

So to the extent any doctor can read Staffa, that doesn't mean any doctor satisfies Daubert's requirements for qualifications and expertise. I think the case law bears that out.

And as to Dr. Dorfman, he was asked by Plaintiffs' counsel in his deposition about adverse event data. He has no opinion in his expert report in which we've proffered him to make comparisons of drug safety and it's only after he was asked those questions that our lawyer established his view as to the unreliability of the data.

So I think it's a little unfair to suggest Dr. Dorfman has affirmatively staked out an opinion on drug safety given that he's a neurologist. We have not asked our

neurologist to give an opinion in the area that we've challenged their neurologist from giving an opinion.

And counsel spent a great deal of his remarks talking about the potential for permanent injury after rhabdomyolysis and he showed some examples of cases. All those cases, including the ones that he has shown, have settled. They are no longer a part of this MDL.

And to the extent that there is a severe enough case of rhabdomyolysis where questions of residual injury can be addressed, to the extent one of those cases ever comes back into this MDL, we can deal with that on a case-specific challenge to any such claim of residual injury. But rhabdomyolysis is no longer really a part of this MDL. Instead we have a thousand, more or less, muscle ache cases.

And so there's a great deal of discussion of medical literature, citations to Dr. Dorfman, our expert, where they posit if you hypothesize a severe enough case of rhabdomyolysis, 350,000 CK, can you have some residual injury? That's not what we're dealing with anymore in this MDL. And so what our motion was directed at is the remainder of the cases, not a hypothetical case that's not here.

And what we have stated is that when a patient -- and then we had the statement from counsel, and I don't know

to what extent it's binding on the rest of the PSC since it was only made in the context of Dr. Richman, but the very clear statement if there's no elevated CK, we're not claiming that the system -- the symptoms can persist following discontinuation of the statin. If I have misstated it, somebody can tell me if I have, but that's what I understood Dr. Richman's -- or Mr. Arbitblit's position to be with respect to Dr. Richman.

MR. ARBITBLIT: With the Court's permission, I would like to clarify that that was intended to be the position of the PSC and its experts, that if the CK is tested and it's never elevated, that we do not claim that there's a possibility of permanent injury.

MR. ISMAIL: So now we have --

THE COURT: I think it's been said three times.

MR. ISMAIL: So now we have counsel's statement that what he characterized as the easy case, that it's been tested, it's normal, there's no permanent injury, that this group of plaintiffs is not claiming that that type of injury exists.

But, of course, we have such reports in this MDL and in part that's what we have addressed our motion to, that under Daubert and as apparently joined by the Plaintiffs' Steering Committee, there is no reliable science on that theory.

So then we get to a group of cases where CK was not tested and there is no contemporaneous diagnosis of the myopathy, there's no objective indicia of the myopathy. I am unclear as to whether the PSC thinks there's a permanent injury that results or can be present there, but we have brought in our -- sought in our motion to exclude such theories.

If there is no -- it's only in the rarest of rare rhabdomyolysis cases do you have some residual injury, not in cases where you have -- and if a patient's CK is not tested, that patient didn't have rhabdomyolysis; or if that patient's myoglobinuria -- if there's no diagnosis of myoglobinuria, that patient didn't have rhabdomyolysis. Doctors know to make these laboratory tests.

So if here we have a patient who after the fact reports I had muscle aches and pains on Baycol and there's no -- and of course the treating physician never drew a CK because these are complaints that arise after the fact, those patients can't claim a statin myopathy that continues months and even years after they've stopped taking Baycol.

Just like there's no science to support affirmative normal CK, there's no science to support the idea that we can have this ongoing statin myopathy for which there's no evidence that the patient ever had injured muscles.

So in that respect we would extend the PSC's concession to even those patients in which there was no contemporaneous CK or other indicia of myopathy at the time. So we don't need to address the rhabdomyolysis hypothetical here because that's not what's left in this MDL.

And I don't want to, again, be ships passing in the night or otherwise try to convince them that their experts have a theory that they've disavowed here, but they have in their expert reports said myopathy may include patients who had no elevations of CK, that's one part of their opinion, and then another part, patients with myopathy can have chronic or residual or permanent disability. So they define "myopathy" to be normal CK and then they define "permanent injury" or "chronic injury" in patients who have a myopathy.

So it's not ships passing in the night to worry that there's a theory being staked out here that myopathy can be a chronic permanent injury, and it's to that theory that we brought our motion and responded to every one of their articles and case reports showing all those patients had their symptoms resolved. Even in the Hansen review that we've talked about, every one of those patients had their symptoms resolved. And so it is on that basis that we seek to exclude the theory in line with the Leathers opinion, in

line with the concessions made today by counsel.

And so in light of that, unless Your Honor had specific questions -- and then on diagnosis, CK isn't the only objective indicia. It's the most common. But we have said in our papers and our expert discussed EMGs or biopsies or quantitative strength tests.

So I know this goes back to Mr. Hopper's point that we've attempted to -- I don't know what he said -- drill a hole in the ground with CK and put them in it. That's not the only objective indicia of myopathy that exists. There are others.

And Dr. Mayer, whose deposition I played much earlier this afternoon, he talked about the four objective indicia, EMG, biopsy, CK, quantitative strength test. So it's acknowledging that those possibilities exist, but understanding that there has to be some contemporaneous proof of the myopathy.

Are there any issues you want me to address, Your Honor?

THE COURT: Thank you.

MR. ISMAIL: How do you want to proceed at this point? There's three more Bayer motions and one Plaintiff motion. I could be relatively quick on the three even though they're -- not a lot of overlap. I could take them seriatim.

THE COURT: Why don't you do that. How much time do you need?

MR. ISMAIL: Ten minutes a motion, would that bother anyone here?

THE COURT: How are you doing down there?

COURT REPORTER: Can we take a five-minute break?

THE COURT: Let's take a five-minute break.

(Recess taken at 5:30 p.m.)

* * * * *

(5:40 p.m.)

IN OPEN COURT

THE COURT: You may continue.

MR. ISMAIL: Thank you, Your Honor. If it's all right with the Court, I would proceed with Dr. Raskin and then since I'm up here and we are already set up, I would go right to Dr. Kapit and Dr. Smith, even though they really don't have anything to do with each other, rather than break down the computers one at a time.

THE COURT: I will give you 30 minutes.

MR. ISMAIL: Thank you. Dr. Raskin first. Dr. Raskin is a cardiologist, practicing cardiologist, and he gives opinions in three areas, comparative drug safety, labeling, and normative opinions about Bayer's conduct in the context which I'll address it as in addition to his chronology, as he sees it, of the Baycol story, which we

believe to be squarely on all fours with the Rezulin decision, which excludes these plaintiff -- excuse me -- partisan arguments dressed up as expert testimony.

I don't want to spend a lot of time on comparative drug safety. The parties' positions are well staked out. Dr. Raskin stated in his deposition he is relying either exclusively or principally on AER data and he had no prior experience with AER data before being retained as an expert in this case. And for similar arguments that we've made with the last group of experts, we sought to exclude that opinion with respect to Dr. Raskin.

On labeling Dr. Raskin gives the opinion that Bayer could have and should have included comparisons of spontaneous adverse event data in its label so that these reporting rate studies that we've heard described today should have been either put in quantitative or qualitative statements in the Baycol labeling.

And as to that question Dr. Raskin has no prior experience in pharmaceutical labeling, at least on the FDA regulations issue. He's never helped draft a drug label, never been a consultant to a pharmaceutical company or FDA in regards to drug labeling.

And as to his opinion, he stated at his deposition Bayer could have on its own included the spontaneous adverse event data in its label through this mechanism called the

changes being effected process by which a company prior to receiving FDA approval changes its drug label. There's an animal in the federal regulatory scheme that allows for this, and he opines that that could have been done.

But prior to submitting his expert report in this case, Dr. Raskin never even heard of the changes being effected process and he states so in his deposition at page 90.

"Is it the case, sir, that when you submitted your expert report in this case you had not even heard of the changes being effected process?"

He said, "No, I just had heard about the 'Dear Doctor' letters.

"Was my statement correct?"

He says, "Yes, sir."

And he flat out admits in his deposition he is not an expert in FDA regulations with respect to drug labeling. He's asked at page 86:

"You are not an expert in FDA regulations?

"Answer: That is right."

Again at page 105 he's asked:

"Do you have any expertise to opine as to whether or not the FDA would have approved a change to the Baycol label to list the number of spontaneous events of rhabdomyolysis?

"No, I don't have any particular knowledge of that."

So he's admittedly not an expert in the FDA scheme for drug labeling and yet he seeks to give an opinion on it. His sole basis for his labeling opinion is stated in his deposition, page 91 of his deposition. Let me try it this way.

"The sum total of your work to prepare an opinion regarding what label changes Bayer could have made to the Baycol label consisted of reading Dr. Kapit's expert report, who is another Plaintiffs' expert, and reviewing the published Code of Federal Regulations?"

And he answers, "Yes."

But as to those two issues he states:

"When you submitted your report in this case you had neither reviewed the Code of Federal Regulations nor reviewed Dr. Kapit's expert report, correct?"

And he answers, "That is correct."

So his sole basis for a labeling opinion is Dr. Kapit and the Code, neither of which he ever saw before he submitted his expert opinion in this case.

So here we have the antithesis of a scientifically reliable methodology. We have an expert who has staked out an opinion, later tried to backfill support for that opinion, but he never had that support when he reached his opinion to begin with. That is not the scientific method. That is not scientifically valid and reliable methodology.

So that's Dr. Raskin on drug labeling and there are cases that we cite that preclude experts -- purported experts from giving opinions on drug labeling who do not have prior professional expertise in FDA regulation of labeling and prior experience in the regulatory process governing pharmaceutical labeling. Dr. Raskin is squarely within that case law.

Dr. Raskin also gives an opinion where he states a couple of things with regard to what doctors knew. He says -- he gives the opinion doctors did not know X, Y, or Z about Baycol and he further states I did not know X, Y, or Z about Baycol. So if you would consider those two opinions on their own.

First of all, his speculation as to what doctors knew is not an opinion that would pass Daubert muster. It is speculative. It's inherently anecdotal. He's got no surveys of what doctors knew. He's not someone who has written in the area of physician prescribing behavior. He's got this general gestalt about what doctors -- what he thinks doctors knew about Baycol and wants to opine that he doesn't think doctors as a whole knew about certain alleged toxicity.

And clearly Dr. Raskin can't testify what a specific doctor knew or didn't know, and that's all that is relevant on issues regarding warnings and learned

intermediary.

Dr. Raskin's opinion as to what doctors knew in the abstract can't go on the questions of relevance and fit, to use the Daubert terminology, to an individual doctor's assessment of the warnings and risks and benefits of the medicine.

And even Dr. Raskin's statements that he personally wasn't aware has no relevance whatsoever to whether other doctors in individual cases were aware.

And I think the Plaintiffs have stated in their papers that somehow we confuse that Dr. Raskin is being offered as both an expert and percipient witness. Well, as a -- he has put these opinions about what he knew and didn't know in his Rule 26 expert report, but he's a percipient witness as to what he knew.

And one of the standards under Daubert is the opinion has to be relevant to the issue at hand. And what Dr. Raskin knew in northern California is not relevant to what a doctor in Minnesota knew or doctors elsewhere around the country. So as to that basis under Daubert, Dr. Raskin's speculation as to what the community as a whole knew and what he knew simply is not relevant.

The last topic on Dr. Raskin is his commentary on what he speculates as to Bayer's corporate state of mind and various normative value, ethical judgments he makes in his

testimony and report.

I think the Plaintiffs don't dispute the general legal proposition that an expert cannot opine as to his view of the ethics or pass value judgments on a company. There's particularly in the mass tort area a great number of cases that have excluded such opinions. It's in the Rezulin case. The Diet Drugs litigation has resulted in similar opinions excluding experts.

But to the extent they agree with the case law, I think they don't agree with the application here and I would like to use an example of where courts have excluded testimony along the lines similar to what Dr. Raskin has done.

Here's Dr. Raskin's expert report, and this is just an example. I'm at paragraphs 18 through 21 and this is just one part of a five- or six-page chronology, as Dr. Raskin sees it, of the Baycol story, so to speak.

And he talks about what he thinks the documents show was Bayer's knowledge. Bayer was aware of evidence, rather than encouraging an open and honest disclosure about Baycol's risks, clearly these are normative value judgments that he's passing, but even more to this whole idea of can an expert become a party's -- provide a party's closing argument and look at internal documents and put them in a chronology that is selective and spoon-fed and biased in its

presentation and call it an expert opinion.

And the Rezulin court very clearly shot down the idea that such opinions pass Daubert. This is the court's opinion in the Rezulin litigation, which we have cited in several of our briefs. As plaintiffs' Rezulin historian, therefore, Dr. Gale does no more than counsel for plaintiff will do in argument, propound a particular interpretation of defendant's conduct. And it goes on to exclude the opinion.

And earlier in the opinion, earlier in the court's opinion, it describes that this expert, Dr. Gale, just went through internal company documents and came to an opinion as to the chronology of events. And Dr. Raskin, if you go through his expert report, has done the same thing.

And whether they call it background or whether they call it the predicate facts upon which he gives his opinion, that is not expert testimony. There is no expertise required there, as the courts found in Rezulin and in Diet Drugs. That is a matter traditionally left to juries and not a matter upon which juries need an expert's guidance.

The lawyers can make the arguments and inferences from the internal documents. They don't need an expert to get up and propound an opinion as to what he thinks the chronology shows.

Turning then to Dr. Kapit, Dr. Kapit is a former

FDA employee who didn't have any prior experience while at the FDA with Baycol. He hasn't practiced medicine in some time and he has no clinical experience with these medicines. He hasn't written on the topics that are at issue in this litigation.

One of the areas that we spell out in our motion is an area of preemption of Dr. Kapit's opinions, and I don't want to take the time here to go over all the analysis there. We rely on our papers.

But Dr. Kapit states in his deposition that Bayer submitted the adverse event reports, submitted the preclinical and clinical data with respect to Baycol, was not remiss in withholding any data, but he thinks Bayer should have given something to the FDA that it was not required to give.

And under Buckman and its progeny, a pharmaceutical company who is complying with FDA regulations shouldn't be in a position to wonder down the line what a plaintiff expert would say or a state court jury would say were its real disclosure obligations.

The FDA gets to decide what it wants to receive and how it wants to receive it. That is not for an expert down the line to second-guess and certainly not an issue that a jury can second-guess.

And so to the extent Dr. Kapit is purporting to

impose on Bayer different disclosure obligations than those that are spelled out by the FDA, such opinions are clearly preempted.

Dr. Kapit also has in his report -- and if Your Honor looks to our papers, we seek to exclude his ethical musings about what he thinks of Bayer's conduct. And again the Plaintiffs don't contest the proposition that an expert is not allowed under 702 to give value judgments as to what he thinks of a party's conduct.

And Dr. Kapit's report very clearly uses words like "ethical" or "irresponsible" or "inappropriate," buzzwords that have been consistently ruled out in federal court cases.

And the PSC's response is to acknowledge that case law and they state very clearly in their report -- or in their opposition, Plaintiffs agree that the Court should preclude Dr. Kapit from using the word "ethics" and its cognates and go on to concede the case law which precludes such ethical opinions.

But where we disagree is what they do next when they say -- this is Plaintiffs' opposition to our motion on Kapit -- A close reading of Dr. Kapit's report indicates that the term "unethical" is often used as a synonym for "irresponsible" or even "reckless." So now we have the PSC being Dr. Kapit's personal thesaurus and wherever he said

"unethical" in his report, he really meant to say "inappropriate."

So there's two ways to view this rewriting of Dr. Kapit's opinion. On the one hand, the lawyers could be changing the substance of the opinion -- there's no supplemental report from Dr. Kapit, there's no subsequent declaration on this issue from Dr. Kapit -- or that the words "ethical" and "inappropriate" or "reckless" mean the same thing.

They're either changing his opinion or they're not. And if they're not changing his opinion, then the word "ethical" is the same substantive opinion as saying it's reckless or inappropriate.

And not even the PSC is pretending that they can after the fact go in and rewrite their expert's report and change the substance of the opinion. So what we have here is we're left with the only other alternative, that the word "ethical" is a 100 percent synonym for the words "irresponsible" and "reckless."

Well, Daubert excludes opinions, not word choice. If ethical opinions are -- do not satisfy muster under Daubert, as they clearly do not and as Plaintiffs concede, then calling it by another name and conceding it's 100 percent the same opinion also has to be excludable. You can't just change the word "ethics" and say, well, he really

meant to say "inappropriate," but they're exactly the same.

So whether they want to call it "reckless" or "inappropriate," "ethical," or some new word, the opinion itself is what we're seeking to exclude, not the word choice. And very clearly the case law would exclude it.

And just to show examples, Your Honor, of what we're talking about on the substance here, this is Dr. Kapit's expert report. He's got a section on Bayer's knowledge of excessive toxicity. Now we have an expert speculating as to Bayer's state of mind and, again, under Rezulin and Diet Drugs such opinions are excludable.

Elsewhere in his report Dr. Kapit has examples of irresponsibility generally. There might be one where he thinks irresponsibility specifically, but here's one on generally. And again he's passing value judgments in the sequence of his views as to Bayer's conduct along the way.

He's even got an opinion -- he's even got a section of his opinion on Bayer's priorities and the company's strategy for Baycol. So he is an expert now, apparently, who can derive Bayer's priorities with respect to Baycol; and of course he is in no position to do that. There's no expertise that he's bringing to Bayer on that issue. He's just speculating as to what he thinks the priorities are.

And then he's got an opinion where he goes through

what he says is the history of Baycol and he goes through his view of the story. It's a story, however, of corporate ambitions for profit and prominence that overcame good judgment.

It reads less like an expert report and more like he's writing a work for general circulation. He's got his view of the Baycol story. There is no expertise that would assist the trier of fact that he's bringing to that question.

And since we haven't had a reference to Vioxx in almost an hour, I will make one now. Dr. Kapit and other experts who have attempted to give state of mind and normative, ethical value and judgment opinion testimony in that litigation have been excluded just like they have in Rezulin and Diet Drugs. So the string of exclusionary rulings in this area that began a few years ago has continued right through this past year.

THE COURT: Don't beat a dead horse on this one.

MR. ISMAIL: Yes, sir.

So then with respect to Dr. Kapit, there's only just one other area and that is the foreign regulatory issues. Dr. Kapit has several references to interactions that Bayer had in other countries and we've sought to exclude that opinion as irrelevant to the issues in the litigation, one of the questions under Daubert, and we have

cited several cases that support that very proposition.

And the Plaintiffs' response is the foreign regulatory proceedings are relevant as to notice and presumably there will be some time on a motion in limine where we can have this fight as to whether as a matter of evidence these interactions can come in as to notice. That is not for this day.

But if the only purpose of these interactions with foreign governments is as to notice, then there's no expertise that Dr. Kapit is bringing to that question. All he is doing now is reciting the facts of the interaction.

And so there's no -- it's no different than him doing a Baycol chronology and putting it in a plaintiff's closing argument sense that these are the facts that he thinks give rise to notice.

And he wants to talk about Australia and Canada. That's not an expert opinion. Those are just facts that a jury does not need, to the extent they are admissible at all, and we have cited in our papers that other Baycol courts have excluded this very evidence, but that's for another day in the federal court system.

But as to the opinion testimony, there's no expertise there. It's just the recitation of facts that a jury can understand and a plaintiff can make the argument and inferences from them.

And so that concludes Dr. Kapit and I'll quickly deal with Dr. Smith, who is a toxicologist, not a medical doctor, and Mr. Beck played a portion of his testimony many hours ago.

He gives -- he has no prior research experience with statins or Baycol or publications, which is not a dispositive factor to preclude him, but it's relevant in this Court's analysis of his opinions.

Dr. Smith states his opinion is that Baycol is the most toxic statin. He relies in part on adverse event data, again, lacking the qualifications there to use that in his analysis, and he relies also on animal and test tube data.

And as far as I can tell, he's relying on three studies, the Matsuyama study, the Matzno study, and an internal Bayer in vitro study. Each of these three studies involved high dose either petri dish or animal testing.

Dr. Smith does not rely on any human pharmacology testing, as far as I can tell, to give a comparative safety opinion. Instead he extrapolates from super high dose test tube and animal studies to give an opinion about human toxicity.

And we have cited case law in the Eighth Circuit, the Glastetter case, and in the Supreme Court the General Electric case which have stated such extrapolations from high dose test tube and animal models to human toxicity does

not meet Rule 702.

The Plaintiffs do not distinguish these cases. They say instead that there's no per se blanket exclusion to rely on animal or test tube data to give an opinion on human toxicity.

And that per se exclusion has never been presented. The Supreme Court or the Eighth Circuit hasn't had to invoke a per se exclusion, but just finding on the facts of those cases that the evidence is not sufficiently reliable.

And we don't believe a per se exclusion is something this Court has to reach either, but instead on the facts of this case, just like in all the others, there is no reliable extrapolation that can be made.

The Plaintiffs do not cite a case finding solely from toxicology high dose animal and test tube models that an expert can give an opinion on general causation. And what they say instead is -- this is their opposition -- they say, well, gee, Dr. Smith is saying -- does not base his opinion on the extrapolation of the results of high dose animal studies to human. He's actually basing his opinion on a comparison of high dose animal studies between statins.

Well, that's a less reliable or greater analytical leap than what the cases have already excluded. You've got high dose animal and test tube studies which courts have

said you cannot extrapolate to humans, but he wants to take those on two different statins and then compare them to each other. He's got multiple layers of unreliability in that analysis, far in excess of what courts have already excluded.

THE COURT: You've set the trap.

MR. ISMAIL: I'm sorry, sir?

THE COURT: You've set the trap. Let's see if they can get out of it.

MR. ISMAIL: Well, in that case --

THE COURT: So save your few minutes to respond to what they've got to say.

MR. ISMAIL: Then I will not proceed further there.

On mechanism, which we have also sought to exclude from Dr. Smith, he's got the opinion that -- you saw this term "apoptosis" in the motion and in the briefs.

Mr. Arbitblit a moment ago said there is no generally accepted view on what the mechanism is for a statin myopathy. Lots of theories have been thrown out and he said there are proponents and detractors for each.

Dr. Smith apparently is a proponent of the apoptosis theory, but he admits there's no human clinical data in support, no pharmacology data in support, no animal data in support, no test tube data in support. He admits

it's just a theory, and we've provided the deposition citations from his own admissions that it's his theory.

However inspired it may be, it is not grounded in scientifically reliable methodology. Instead it's his *ipse dixit*. He says that's the mechanism and he'll be prepared to defend it, but that is all the farther it goes.

He also has an opinion that Bayer's metabolism increased the likelihood of its interacting with other drugs. He admits there's no peer-reviewed literature in support of that opinion.

And we noted for the Court that Plaintiffs' other toxicologist, Dr. Pang, flatly disagrees with Dr. Smith. He said this dual pathway for drug metabolism for Baycol was not a reason to believe they would have a higher susceptibility to drug interaction.

And so, again, it's an interesting theory that he advances, but not one that's been repeated anywhere outside his expert opinion in this case.

Lastly, Your Honor, Dr. Smith joins other experts in giving value judgments about Bayer's conduct. And the response from the Plaintiffs was, well, gee, he is only quoting from Bayer's own internal documents; and that's at page 23 of their opposition to our motion on Dr. Smith. That's not a response to pass muster under Daubert. That's a reason to exclude it under Daubert.

If all he is quoting is internal Bayer documents and putting them in whatever chronology or drawing inferences from them, that's for a jury to do and that's what the cases have held; and Dr. Smith's attempt to the contrary doesn't pass muster under Rule 702.

And with that, thank you, Your Honor.

THE COURT: Thank you.

MR. ARBITBLIT: Your Honor, Mr. Black will be addressing the Kapit motion and I will be addressing Raskin and Smith. We can go in whichever order you prefer.

THE COURT: I will leave it in your hands.

MR. BLACK: And then, Your Honor, I can go directly into the motion on Dr. Arrowsmith-Lowe.

THE COURT: That's fine.

MR. ARBITBLIT: May I provide these and use them as little as possible, Your Honor?

THE COURT: Most definitely.

MR. ARBITBLIT: There's one for Dr. Smith, two copies, and one for Dr. Raskin, two copies.

THE COURT: You've got 20 minutes and the yellow light will come on with 10 minutes to go so you will know to switch gears.

MR. ARBITBLIT: I'll start with Dr. Raskin, Your Honor. The interesting issue with Dr. Raskin is that Bayer called him an expert when they hired him, put him on a

speakers panel and said you're an expert and we'd like you to help us sell Baycol and promote it to other doctors.

And there's, I think, a qualitative and important difference between someone who is simply hired to tell the Rezulin [sic] story as an outsider versus someone who was hired by the company to tell that story to doctors and then found out the story wasn't true and that he was misled and he wasn't told what the company knew.

And so it's not simply -- it's an important distinction in this case and an important contribution that Dr. Raskin can make to what, after all, is a story for a jury. It's not just about science.

And he is a fact witness. He's a percipient witness. He was there. He was told that Baycol was as safe as other drugs at the same time that Bayer was accumulating data, more and more each month, that it was not telling him. As he was going about the business of preparing to tell other doctors how safe Baycol was, he was not being told that they were having these doubts internally and compiling data that was showing that wasn't necessarily so.

Now, Dr. Raskin did testify that he does have some familiarity with adverse event reporting systems. He's not -- he doesn't have to be an FDA expert to testify to that. What he has to do is meet the standard that's in the Diet Drugs case, which is that he is permitted to testify

that the label did not match what was known or scientifically knowable. And that also feeds into the issue of state of mind.

Now, knowledge is an element of the cause of action or a claim for relief for failure to warn. What was known or scientifically knowable defines the duty of a manufacturer to disclose risk. So the idea that knowledge is a forbidden state of mind for an expert to talk about is -- would make the claim for relief unprovable, so that can't be the standard.

When it gets into intent, then perhaps -- then that does cross the line. When it gets into ethics, that does cross the line. But when it's about knowledge, that does not cross the line. That's essential testimony about what was known or scientifically knowable and did it match the label.

Now, the position that Dr. Raskin takes and testified to is that on other occasions throughout his experience as a treater and prescriber he had seen examples of companies that did disclose risks based on adverse event reports and that his notion of what a drug company should tell a doctor was based on that experience and as well as reviewing the Staffa article, which we've had enough discussion about whether there's a consensus on that. I won't go into that again, but we think that he was entitled

to rely on that.

But he was a statin expert. That's why he was asked to be on the panel. He was asked to tell the story of Baycol being as safe as other drugs to other doctors and he is in a unique position factually to say I was not told what they knew; and if I had known, I would not have agreed to be a part of their panel and I would not have prescribed this drug because to me as a prescriber that signal should have been disclosed.

Now, there are two very important factors that support him on that. One is -- and this doesn't get talked about much, but it is important and it is in his report -- on December 15, 1999 Bayer issued a "Dear Doctor" letter.

That "Dear Doctor" letter changed the landscape as far as what doctors were told about Baycol, but it only changed it as to combination use. It said combination use with gemfibrozil is not a good idea, we recommend against it. And that got stronger over time, but that was the initial information to the public.

But what hasn't been said often enough but Dr. Raskin does say it is that at the very same time frame the very same data analysis that Bayer was doing of adverse event reports also showed excess risk for monotherapy. That was not said, but it was in the data. It's in the report. It's in the data.

Dr. Raskin is entitled to say if Bayer could disclose a risk that they got from adverse event reports that they say are so irrelevant but yet they acted on them -- that was the only basis in December 1999 for that warning, was their internal analysis of the adverse event reports compared to other statins -- and they want congratulations for doing the right thing and warning the community, but if they're going to warn about combination use, what insulates them from warning about monotherapy, which is also shown to be elevated in the same database? Why is Dr. Raskin somehow precluded from testifying they told me about one, why didn't they tell me about the other? He shouldn't be precluded.

He testified that other companies had given him the opportunity to do the right thing by giving him information when there was adverse event spikes that showed that there was a potential problem.

Now, the other thing that supports him is that Dr. Dorfman agreed with him. And the testimony of -- Dr. Dorfman, who also believed that he had received the "Dear Doctor" letter of December 15, 1999 and said at his deposition in September of 2004 that that was the type of information he expected to receive from drug manufacturers, testified as follows: And this is at slide 10 of the Raskin presentation.

"Question: Are you suggesting it would be prudent for the manufacturer to let doctors know if they discover a particular signal of higher adverse event reporting even if they haven't yet concluded that the relationship is definitely there?

"Answer: Yes.

"Question: Would your answer be the same whether the data showed increased reporting rate relative to prescription numbers for Baycol in monotherapy as opposed to this December 1999 letter pertaining to combination therapy with gemfibrozil?

"Answer: I don't see why there should be a difference."

And frankly, Your Honor, neither do I see why there should be a difference. And the point is that Dr. Dorfman expected that type of information to be disclosed as a treating doctor so that he could make treatment decisions that were based on the knowledge that the company had. Dr. Raskin is entitled to say as well that the label did not disclose what was known or scientifically knowable.

And I believe that the report of Dr. Raskin, for example, in the last paragraph, indicated that in summary Bayer did not tell practicing cardiologists or the medical community what it knew about the risks of muscle toxicity associated with Baycol.

That goes to knowledge. That's a state of mind that is not off limits. It's within bounds. It's necessary to proving the failure to warn because what has to be proved is that there's something that's known or scientifically knowable.

And with that I would like to move on to Dr. Smith, with the Court's permission.

THE COURT: You may.

MR. ARBITBLIT: Thank you, Your Honor. Now, the issues with Dr. Smith, I'm sorry, I'm going to have to rush through them because they are somewhat more complicated. In fact, even some of the names of the authors are hard to pronounce.

But the point is that you don't -- I don't believe that it's a fair interpretation of the law on animal studies that you start with the presumption that they're out. The presumption is the opposite. The Reference Manual says that there is a role to play for animal studies. They are a part of the entire picture.

They're not the only evidence of Baycol's greater toxicity. Whether it's Dr. Smith or someone else testifying, there's plenty of evidence in this case about Baycol's greater toxicity.

And to exclude someone talking about animal evidence that's within their speciality, first of all, he --

I believe that he is entitled to rely on the literature as far as whether he thinks it showed excess toxicity based on Staffa and a few people that cited her with approval as of the time he wrote his report.

But in addition to that, this evidence on what the animal studies show is not in isolation. You can't take one expert and say this expert is divorced somehow from the other evidence in the case.

If there's evidence in the case of greater toxicity, which there is plenty of evidence that we've talked about today, someone else talking about what the animal studies show is relevant to the entire evidentiary portrayal. And so this is a piece of the puzzle, not the entire puzzle.

In addition, I would point out that we've -- first I'll just cite to the Reference Manual at 206 -- 2006, page 405 and 569, on the issue of using animal studies. One can usually rely on the fact that a compound causing an effect in one mammalian species will cause it in another species. That's a quote. So the presumption is that it should be permitted, not that it shouldn't.

The Bayer documents about the steep dose-response curve are mirrored in the recent literature on -- for example, the Bays article that we talked about earlier that talks about a threshold dose being reached for Baycol at

marketed doses at .4 and going way up with .8 that wasn't happening with other marketed doses of other statins. So there's a -- it's not just -- what we're seeing is later research again validating the opinions that Dr. Smith had on this narrow window.

Now, as far as human data, well, bioavailability on average 60 percent, much higher than the bioavailability of other statins. That's based on human data. So the assertion that there's no human data in Dr. Smith's report is wrong. He does talk about the human data.

And bioavailability is part of what the literature says is a reason -- bioavailability means more of the drug gets into your system where it can do some harm instead of getting excreted where it's harmless.

So the literature that we've submitted does include many references to bioavailability as one of the things that could be contributing as a plausible mechanism to the greater toxicity of Baycol for human muscles.

Now, another example of recent literature -- and I think this is important because it's the first study as scientists continue to progress and I think supporting the opinions he came to previously -- at slide 11 there's a reference to the Yamazaki article, which is a 2006 study that said in human skeletal muscle cells that cerivastatin was the most potent inhibitor of cholesterol biosynthesis

and showed the most cytotoxicity, which means cell killing.

So this is human skeletal muscle and that's a scientific advance that confirms what Dr. Smith was saying based on the animal studies. There were no human skeletal cell studies as of the time of his opinion. Now there are. They confirm what he said previously.

The narrow safety margin that Dr. Smith talks about is again something that has been confirmed in the Bays article, about going up to a .4 and you have exceeded the threshold dose for toxicity. That's because you have a narrow window between the threshold for efficacy and for toxicity.

Good drugs, as Dr. Smith testified, have a large window so that when you are getting what you want out of the drug, you're not risking what you don't want. Bad drugs are too close together where what you need to lower cholesterol is too close to what you have for killing cells.

So that narrow window is talked about in Bays, it's talked about in Jacobson, and it is a serious issue for Baycol.

Now, on the dual metabolic pathway, well, this is -- I hope I have time to explain this as I would like to, Your Honor, but the situation is if you would like to look and see if this would help at all, it's starting at slide 14, that the issue with drug-drug interaction is that

if -- drugs are taken out of the body through various pathways that metabolize them. You take it in and you have to get rid of it.

If you don't get rid of it soon enough, it builds up as you keep on taking more of the drug. So that means that your body concentration gets higher and higher and exceeds a threshold dose and then you have cell killing.

The problem with Baycol that makes it more susceptible -- and there are examples given in the slide presentation and the biggest one is gemfibrozil itself, which is found to be a special case for Bayer, for Baycol, where it's more toxic with Baycol than with any other drug. And the reason is the dual pathways because, as it's now been published, there's the second pathway.

They have these acronyms. CYP3A4 is a very common pathway for four of the statins to be metabolized, but CYP2C8 is crucial, it's called crucial to the metabolism of Baycol, not to the other statins. So if you have another drug that's taking up the CYP2C8 or inhibiting it, then you can't get rid of the Baycol.

And that's what they found that gemfibrozil does. It increases the concentration called the area under the curve which measures your systemic exposure over time. It increases it six-fold with Baycol, but not with other statins.

And that's an example of confirming what Dr. Smith testified, that if you couldn't see that that was a possibility, it was weak thinking; and he's been proven right.

The research shows that CYP2C8 is the reason why gemfibrozil is so bad in combination with Baycol but not other statins, because it's using up the stuff that would get rid of the Baycol, in plain English. If you had more CYP2C8, then you could get rid of the Baycol. If you've got gemfibrozil using it up, then you can't get rid of the Baycol.

And so there are examples in here -- now, I do want to talk about Dr. Pang. Again, Dr. Pang had just seen Dr. Smith's rebuttal report on these dual pathways. And if you look at slide 19, the part that was not included in the excerpt provided by defense counsel is that she says she doesn't agree with Dr. Smith, but then she does. She says both things. Well, that's not much of an opposition to his opinion.

She says -- and this is the part that was left out -- "But of course if you have two enzymes, the incidences of drug-drug interaction, as Dr. Smith pointed out, become higher because you have two different components that could be interacted with."

And that's what's happening with Baycol having the

CYP3A4, which interacts with drugs like cyclosporine and many others and causes a higher rate and also with gemfibrozil, which is one of the acknowledged bad combinations. And we cite to the literature that also talks about those interactions at slide 20.

Let's see. We acknowledge that Dr. Smith will not testify as to whether Bayer acted ethically, but, again, the issue is that statements in Bayer's documents that they made publicly and that they've made to the FDA are not only relevant to a fraud on the FDA claim, as the Kittleson case points out in this district, statements made to the FDA are evidence of negligence for the main claim of failure to warn the patient and the patient's doctor. A failure to -- an FDA fraud claim means that the individual is trying to claim a private right of action because the FDA was defrauded.

And that's not what these plaintiffs are alleging in the Baycol cases. They're alleging, as in Kittleson, their own right under a failure to warn theory and, as in Kittleson, statements to the FDA that are not accurate are evidence of negligence, not evidence of a fraud on the FDA.

And so Dr. Smith is entitled to talk about what they said that was contrary to known or knowable scientific information at the time, and that's what he did.

Thank you, Your Honor.

THE COURT: Thank you.

MR. BLACK: Your Honor, if I might approach, I have PowerPoints prepared. In the interest of time I would like to pass both of them up at once.

THE COURT: You may.

MR. BLACK: I've handed one to counsel as well.

With regard to Dr. Kapit on preemption, Your Honor, there's two kinds of preemption at issue. There's preemption of fraud on the FDA --

THE COURT: First off, how much time do you need? Ten for Kapit. On your motion how much time do you need?

MR. BLACK: I would think five minutes, Your Honor.

THE COURT: The yellow light will go on in five minutes. As you can tell, the GSA has turned off the ventilation, so that five minutes may be cut down to a couple of minutes.

MR. BLACK: We'll move along, Your Honor. I understand. May I proceed, Your Honor?

THE COURT: You may.

MR. BLACK: With regard to Dr. Kapit and preemption, there's two kinds of preemption at issue. There's the preemption of fraud on the FDA claims under Buckman. It's in the PowerPoint. It's in our briefing.

In the Vioxx litigation Judge Fallon held that Buckman had no bearing at all on the admissibility of

Dr. Kapit's testimony, a specific ruling on exactly this point.

In this district there have been three rulings all holding that Buckman did not preempt the use of evidence about communications to the FDA to prove claims of negligence or failure to warn.

And those cases -- the most recent one is the Medtronic decision in which Chief Judge Rosenbaum said you can't use the evidence solely to show fraud on the FDA, but you can use it to establish a failure to warn claim or other state tort law claims. In 2004 Judge Tunheim in the St. Jude case held similarly and in Kittleson, to which Mr. Arbitblit has already referred, Chief Magistrate Noel similarly held.

So that's all I will say on Buckman unless the Court -- unless Your Honor has some questions about that.

With regard to Geier, Geier is the idea that regulations establish both a floor and a ceiling. Geier was a case about air bags. And after the Department of Transportation had explicitly rejected a proposed regulation that would require air bags on all cars, plaintiffs go into court and say that a Honda is defective because it doesn't have an air bag. And that's the Geier case.

The Supreme Court said, no, under those circumstances, when the agency has explicitly ruled upon the

very action that you want the defendant to have taken, then it's preempted. And I don't believe that applies here at all, Your Honor.

There's also been a preamble to some rules that came out about a year ago where the FDA was pushing this idea of Geier preemption. The FDA has recently clarified that in a letter brief that was submitted I think it's in the Eastern District of Pennsylvania. It's in the Perry case, Perry vs. Novartis.

And what's interesting about that is that there the FDA makes clear that all we're talking about is language that the FDA explicitly rejected or would have rejected. And I don't think either of those applies here.

Bayer never went to the FDA and said, Please, please, can we add some warning language about monotherapy myopathy? That was never done. That was never explicitly rejected.

And as to the would have rejected, we know what happened when the FDA finally learned. On August 3rd there was a letter sent to Bayer saying we think there's real problems with this drug, and the details I'll leave to Your Honor to read the exhibit yourself.

And there was an August 17th memorandum in which the FDA addressed the situation and, among other things, raised serious questions about PacifiCare, raised serious

questions about the adverse event evidence, what the adverse event evidence showed about Baycol.

So it's pretty clear that the FDA would not have rejected a stronger warning had Bayer proposed it; therefore, you don't have either rejected or would have rejected.

And finally on that point, the Perry court, the court to which that letter brief was submitted, rejected the brief. It said we don't accept that argument at all. So even if you accept the brief as the outer limits of Geier preemption, it doesn't apply here.

And a number of courts have said -- have not recognized the FDA's argument on that, and it isn't just the Perry court. The majority of courts that have considered the argument have rejected it, and those cases are listed in our briefing or in the PowerPoint.

With regard to ethics, I don't want to beat this horse anymore, Your Honor. I don't think -- first of all, Dr. Kapit's report is not going to come into evidence; or if we for some reason wanted to put it into evidence, we would have to redact it and have to agree on some redaction with Bayer. So that's not an issue.

And I don't think there would be an issue with any testimony he'd give. He'll be testifying about things like -- as Mr. Arbitblit explained with regard to

Dr. Raskin, he would be testifying to things like this is what Bayer did, this is the information Bayer had available to it, this is what I saw other companies do when they had similar information available to them, this is how they reacted; and therefore, I don't think that Bayer acted with what I would typically expect -- within what I would typically expect a pharmaceutical company to do. That's the kind of testimony he's going to give.

And in the PowerPoint I've suggested and I think for purposes of today it's about as far as we can go. We are not going to be giving -- we are not going to be eliciting testimony from Dr. Kapit about ethics or state of mind. We'll state that clearly on the record.

And I would suggest that Your Honor take the approach that Judge Fallon did in the Vioxx litigation and issue a ruling to that effect and leave the details to objections at trial should the issue arise at trial.

That's all I had to say about the ethics. As to the foreign regulatory actions, what Dr. Kapit is relying upon is not only the fact that there were communications from foreign regulatory agencies to Bayer about Baycol, but also relying on the scientific substance of those communications.

So to the extent that the Australian Therapeutic Goods Administration is a scientific agency, as the FDA is,

and the Therapeutic Goods Administration found that there was an elevated rate of muscle problems with Baycol as compared to other statins, that's scientific information on which Dr. Kapit is perfectly -- or should be allowed to rely and about which he should be allowed to testify.

And that's the way he would be using that. So it's both for the scientific findings of foreign regulatory agencies as well as for notice, that information of which Bayer should have taken notice.

And that's all that I have to say on Dr. Kapit. If the Court is willing, I'll move on to Dr. Arrowsmith-Lowe.

THE COURT: All right.

MR. BLACK: I think I will do this in two minutes, Your Honor. This issue is very, very narrow.

There were several documents, in particular a document prepared by an individual named Steve Niemcryk, I think I have pronounced that correctly, but also other comparisons of adverse event reporting rates that were conducted by Baycol and never provided to the FDA.

I'm not sure they have been provided to the FDA even today, but certainly up through August of 2001, when the drug was taken off the market, that information had never been provided to the FDA.

There's a rule that clearly states that you have

to report on studies undertaken during a three-month period or one-year period in a periodic safety update report. During the time at issue here it would have been every three months that one of these reports had to be submitted. That's what the regulation clearly states.

So you've got this study. Again, we're talking about something that happened two and a half -- two years to a year and a half before the drug is finally off the market Bayer is conducting these studies and during that whole period of time never tells the FDA.

Your Honor, that simply cannot be right. It clearly falls within the regulation and Dr. Arrowsmith-Lowe should not be allowed to give testimony to the contrary. I think you've got the documents in front of you and I think you can rule based on that.

THE COURT: Thank you.

MR. BLACK: Thank you, Your Honor.

THE COURT: Short response.

MR. ISMAIL: May I make a couple of comments on the three motions that I referenced earlier, very briefly?

I have nothing to comment further on Dr. Smith, but as to Dr. Raskin, I think Mr. Arbitblit tried to limit his testimony, but then walked right back into the case law when he says he wants to opine as to what Bayer knew. Bayer didn't tell me what they knew, well, that requires him to

speculate as to what he thinks Bayer knew.

And they say in their brief Dr. Raskin feels duped. Well, that's not a fact in relevance in any one of these cases. Whether -- Dr. Raskin's personal feelings about what he thinks Bayer knew is not at issue and wouldn't be relevant under Daubert.

And just to clarify this suggestion that Dr. Raskin was part of the Bayer family, so to speak. He went to one meeting, never spoke on behalf of Bayer. It was in 1999 in which other cardiologists were invited to participate.

And if Dr. Raskin actually wanted to give an opinion about cardiology or lowering lipids or whether he thinks Baycol was a lousy statin or whether he thinks lowering cholesterol isn't really as good as Bayer made it out to be, well, then that would be an area in which he is qualified and an area in which he participated in this lipid conference.

But not for him instead to comment about things in which he's admittedly not an expert, what he thinks Bayer could have done and the FDA regulations, comparative drug safety and what he thinks Bayer knew.

Lastly, on Dr. Kapit under Geier preemption, FDA had the very data that Plaintiffs say we are obligated to put in the label. We got it from the FDA. In fact, the FDA

did its own comparative analyses. Mr. Beck showed it earlier.

So this idea that under Geier preemption what the FDA would have done had this information sought to be included in the label, we have conclusive proof that the FDA had the data, had the analyses. Not only did they not require it to be added to the label, they subsequently approved the .8 dose, the doubling of the dose. So this idea that FDA would not -- or would have acted had the information been provided to it is just flat-out wrong.

And lastly, I don't want to spend any more time, but if you read Dr. Kapit's report, it is replete with his normative and state of mind hypotheses. And accepting counsel's attempt to put boundaries around it may be very well good in this situation, but we have an expert report that is going to travel on remand and we have an expert who clearly can't give the opinions he wants to give.

And Mr. Black saying, well, that's not what I'm going to ask him really doesn't do us any good in this context. What we're seeking to have is the entirety of those opinions excluded on state of mind and ethics and what he thinks a company should have done in similar circumstances.

And with that, I am going to turn the Dr. Arrowsmith-Lowe response to Mr. Baum, our colleague.

MR. BLACK: I hate to do this at this hour, Your Honor, but just one very brief surreply with regard to what the FDA knew.

This is sort of a situation where they told the FDA, they told the FDA. They hid the data. They didn't break any rules necessarily because it's sort of somewhere in the document, but there's no evidence that the FDA considered all that data. And they certainly did not provide the comparative analyses that they had done. The FDA never considered that.

If that's the argument on preemption, if the FDA actually had adequate data to reach a decision, then I think what you have is a factual issue that you have to get into in order to deal with preemption; and that's not something we're going to do here today. That requires another hearing on preemption and that would make Dr. Kapit's testimony on how the FDA works and processes information even more relevant and admissible.

THE COURT: Thank you.

MR. BAUM: Good evening, Your Honor. I'll be very brief in responding to the Arrowsmith-Lowe motion.

THE COURT: Good evening.

MR. BAUM: I would like to start by focusing on what the PSC does not dispute in its motion.

First, the PSC does not dispute that the subject

matter of Dr. Arrowsmith-Lowe's testimony is proper subject matter for expert testimony generally. Here we have an undisputed FDA expert interpreting FDA regulations and applying them to relevant issues in the case. I would note the PSC has disclosed its own FDA expert, Dr. Kapit, to opine on the very same matters.

Second, the PSC does not dispute that Dr. Arrowsmith-Lowe is sufficiently qualified as an FDA expert.

Third, the PSC does not dispute that Dr. Arrowsmith-Lowe employed a proper methodology in reaching her opinion. Here Dr. Arrowsmith-Lowe reviewed the relevant regulations, applied them to the documents at issue, and using her undisputed experience and expertise determined that the documents did not fall within the scope of the reporting requirements. Notably, the PSC -- neither in its motion nor in its argument has the PSC offered some other mode of methodology that would have been more proper in this circumstance.

And fourth, the PSC does not dispute that Dr. Arrowsmith-Lowe's opinion is relevant to the issues in this case.

So that brings us to the one thing that the PSC does dispute in its motion and that is Dr. Arrowsmith-Lowe's conclusion that Bayer was not obligated to provide the

specific data compilations of rhabdo AER data pursuant to Section 314.80.

Again, a party's disagreement is not a basis for excluding evidence under Daubert. Daubert itself states, and I'm quoting here from page 595 of Daubert, The focus, of course, must be solely on principles and methodology, not on the conclusions that they generate.

Here the PSC has not challenged the principles or methodology used by Dr. Arrowsmith-Lowe in any way. The sole basis of the motion is that Dr. Arrowsmith-Lowe is, quote, simply wrong.

Dr. Arrowsmith-Lowe adequately provided her reasoning for her opinion. She stated on pages 187 and 188 of her deposition that, first, the sort of data contained in these documents is not the sort of data that allows for reliable conclusions about comparative drug safety. That's the same position as espoused by the FDA in the caveats document we saw earlier today.

And second, at page 183 Dr. Arrowsmith-Lowe testified that these data compilations were not studies within the meaning of the regulation cited by Mr. Black. They weren't preclinical or clinical trials. They weren't epidemiology studies. They had none of the indicia of a study in the traditional sense. There was no formal protocols, no inclusion or exclusion criteria, no generation

of new data at all. Bayer simply took data mostly from the FDA and put it into a tabular form.

By way of contrast, I would point to the PacifiCare study or the Baycol/gemfibrozil interaction study. Those clearly were studies that were initiated in response to adverse experiences. The same cannot clearly be said of the Niemcryk or Sprenger analyses. And in the opinion of the expert in this case, Dr. Arrowsmith-Lowe, it can't be said at all.

So simply put, Defendants believe that the PSC has raised no Daubert challenge at all. It's not an adequate basis to disagree with the conclusion. And certainly Plaintiffs are free to cross-examine Dr. Arrowsmith-Lowe at trial regarding this opinion, but it's not a basis, in our opinion, to exclude the testimony.

That's all I have.

THE COURT: Thank you very much.

Anything further? If not, I'll take everything under advisement and next time I might listen to Mr. Lockridge when he says everything should be submitted on the record.

MR. LOCKRIDGE: We tried, Your Honor.

THE COURT: No, I prefer oral argument and I would not change my ruling on that. I thank you for being patient with me and getting everything done this evening.

You should really thank Mrs. Simpson because we start up trial tomorrow at 9:00 and she will have a few minutes to ice her fingers before we get started again.

So have safe journeys and it's good seeing you all again and I'll get the order out as quickly as possible.

COUNSEL: Thank you, Your Honor.

(Court adjourned at 6:50 p.m.)

* * *

I, Lori A. Simpson, certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

Certified by: _____
Lori A. Simpson, RMR-CRR