IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

In re: AVANDIA MARKETING SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	:	MDL No. 1871 Case No. 2:07-cv-05360-CMR
THIS DOCUMENT RELATES TO: DEBORAH A. BURFORD, et al., Plaintiffs, v. SMITHKLINE BEECHAM CORPORATION d/b/a GLAXOSMITHKLINE, Defendant.	:	

PLAINTIFFS' PRETRIAL MEMORANDUM

Plaintiffs Deborah Burford, et al., by and through undersigned counsel of record submit the following pretrial memorandum and accompanying attachments pursuant to local rule 16.1(c) and Pretrial Order 124.

I. JURISDICTIONAL STATEMENT

The Court has diversity jurisdiction over this case pursuant to 28 U.S.C. § 1332, in that the parties are citizens of different states, and the amount in controversy exceeds $75,000. The Plaintiffs are citizens of North Carolina, while defendant GlaxoSmithKline is a corporate citizen of Pennsylvania. Additionally, this Court has jurisdiction as the MDL court for the Avandia litigation, as designated by Judicial Panel on Multidistrict Litigation pursuant to its authority under 28 U.S.C. § 1407(a).

II. STATEMENT OF THE FACTS OF THE CASE

James Burford lived in Advance, North Carolina, with his wife of 27 years, Debbie, and their two children, Sarah, 10 and Michael, 16. He worked as an electrical parts salesmen for the same company for twenty years.

In 2004, only two years before his death, Jim was diagnosed with Type II diabetes. Like most persons with diabetes, he struggled with his weight, had high blood pressure and high cholesterol. He proactively managed these health issues and stayed active.

When Jim was first diagnosed with diabetes, his family doctor, Dr. Spencer, prescribed Metformin. Metformin is well known as the "gold standard" first-line treatment for Type II diabetes. On August 22, 2005, Dr. Spencer suggested that Jim add Avandia to his Metformin regimen. He began taking 4 mg of Avandia daily. Unfortunately, Avandia was not effective at controlling his blood sugar levels. On December 23, 2005, Dr. Spencer doubled the dose to 4 mg twice per day, the maximum approved dose of the drug. Jim compliantly took his new dose.

About three weeks after doubling his dose of Avandia, Jim had an episode where he awakened in the middle of the night sweating and felt his heart was beating fast. All experts in this case have described the event as likely a "myocardial ischemic attack." As noted, it occurred within weeks of Jim doubling his Avandia dose. Because Avandia, even at the highest dose, was not working, in October Dr. Spence added glyburide, a sulfonylurea, to Jim's prescriptions.

Later that year, on Sunday, November 19, 2006, Jim was not feeling well. He told his wife that he was extremely fatigued, was suffering from a headache, had shortness of breath, and was experiencing leg cramps. At Mrs. Burford's deposition, she recalled that her husband's face looked "puffy" in the month prior to his death, and that he was experiencing difficulty removing his wedding band. The following day, Monday, Jim continued to have a headache and stayed home from work. On Tuesday, he drove his son to school and went to work. But, by 2 p.m. on the afternoon of November 21, 2006, Jim was feeling so poorly that he returned home.

About an hour later, Debbie Burford returned home from work after picking up her 10-year-old daughter, Sarah, and one of Sarah's friends from school. As Debbie Burford entered the house, she called out Jim's name, but she got no response. As she came into the family room, Debbie noticed that Jim was lying on the sofa with his eyes partially open, and that he looked kind of bluish around the lips. Mrs. Burford grabbed the phone and started to call 911. Sarah and her friend came in the front door, and upon seeing her mother's fright, she asked her mother what was wrong. Debbie whispered "I think Daddy's asleep," and shooed Sarah and her friend off to play in her room upstairs. Mrs. Burford called 911, told them she feared her husband had died, and was given instructions on what to do to resuscitate him. She testified that she "tried to

resuscitate him and tried to, you know, give him mouth-to-mouth; and there were already fluids in his mouth. It was gurgling."

Minutes later, the school bus carrying Michael Burford pulled up outside. He saw the driveway was filled with EMS vehicles. He got off the bus and ran home. When he came in, he saw his father to the left laying down "with his feet up on the seat like he always did to watch TV, and there were a bunch of people around him, and there was a blanket or something over his face." Jim Burford was pronounced dead. He was 49 years old.

Because the death was unexpected, particularly in someone so young, Dr. Spencer ordered an autopsy. The autopsy revealed that Jim had suffered from a myocardial infarction – a heart attack. A thrombus (blood clot) was found in one of the arteries that provides blood to the heart, his right coronary artery. Both the autopsy report and death certificate state that Jim died of a myocardial infarction.

Dr. Spencer testified that it was his practice to talk with his patients about medication options, the reasons for the medications, and the risks involved. When prescribing Avandia, Dr. Spencer did not discuss the increased risk of myocardial infarction that comes from use of the drug. In November 2006, Dr. Spencer could not know that Avandia had been shown to cause heart attacks because GSK had not warned physicians in the United States about the risk. In Europe, one month before Jim Burford died, GSK added a warning to the label saying Avandia had been shown to increase the risk of myocardial ischemic events, such as heart attacks. GSK did not put that warning in the U.S. label until a year after Jim's heart attack.

Dr. Spencer testified that he now believes that the other commercially available thiazolidindione (TZD), Actos, is safer than Avandia, "with no apparent increased risk of myocardial infarction or heart attack in patients with Type II diabetes that take Actos." Further,

Dr. Spencer testified that had GSK timely warned of the increased risk of myocardial ischemic events, he would have prescribed the safer alternative for Jim, Actos. He also testified that Jim's death, only 2.5 years after being diagnosed with diabetes, was "uncommon."

Plaintiffs will demonstrate that Glaxo knew of the heart danger risks of its drug Avandia. That it manufactured and sold this drug to a population that was already vulnerable to these risks. Moreover, Plaintiffs will show Glaxo failed to warn physicians and patients, including Jim Burford and his physician, of these risks. Finally, had Glaxo warned physicians and patients of this dangers, Jim Burford would not have been prescribed Avandia and would not have had a heart attack and died at age 49.

III. ITEMIZED DAMAGES FOR THE ESTATE OF JAMES BURFORD

Economic Damages

Damage	**Amount**
Lost Wages:	$ 1,159,700.00
Lost Value of Household Services:	$ 215,400.00
Funeral Expenses:	$ 11,286.93
Davie County EMS:	$ 1,142.36
TOTAL[1]	**$ 1,387,529.92**

Non Economic Damages

Damage	**Amount**
Pain and Suffering, James Burford	to be determined by a jury
Emotional Distress, Deborah Burford	to be determined by a jury
Emotional Distress, Michael Burford	to be determined by a jury

[1] Plaintiffs damages may be trebled if they prevail on their claim under North Carolina law for unfair and deceptive trade practices.

Loss of Consortium, Deborah Burford		to be determined by a jury
Loss of Services/Society Michael Burford		to be determined by a jury
Loss of Services/Society Sarah Burford		to be determined by a jury
Punitive Damages		to be determined by a jury
	TOTAL	**to be determined by a jury**

IV. LIST OF INTENDED WITNESSES (DESIGNATED SEPARATELY FOR LIABILITY AND DAMAGES)

Please see Attachment A to this Pretrial Memorandum for the list of intended witnesses to testify at trial.

V. SCHEDULE OF EXHIBITS TO BE OFFERED AT TRIAL

Please see Attachment B to this Pretrial Memorandum for the list of exhibits to be offered at trial.

VI. ESTIMATE OF REQUIRED TRIAL TIME

Plaintiffs anticipate needing six full days of trial time.

VII. STIPULATIONS

The Parties will continue to work toward stipulations regarding all issues, including evidentiary matters.

VIII. AMENDMENTS OF PLEADINGS OR OTHER APPROPRIATE MATTERS

None at this time.

IX. PROPOSED VOIR DIRE QUESTIONS

Plaintiffs' proposed voir dire questions are attached to Plaintiffs Pretrial Memorandum at Attachment C.

X. PROPOSED JURY INSTRUCTIONS (ONE POINT PER PAGE)

Plaintiffs' proposed jury instructions are attached to Plaintiffs Pretrial Memorandum at Attachment D.

XI. PROPOSED JURY INTERROGATORIES

Plaintiffs' proposed jury interrogatories are attached to Plaintiffs Pretrial Memorandum at Attachment E.

XII. SPECIFIC LEGAL ISSUES INVOLVED IN THE CASE

A. Plaintiff Must Demonstrate Glaxo Failed to Warn Doctors and the Public

During the recent *Daubert* hearing, Glaxo took the position that its conduct in this case should be measured solely by reference to what it told Jim Burford and his doctor and what Avandia did to Jim Burford. In essence, Glaxo wants to limit all evidence in this case to issues of specific causation. To do so, would prevent Plaintiffs as a matter of law from meeting the burdens imposed upon them to prove their entire case.

Plaintiffs have alleged that Glaxo failed to warn of the heart dangers of its drug, Avandia. Under North Carolina law, to prove such a claim Plaintiffs must demonstrate, among other things, that at the time Avandia left the control of the defendant without an adequate warning or instruction:

1. Avandia created an unreasonably dangerous condition;

2. that the defendant knew or, in the exercise of ordinary care should have known, posed a substantial risk of harm;

3. to a reasonably foreseeable claimant.

See Plaintiffs' Proposed Jury Instructions, Failure to Warn. For purposes of this instruction, "Ordinary care means that degree of care which a reasonable and prudent

manufacturer would use under the same or similar circumstances to protect others from injury or death." *Id.*

Hence, Plaintiffs must demonstrate not only that Avandia was dangerous to Jim Burford's heart (as Glaxo would limit the proof), but that Glaxo knew or should have known that it was dangerous to the heart of a reasonably foreseeable user (i.e., patients with diabetes). As such Glaxo's knowledge about the medical risks Avandia posed to diabetes patients in general is fundamental to Plaintiffs meeting their burden of proof.

The actions it takes or refuses to take to gain the appropriate knowledge of the dangers are measured against what a reasonable and prudent manufacturer would do under the same circumstances. Glaxo has not, and will not, stipulate to this element upon which the Plaintiffs bear the burden. In fact, to this day, Glaxo denies both that Avandia is dangerous to the hearts of patients with diabetes and that it had any knowledge of Avandia's unreasonably dangerous condition.

Hence, pursuant to F.R.E. 401, Plaintiff must be permitted to introduce that evidence which has a tendency to show Glaxo knew or should have known Avandia was dangerous to the hearts of diabetes patients. In addition, Plaintiffs must be permitted to introduce evidence of the circumstances to demonstrate whether Glaxo acted in a reasonable manner in those circumstances. To satisfy this burden, Plaintiff will present evidence that:

- In 1994, Glaxo knew Avandia increased heart problems in pre-clinical animal studies;
- In 1998, in Glaxo knew Avandia increased LDL or bad cholesterol, a clear marker of cardiovascular risk;

- In 1998, Glaxo knew Avandia increased ApoB, a clear marker of cardiovascular risk;

- In 2000, Glaxo knew Avandia increased Lp-PLA2, a novel marker of cardiovascular risk;

- Glaxo scientists had multiple exchanges with scientists, analysts and regulators about the increase in myocardial ischemic events with the use of Avandia.

Glaxo's counsel seeks to exclude this evidence. They claim it is irrelevant here by asserting that the specific patient, Jim Burford, did not experience some of these negative effects of Avandia. They argue that the warning and concerns of scientists and regulators notifying Glaxo of the risks are irrelevant to Jim Burford's heart attack or what his personal physician knew or did not know. However, all of this evidence goes directly to demonstrate that Glaxo knew or should have known under the circumstances existing at the time that Avandia was dangerous to the heart. This is a fundamental element of Plaintiffs' liability case. If the Court should exclude this notice evidence, Glaxo will surely move for dismissal claiming lack of proof as to its knowledge of Avandia's unreasonably dangerous condition. Repeated signals and notifications of the heart risks of Avandia should be presented for the jury's consider as to whether Glaxo knew or should have known of the heart dangers of the drug.

Clearly, Glaxo will contend that the evidence was not robust enough to put it on notice. It is welcome to do so. However, Plaintiffs must be permitted to demonstrate to the jury that when confronted with such evidence a reasonable manufacturer should have known and therefore warned physicians and patients of Avandia's dangerous condition.

B. Glaxo's Duty to Inform Goes Not Only to Jim Burford and His Physician, But to all Doctors and patients who might be foreseeable recipients of that information

Plaintiffs must also demonstrate that, when confronted with this notice of the risks of Avandia, Glaxo unreasonably failed to inform physicians and patients. Again, the extent of Glaxo's duty and the test of its reasonableness are not limited to Jim Burford and/or his physician, as Glaxo has represented. In fact, Glaxo's legal obligation as set forth in the applicable regulations is not tied to Jim Burford or Dr. Spencer. Glaxo must revise its label "as soon as there is reasonable evidence of an association of a serious hazard with a drug." This legal duty runs to all reasonably foreseeable physicians and patients.[2] Hence, evidence of Glaxo's failure to inform physicians and patients about the heart dangers of Avandia is essential to Plaintiffs' ability to prove their case. To meet their burden, Plaintiffs must be permitted to demonstrate what Glaxo did and did not do in response to the knowledge of the cardiovascular risks. For example, Plaintiffs must be permitted to present evidence that, while knowing of the heart dangers:

- Glaxo affirmatively marketed Avandia as cardio-protective;
- Glaxo did not publish data and studies showing the heart dangers;
- Glaxo designed studies to avoid showing heart dangers;
- Glaxo chose to warn physicians and patients of the heart dangers in countries outside of the United States while not informing physicians here;
- Glaxo sales materials minimized the heart dangers of Avandia;
- Glaxo refused to let physicians discuss the heart dangers.

All of this evidence, and more, has some tendency to show Glaxo did not act as a reasonably prudent manufacturer should have acted when knowing of the heart dangers of a

[2] In addition to their failure to warn claim, Plaintiffs have alleged that Glaxo's sales of Avandia constituted an unfair and deceptive act. To meet their burden on this claim, Plaintiffs must show Glaxo knew "that taking Avandia increases the risk of suffering a heart injury and fail[ed] **to warn doctors or the public about that risk**."

drug. Assuming the evidence is otherwise admissible, Plaintiff should be permitted to introduce it to the jury.

Finally, under North Carolina law, this evidence goes directly to prove proximate causation. Contrary to Glaxo's assertions at the *Daubert* hearing, Plaintiff may prove proximate causation through Glaxo's failure to warn the medical community of Avandia's dangers. "[T]he North Carolina Court of Appeals has specifically concluded that proximate cause may be established based on failure to warn not only the prescribing physician, but also other "foreseeable" treating medical professionals pursuant to "standard principles of negligence law." *See Fussman v. Novartis Pharmaceuticals Corporation, Slip Copy, 2010 WL 4104707, *2* (M.D.N.C. 2010) (citing *Holley v. Burroughs Wellcome Co.*, 74 N.C.App. 736, 746, 330 S.E.2d 228, 235 (1985). Hence, the North Carolina Supreme Court "thus [extended] proximate cause to treating medical personnel (not just the prescribing physician), based on information provided by the manufacturer to the medical profession generally through 'medical journals, professional literature distributions and package inserts." *Id.*

C. Plaintiff Need Not Prove that Avandia Was the Sole Cause of Jim Burford's Heart Attack

In the instant action, Plaintiffs must prove by a preponderance of the evidence that Glaxo's conduct was *a* proximate cause of Jim Burford's heart attack. Glaxo, by invoking the "but for" standard, has suggested to the Court that to establish proximate cause Plaintiffs must prove to a medical certainty through expert testimony that Avandia was the sole and exclusive cause of Jim Burford's heart. This is incorrect.

North Carolina law is very clear: Plaintiffs need only demonstrate Avandia was *one* cause of Jim Burford's heart attack. Moreover, Plaintiffs need not prove it with certainty. As one court applying North Carolina law has stated: "Proximate cause is ordinarily a question of fact

for the jury, to be solved by the exercise of good common sense in the consideration of the evidence of each particular case' .... [and] '[c]ausation is an **inference** of fact to be drawn from other facts and circumstances.'" *Fussman v. Novartis Pharmaceuticals Corp*., Slip Copy, 2010 WL 4104707 (M.D.N.C. 2010).

Under the North Carolina Pattern Jury Instructions, a defendant's conduct need not be the sole cause of plaintiff's injuries but rather one proximate cause. *See N.C. Pattern Jury Instructions* 102.19.[3] Similarly, North Carolina's Pattern Jury Instructions for a products liability claim of inadequate warning or instruction provide:

...Proximate cause is a cause which in a natural and continuous sequence produces a person's [injury] [death] [damage], and is a cause which a reasonable and prudent person could have foreseen would probably produce such [injury] [death] [damage] or similar injurious result. There may be more than one proximate cause of [an injury] [a death] [a damage]. Therefore, the plaintiff need not prove the defendant's failure to provide an adequate warning or instruction was the sole proximate cause of the [injury] [death] [damage]. The plaintiff must prove, by the greater weight of the evidence, only that such failure was a proximate cause.

N.C. Pattern Jury Instructions 741.70.[4] Both of these instructions (negligence and failure to warn) establish that the defendant's negligence need only *a*, not the sole, proximate cause in bringing about the plaintiff's injuries and not the only cause.[5]

[3] "There may be more than one proximate cause of [an injury] [damage]. Therefore the plaintiff need not prove that the defendant's negligence was the sole proximate cause of [injury] [damage]. The plaintiff must prove, by the greater weight of evidence, only that the defendant's negligence was a cause."

[4] Pattern Instructions regarding claim of inadequate design or formulation utilizes substantially the same language. *See N.C. Pattern Jury Instructions* 741.71

[5] North Carolina Courts continue to use the "substantial factor" test in determining issues of proximate cause. *See, e.g.* Self v. Yelton, No. COA09-207 (N.C. App. January 5, 2010) ("it must be shown that the defendant's actions were a substantial factor...of the particular injuries for which the plaintiff seeks recovery."

This result is clear in the North Carolina case law as well. A review of the case law in North Carolina shows that where an action was a substantial factor in bringing about the injury the court may find causation. In *Peal v. Smith*, 115 N.C. App. 225, 234 (1994), the court found there was sufficient evidence for a jury to find that defendant's failure to enforce an employment policy that prohibited an employee from being on a project work site under the influence of alcohol was a substantial factor in brining about the injuries sustained by the plaintiff in a car accident caused by defendant's employee after consuming alcohol at the work site. In making this finding, the court stated, "[a]n actor may be liable if his negligence is a substantial factor in causing an injury, and he is not relieved of liability because of the intervening act of a third person if such act was reasonably foreseeable at the time of his negligent conduct..." *Id*. at 234.

Glaxo's contention that liability in this case arises only as a result of "but for" proximate causation stands in stark contrast with the North Carolina Pattern Jury Instructions and well settled case law.[6] Plaintiffs need only prove that GSK's conduct (i.e., negligent design, failure to warn, etc.) was *a* substantial factor in causing James Burford's myocardial infarction and premature death. Plaintiffs, however, need not establish that Glaxo's conduct was the sole cause of James Burford's injuries; other contributing causes may exist.

[6] Both parties are in agreement that North Carolina substantive case law controls the instant action.

Respectfully submitted this 7th day of January, 2011.

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CERTIFICATE OF SERVICE

I hereby certify that on this 7th day of January, 2011, a true and correct copy of Plaintiffs' Pretrial Memorandum was served via the court's electronic filing system upon the following counsel:

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