No. 15-____

IN THE
Supreme Court of the United States

IN RE: AVANDIA MARKETING, SALES PRACTICES & PRODUCTS LIABILITY LITIGATION:

GLAXOSMITHKLINE LLC,
Petitioner,

v.

ALLIED SERVICES DIVISION WELFARE FUND, UFCW LOCAL 1776 AND PARTICIPATING EMPLOYERS HEALTH AND WELFARE FUND, AND UNITED BENEFIT FUND,
Respondents.

On Petition For A Writ Of Certiorari To The United States Court of Appeals For the Third Circuit

PETITION FOR A WRIT OF CERTIORARI

Nina M. Gussack
Anthony C.H. Vale
Yvonne M. McKenzie
PEPPER HAMILTON LLP
3000 Two Logan Square
Eighteenth & Arch Streets
Philadelphia, PA 19103
(215) 981-4000

John H. Beisner
Counsel of Record
Jessica D. Miller
Geoffrey M. Wyatt
SKADDEN, ARPS, SLATE, MEAGHER & FLOM LLP
1440 New York Ave., NW
Washington, DC 20005
(202) 371-7000
john.beisner@skadden.com

Attorneys for Petitioner

QUESTIONS PRESENTED

This case involves claims by third-party payors ("TPPs") that they overpaid for Avandia, a prescription diabetes medication manufactured by petitioner, GlaxoSmithKline ("GSK"). The TPPs claim that GSK failed to disclose risk information, entitling them to recovery under the Racketeer Influenced and Corrupt Organizations Act, even though they do not allege that Avandia was ineffective; that it injured any one of their plan participants; or that they stopped covering it after learning about the drug's alleged risks. The Third Circuit nevertheless held that the TPPs could plausibly allege that GSK's representations had an "inflationary effect" on the drug's price. In so ruling, the Third Circuit expressly declined to follow the Eleventh Circuit, which had previously rejected similar claims, and also departed from several other appellate decisions rejecting similar "fraud on the market" theories. The Third Circuit also concluded that the TPPs plausibly alleged proximate and factual causation, again contradicting the decisions of other circuits. The questions presented are:

1. Whether a TPP states a plausible RICO injury by alleging that a manufacturer's failure to disclose risk information inflated the price of a medication.

2. a. Whether the independent decisions of prescribing doctors break the causal chain under RICO where a TPP alleges that it paid more because a manufacturer's misrepresentations caused doctors to write more prescriptions for a medication.

b. Whether a TPP must allege specific facts tying an alleged fraud to its own decision to cover a drug under its prescription plan in order to properly plead factual causation.

CORPORATE DISCLOSURE STATEMENT

Petitioner GlaxoSmithKline LLC is owned, through several levels of wholly-owned subsidiaries, by GlaxoSmithKline plc, a publicly traded limited company organized under the laws of England. To the knowledge of GlaxoSmithKline LLC and GlaxoSmithKline plc, none of the shareholders of GlaxoSmithKline plc owns beneficially 10 percent or more of its outstanding shares. However, the Bank New York Mellon ("BNYM") acts as Depository in respect of Ordinary Share American Depositary Receipts ("ADRs") representing shares in GlaxoSmithKline plc. In that capacity, BNYM is the holder of more than 10 percent of the outstanding shares in GlaxoSmithKline plc.

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PETITION FOR A WRIT OF CERTIORARI

Petitioner GlaxoSmithKline LLC ("GSK") respectfully petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Third Circuit in this case.

OPINIONS BELOW

The opinion of the Court of Appeals (App. 1a-29a) is reported at 804 F.3d 633. The opinion of the United States District Court for the Eastern District of Pennsylvania (App. 30a-62a) is unpublished but available at 2013 U.S. Dist. LEXIS 152726.

STATEMENT OF JURISDICTION

The Court of Appeals issued its decision on October 26, 2015. On November 9, 2015, GSK filed a petition for panel rehearing or rehearing *en banc*. The Court of Appeals denied this request on November 25, 2015. This Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

The Racketeer Influenced and Corrupt Organizations Act ("RICO"), states, in relevant part, that "[a]ny person injured in his business or property by reason of a violation of section 1962 of this chapter [18 U.S.C. § 1962] may sue therefore in any appropriate United States district court and shall recover threefold the damages he sustains and the cost of the suit, including a reasonable attorney's fee . . . ." 18 U.S.C. § 1964(c).

STATEMENT

This case presents important and recurring questions that have divided the lower courts in cases involving RICO claims brought by third-party payors ("TPPs") against drug manufacturers. In particular,

the decision below approved a theory of RICO injury based on allegations by TPPs that they paid too much for a drug – even though they do not allege that the drug was ineffective or injured any of their beneficiaries. The Third Circuit's decision squarely conflicts with the Eleventh Circuit's ruling in *Ironworkers Local Union 68 v. AstraZeneca Pharmaceuticals*, 634 F.3d 1352 (11th Cir. 2011), which expressly held that a plaintiff TPP cannot establish the requisite loss to support a RICO claim against a drug manufacturer based solely on an allegation that a drug was misrepresented and that cheaper alternatives were available, *id.* at 1363-64. The Court of Appeals acknowledged *Ironworkers* but declined to follow it, suggesting that *Ironworkers* was wrongly decided and concluding that the respondents could proceed on the theory that GSK's alleged misrepresentations or omissions about cardiovascular safety caused them to pay more for the diabetes drug Avandia than they otherwise would have. This price-inflation theory – which was not pressed by respondents and was co-opted by the court below from the antitrust context – also conflicts with other courts of appeals that have rejected price-inflation theories in the prescription-drug context and is tantamount to a fraud-on-the-market theory that many other courts have rejected under RICO.

The decision below also contravened the holdings of this Court and many lower courts regarding the sufficiency of causation under RICO in two ways. First, the Third Circuit parted ways with the Second and Ninth Circuits, as well as several district courts, in failing to hold that the intervening decisions of prescribing doctors break the causal chain and render causation too attenuated under this Court's

RICO precedents, which hold that proximate causation is lacking where the alleged causal connection between a RICO violation and injury is not sufficiently direct. Second, the Third Circuit permitted the TPPs to rest on conclusory allegations of reliance that did not offer any factual detail about the alleged misrepresentations they received or how the TPPs relied on them – contrary to an Eleventh Circuit ruling in a similar case and this Court's decisions in *Twombly* and *Iqbal*, which expressly held that courts must not "unlock the doors of discovery for a plaintiff armed with nothing more than conclusions."

These important issues repeatedly arise in TPP suits against drug manufacturers, which comprise a significant and growing segment of prescription-drug litigation in this country. The pattern in such cases is typically the following: a study raises questions about the risk-benefit profile of an FDA-approved drug, prompting a debate in the scientific community. As the debate continues, TPPs and others bring suit claiming that they would have refused to cover the drug or paid less for it if the risk had been discovered earlier. In nearly all such cases, including this one, the TPPs continue to cover the drug after filing their lawsuits, undermining their own claims that they were duped into paying for it. And additional studies are often published after a lawsuit is filed, refuting the initial study results that led to litigation in the first place. This case is a particularly compelling example of that pattern: over the course of the Avandia controversy, the FDA required a so-called "black box" warning and imposed a restrictive-prescription program, only to reverse course and eliminate both the warning and the restrictions a few years later.

Unfortunately, plaintiffs rarely wait for the science to settle. The promise of treble damages increasingly drives many litigants – even TPPs, which face their own share of dubious RICO suits – to label ongoing scientific debate and differences of opinion as "fraud." The implications for the entire pharmaceutical industry are enormous – threatening virtually limitless liability in many cases in which the *drug worked* and *none of the TPP's beneficiaries is alleged to have been injured*. For these reasons, it is especially important that the questions presented in this case are resolved correctly and that RICO requirements are applied in the same way across the circuits.

A. Avandia

Avandia belongs to the class of drugs known as thiazolidinediones ("TZDs"). TZDs were developed in the 1990s as a new form of treatment for the most common form of diabetes: Type 2. Avandia was approved for sale in the United States by the Food and Drug Administration ("FDA") on May 25, 1999.[1] Since Avandia's introduction, more than one million individuals in the United States have used the drug on a regular basis. Prior to the introduction of TZDs, Type 2 diabetes was generally treated with metformin, sulfonylureas, or injected insulin.

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[1] This case also involves two related drugs, Avandamet and Avandaryl. Avandamet, which combines Avandia and metformin in one pill, was approved by the FDA on October 10, 2002. Avandaryl, which combines Avandia and glimepiride in one pill, was approved by the FDA on November 23, 2005. Because the allegations do not meaningfully distinguish among these drugs, they are referred to collectively as "Avandia."

Following Avandia's introduction to the market in 1999, the FDA required GSK to amend its warning for Avandia on several occasions. In 2001, GSK added a warning to its prescription label, cautioning doctors that use of Avandia could cause fluid retention. In 2006, GSK added data on a non-statistically-significant increased incidence of heart attack and heart-related chest pain in some patients taking Avandia. The following year, in November 2007, the FDA required GSK to add a "black box" warning regarding the potential increased risk of heart attacks and other ischemic events. The FDA's action in November followed publication of a meta-analysis in *The New England Journal of Medicine*, which reported that Avandia was associated with a statistically significant increase in the risk of myocardial infarction and a borderline-significant increase in the risk of death from heart-related diseases compared to competing diabetes medications. Although some TPPs discontinued coverage of Avandia following release of the May 2007 meta-analysis, the TPPs in this action did not remove Avandia from their formularies or restrict coverage of the drug. (App. 51a.)

In September 2010, after reviewing developing data regarding cardiovascular risks, the FDA went further, limiting Avandia to: (i) patients already using the medication (as long as the patient's doctor advised the patient of potential cardiovascular risks) or (ii) new patients whose blood sugar was inadequately controlled with other medications and who decided, in consultation with their physician, not to take Actos (another TZD). (App. 39a; see also App. 192a-193a.)

Then, in 2013, the FDA dramatically shifted course. After "determin[ing] that recent data" for

Avandia "do not show an increased risk of heart attack compared to the standard type 2 diabetes medicines metformin and sulfonylurea," the FDA removed restrictions on the drug. See FDA, *Drug Safety Communication*, Nov. 25, 2013 ("FDA Nov. 25 Communication"), *available at* http://www.fda.gov/Drugs/DrugSafety/ucm376389.htm (last visited Feb. 23, 2016). And in December 2015, the FDA announced that it had "continued monitoring" Avandia, "identified no new pertinent safety information," and determined that special regulatory oversight of the medication was no longer necessary. FDA, *Drug Safety Communication*, Dec. 16, 2015, *available at* http://www.fda.gov/Drugs/DrugSafety/ucm476466.htm (last visited Feb. 23, 2016). As a result of these developments, the Avandia label no longer contains a black-box warning about the risk of heart attacks, and the "Warnings and Precautions" section has been revised to include, in addition to the 2007 meta-analysis, the FDA's latest conclusion that studies of Avandia "do not show an increased risk of heart attack compared to the standard type 2 diabetes medicines metformin and sulfonylurea." *See* FDA Nov. 25 Communication.[2]

B. Respondents' Allegations

Respondents are union health and welfare funds that provide medical and prescription drug coverage to their beneficiaries and their beneficiaries' dependents. Most TPPs obtain administrative services from

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[2] Although these developments post-dated the complaints at issue here, the Court may take judicial notice of the statements of a federal agency. See Fed. R. Evid. 201(b); see, *e.g.*, *Funk v. Stryker Corp.*, 631 F.3d 777, 783 (5th Cir. 2011) (affirming judicial notice of FDA letter).

companies known as Pharmacy Benefit Managers ("PBMs"), which are responsible for preparing a formulary – a list of drugs that are approved for coverage when prescribed to the TPP's beneficiaries.

Respondents, which covered Avandia under their formularies, filed putative class actions against GSK, alleging that it failed to disclose the heart-related risks of Avandia and asserting claims for: (1) violations of RICO and state consumer protection laws; and (2) unjust enrichment. Respondents alleged subject-matter jurisdiction under the Class Action Fairness Act, 28 U.S.C. § 1332(d)(2). (App. 86a, 180a, 279a.)[3]

The thrust of respondents' allegations is that GSK failed to disclose that Avandia poses an alleged heart-attack risk. Respondents further allege that "PBMs and pharmacy and therapeutic committees relied on Defendant's misrepresentations regarding Avandia's safety when approving and/or placing Avandia on formularies" and that "[TPPs] relied on the Defendant's misrepresentations regarding Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their" beneficiaries. (App. 141a-142a, 235a (same), 332a (same).) Respondents also contend that (i) "[b]ut for Defendant's actions, [TPPs] would not have paid for Avandia but would instead have paid for safer, equally efficacious drugs like metformin and/or sulfonylureas" (App. 142a, 235a (same), 332a (same)); and (ii) "Defendants' deceptive and misleading marketing scheme increased the number of prescriptions of Avandia

[3] The Court of Appeals determined that the district court had jurisdiction pursuant to 28 U.S.C. § 1331, and that it had appellate jurisdiction pursuant to 28 U.S.C. § 1292(b).

written and filled during the Class Period" (App. 139a-140a, 233a (same), 330a (same)).

Notably, respondents did not plead *any facts* in support of *their* generalized allegations of reliance on GSK's alleged misrepresentations; instead, they made only broad statements about *all* purchasers of Avandia.[4] Nor did respondents allege that, after learning about Avandia's alleged risks, they refused to pay for Avandia prescriptions – or that they restricted its coverage in any way. For example, although respondents' complaints focus on safety concerns raised by Dr. Steven Nissen in 2007, there is no allegation that *any one* of the respondents restricted coverage of Avandia or removed it from their formularies after being informed of the alleged risks. Respondents also failed to allege that Avandia was ineffective, that it injured any of their beneficiaries, or that the physicians who prescribed Avandia to their beneficiaries stopped prescribing Avandia when additional risk information became available in 2007 or at any time thereafter.

Importantly, respondents also failed to plead facts in support of their assertion that they would have saved money if their beneficiaries had used an alternative medication. Respondents alleged that a one-

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[4] (See, *e.g.*, App. 235a ("Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors relied on the Defendants' misrepresentations of Avandia's safety. . . . PBMs and pharmacy and therapeutic committees relied on the Defendants' misrepresentations of Avandia's safety when approving and/or placing on their formularies. Third-party payors relied on the Defendants' misrepresentations of Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their [beneficiaries]."); App. 332a (same); App. 141a (same).)

month supply of Avandia sold for $90 to $220, with TPPs typically covering $135 to $140 per prescription and the patient paying the balance. Although respondents also alleged that a one-month supply of metformin (an older diabetes drug) cost approximately $45 to $55, with a TPP covering $40 to $50 of that amount, they did not provide the cost of any other TZD (such as Actos – the drug that respondents themselves alleged to be an "alternative" to Avandia). This omission is significant because, as the district court noted, Avandia was generally only prescribed when older medications such as metformin were unsuccessful for a patient. (3d Cir. JA 314.) And although respondents' complaints contain bland allegations that they "overpaid" for Avandia (see App. 252a; App. 349a; App. 158a), there is no allegation that the price of Avandia declined after the alleged risks were disclosed in 2007 or in subsequent years. As such, plaintiffs did not allege facts sufficient to support the conclusory allegation that they would have paid less but for GSK's supposed misconduct.

C. GSK's Motion To Dismiss

GSK moved to dismiss the respondents' complaints in the district court, arguing, among other things, that respondents lacked standing to pursue their RICO claims because they had not adequately alleged injury and causation.

With respect to injury, GSK argued that paying for a drug that allegedly contains undisclosed risks does not amount to an economic injury under RICO unless the drug is alleged to have been ineffective or harmful. GSK further contended that even if such a theory were generally cognizable, plaintiffs' allegations failed to set forth sufficient facts to show that

their beneficiaries' doctors would have prescribed cheaper alternative drugs instead of Avandia.

GSK also argued that respondents failed to state plausible theories of causation. With respect to respondents' first causation theory – that they would have refused to pay for Avandia but for GSK's allegedly fraudulent conduct – GSK argued that respondents did not plead any *facts* to support this theory, rendering their conclusory allegations implausible. With respect to respondents' alternative causation theory – that they were injured because physicians would have written fewer Avandia prescriptions but for GSK's fraudulent conduct – GSK argued that this theory of causation was too attenuated and failed due to, among other things, the intervening independent judgment of the prescribing physicians. GSK further argued for dismissal of respondents' consumer-fraud and unjust-enrichment claims for similar reasons – specifically, that these claims (like the RICO claims) require allegations of causation and injury, which were not sufficiently alleged for the same reasons set forth in support of dismissal of the RICO claims.

D. Rulings Below

The district court largely rejected GSK's arguments, denying the motion to dismiss as to all of the TPPs' claims except their claims for unjust enrichment. The district court first held that the TPPs "sufficiently allege[d] economic injury at th[e] pleading stage of the litigation" to support their RICO and consumer protection claims by asserting that, if GSK had not misled them about the safety of Avandia,

they would not have covered the drug. (App. 44a.)[5] The court asserted, without explanation, that this conclusion was "unaffected by whether any given patient who ingested Avandia became ill." (*Id.*) At the same time, however, the district court dismissed the TPPs' unjust enrichment claims on the ground that they "received the benefit of their bargains" in the form of an effective diabetes medication that was not alleged to have injured any of their beneficiaries. (App. 62a.) The court did not attempt to reconcile those two rulings.

The district court also rejected GSK's causation arguments. While noting that "it is not clear from the Complaints the extent to which [GSK's] alleged misrepresentations and concealments were directed at the TPPs or their PBMs," the court found that respondents had adequately alleged causation because their complaints generally alleged that "PBMs routinely rely upon existing scientific literature when making formulary decisions, and that they did rely upon such literature when making formulary decisions about Avandia" – notwithstanding respondents' failure to allege what scientific literature they purportedly relied on or when they considered it.

The district court also rejected GSK's argument that the intervening decisions of doctors destroyed proximate causation. According to the court, "first-party reliance is not a necessary element of proximate cause in every private RICO claim." (App. 46a.)

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[5] The district court acknowledged that the TPPs had failed to allege that they would have saved money by covering another TZD (*e.g.*, Actos) instead of Avandia, but held that this "argument is more relevant to summary judgment or the calculation of damages." (App. 44a.)

Thus, "[w]here misrepresentations are directed at prescribing doctors, rather than TPPs, but a TPP, as payor, is a primary and intended victim," "the doctor's independent actions do not break the causal chain" because injury to the TPP is foreseeable. (App. 46a-47a (internal quotation marks omitted).)

On interlocutory review under 28 U.S.C. § 1292(b), the Court of Appeals affirmed. Relying on inapposite antitrust case law, the Court of Appeals determined that respondents had alleged a tangible economic harm under RICO based "on the inflationary effect that GSK's allegedly fraudulent behavior had on the price of Avandia" – an injury that the Court of Appeals determined "d[id] not depend on the effectiveness of the Avandia that [respondents] purchased." (App. 15a.) The Court of Appeals further determined that "the presence of intermediaries, doctors and patients" did not destroy proximate causation. (App. 27a.) Despite concluding that "many of these issues will resurface in the future" and declining to "opine on the likelihood of plaintiffs' success down the road," the Court of Appeals allowed the case to proceed, explaining that "[a]t this stage in the litigation, plaintiffs 'need only put forth allegations that raise a reasonable expectation that discovery will reveal evidence' of proximate causation." (App. 29a (quoting *Fowler v. UPMC Shadyside*, 578 F.3d 203, 213 (3d Cir. 2009)).)

Following this decision, GSK filed a petition for panel rehearing or rehearing en banc. In its petition, GSK argued that the Court of Appeals erred in three significant ways. First, the court adopted an "inflationary effect" injury that was not advanced by respondents and is not cognizable under RICO. Second, the panel opinion ignored one of GSK's key

arguments on appeal: that respondents' complaints did not plead facts sufficient to establish but-for causation because the allegations sounded in reliance but failed to set forth facts showing how any reliance by respondents or anyone else caused *their* alleged injuries. The TPPs did not allege that they actually received and acted on an alleged misrepresentation by GSK or that doctors relied on the alleged misrepresentations in prescribing Avandia to the three TPPs' beneficiaries. Third, the panel's proximate-causation analysis ignored plaintiffs' "quantity-effect" theory, which depends on the independent decisions of third-party physicians.

The Court of Appeals denied the request for rehearing on November 25, 2015. This petition for certiorari timely follows.

REASONS FOR GRANTING THE WRIT

I. The Third Circuit's Holding that Alleged Overpayments for an Effective Drug Suffice to Establish RICO Injury Directly Conflicts with Eleventh Circuit Precedent and Contravenes the Decisions of this Court and Other Circuits.

First, the decision below squarely disagreed with the Eleventh Circuit over whether a TPP sustains a cognizable RICO injury by allegedly paying too much for a drug even though there is no allegation that the drug was ineffective or injured any of the TPP's beneficiaries. According to the Third Circuit, the TPPs stated an injury irrespective of "the effectiveness of the Avandia that they purchased" (App. 15a), a ruling that directly conflicts with the Eleventh Circuit's contrary holding in a similar case.

RICO confers standing only upon a person claiming to be "injured in his business or property by reason of a violation of section 1962." 18 U.S.C. § 1964(c); see *Sedima, S.P.R.L. v. Imrex Co.*, 473 U.S. 479, 496 (1985) ("the plaintiff only has standing if, and can only recover to the extent that, he has been injured in his business or property by the conduct constituting the violation"). A "defendant who violates section 1962 is not liable for treble damages to everyone he might have injured by other conduct, nor is the defendant liable to those who have not been injured." *Sedima*, 473 U.S. at 496-97 (internal quotation marks and citation omitted). Thus, section 1964(c)'s "limitation to a person 'injured in his business or property' has a 'restrictive significance,' . . . which helps to assure that RICO is not expanded to provide a federal cause of action and treble damages to every tort plaintiff." *Steele v. Hospital Corp. of Am.*, 36 F.3d 69, 70 (9th Cir. 1994) (quoting *Reiter v. Sonotone Corp.*, 442 U.S. 330, 339 (1979); other internal quotation marks and citation omitted).

Consistent with this important statutory limitation, some courts have rejected RICO theories of injury in cases, such as this one, alleging that a drug was fraudulently marketed, where the plaintiff does not allege that the drug failed to work or that it suffered injury from any of those risks. In *Ironworkers Local Union No. 68 v. AstraZeneca Pharmaceuticals, LP*, 634 F.3d 1352, 1356 (11th Cir. 2011), for example, the Eleventh Circuit reviewed the dismissal of a RICO action brought by several TPPs (and others) against AstraZeneca, in which the TPPs alleged that the drug manufacturer had fraudulently induced physicians to prescribe the medication Seroquel for numerous off-label uses. *Id.* The TPPs claimed that

AstraZeneca's allegedly fraudulent off-label marketing campaign caused them "'to unnecessarily pay for [the more expensive] Seroquel off-label prescriptions.'" *Id.* at 1357 (quoting complaint). The TPPs sought to recover the difference between the price of the off-label Seroquel prescriptions and the amount that they would have paid for the less expensive alternatives. *Id.* On appeal, the Eleventh Circuit affirmed the dismissal, finding, among other things, that the TPPs failed to allege a cognizable economic injury under RICO.

In its ruling, the Eleventh Circuit concluded that a TPP does not suffer economic injury merely by paying for "a more expensive drug." *Id.* at 1363. As the court explained, because prescriptions are based on the medical judgment of doctors, "a patient suffers no economic injury" by being prescribed one drug simply because cheaper alternatives are available. *Id.* Neither, by extension, does a TPP suffer injury in such circumstances. *Id.* at 1366. After all, TPPs and PBMs make actuarial calculations in establishing premiums to ensure that they can cover a predicted number of prescriptions of a drug and still make a profit – calculations that are not affected by a drug manufacturer's representations to doctors because TPPs "ha[ve] to pay regardless of the facts surrounding [a] prescription." *Id.* at 1365-66. Thus, to state a cognizable injury under RICO, a plaintiff must show something more – e.g., that its beneficiaries' physicians, "would not have prescribed the drug under the standards of sound medical practice" if they had known the allegedly undisclosed information, "because [it] was unsafe or ineffective in treating the [enrollees'] condition." *Id.* at 1363.

Several other decisions have applied similar logic. See, *e.g.*, *Health Care Servs. Corp. v. Pfizer, Inc.*, No. 2:10-cv-221, 2012 U.S. Dist. LEXIS 89759, at *7-8 (E.D. Tex. Apr. 23, 2012) (recommending dismissal of RICO claim by TPP for lack of a RICO injury because, *inter alia*, there was no allegation that the purchased drugs were "either unsafe or ineffective for their prescribed use"), *report and recommendation adopted*, 2012 U.S. Dist. LEXIS 89758 (E.D. Tex. June 28, 2012). As the U.S. Court of Appeals for the Fifth Circuit explained in applying Article III's injury requirement, a plaintiff does not allege a plausible economic injury by claiming that a drug contained a risk that only affected *other* individuals. *Rivera v. Wyeth-Ayerst Labs.*, 283 F.3d 315, 320 (5th Cir. 2002); see also *Dist. 1199P Health & Welfare Plan v. Janssen, L.P.*, 784 F. Supp. 2d 508, 521, 523 & n.23 (D.N.J. 2011) (dismissing RICO claims by TPPs for lack of injury where they "d[id] not identify any participant in their health plans who received an ineffective or off-label Risperdal prescription"; allegations that "alternative medications were more effective or safer than Risperdal" were insufficient); *In re Schering-Plough Corp. Intron/Temodar Consumer Class Action*, No. 2:06-cv-4774, 2009 U.S. Dist. LEXIS 58900, at *67 (D.N.J. July 10, 2009) (TPPs lacked standing under RICO where they failed to plead that any beneficiaries "received inadequate [or] inferior [drugs] or even worse, suffered personal injuries as a result of [d]efendants' alleged misrepresentations") (internal quotation marks and citation omitted).

The Third Circuit acknowledged the Eleventh Circuit's ruling in *Ironworkers* – and indeed expressly noted that the case involved "facts similar to these"

(App. 17a-18a) – but declined to follow it. According to the Third Circuit, it is improper to make any "presumption at the motion-to-dismiss" stage regarding the manner in which TPPs set their premiums (App. 18a) – even though it was the *plaintiffs'* burden to plead facts showing that they sustained injury. The Third Circuit also expressed its concern that the Eleventh Circuit's holding "lacks a limiting principle" and would give a green light to fraudulent conduct by drug manufacturers (*id.*), ignoring the fact that the heavily regulated drug industry already has several disincentives to engage in fraud, in the form of FDA sanctions, Medicaid fraud suits brought by state attorneys general, and consumer and personal injury suits, to name a few.

Instead, the Third Circuit chose to part ways with its sister circuit and create an entirely new theory of RICO injury for drug cases that respondents had not even advocated: i.e., that an insurer can recover for the supposed "inflationary effect that [a drug manufacturer's] allegedly fraudulent behavior had on the price of" a drug. (App. 15a.)[6] The Court of Appeals

[6] The Third Circuit did not appear to embrace either of the theories of injury that respondents actually advanced – i.e., that they were injured by paying for Avandia because cheaper drugs were available or that they were injured because physicians prescribed the medication with more frequency than they otherwise would have. These theories of injury would also fail as a matter of law under *Ironworkers* because the TPPs do not allege that the drug was ineffective or that it caused physical injury to their beneficiaries. In addition, the TPPs' first theory – that the TPPs would have covered cheaper drugs – lacks sufficient support in the pleadings. As noted above, the TPPs alleged that metformin was cheaper than Avandia, but they did not offer any allegations comparing the price of Avandia to that of Actos – the only drug in the same class as Avandia that is mentioned in the

did not cite any RICO precedent from its own decisions or those of any other court in support of its conclusion, presumably because courts have rejected this theory time and again. As this Court held in *Anza*, the price a defendant sets for its products is "entirely distinct" conduct from the same party's allegedly fraudulent statements; after all, the decision to set a particular price "in no sense require[s] [a company] to defraud" anyone. *Anza v. Ideal Steel Supply Corp.*, 547 U.S. 451, 458-59 (2006). Thus, a theory of injury that depends on the notion that a defendant's alleged fraud allowed it to set a certain price for its products is too attenuated to be sustainable under RICO. See *id.* As one court put it, "'such a theory is patently absurd'" because it "depend[s] on the faulty premise that the price of [a medicine] fluctuates based on the public's knowledge of [the medicine's] benefits, even though drug prices (unlike stock prices which are necessarily set by the price at which buyers are willing to buy, or sellers willing to sell) are fixed by the product's manufacturer." *Prohias v. Pfizer, Inc.*, 485 F. Supp. 2d 1329, 1337 (S.D. Fla. 2007) (quoting *Heindel v. Pfizer, Inc.*, 381 F. Supp. 2d 364, 380 (D.N.J. 2004)).

Consistent with this reasoning, other federal courts – including several other courts of appeals – have squarely rejected price-inflation theories under RICO. As the Second Circuit has explained, such a

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complaints. The Third Circuit dismissed this deficiency as a "factual dispute" (App. 27a), but the TPPs have the burden of pleading sufficient facts to show an injury, and absent allegations that Actos was cheaper or that the TPPs would only have covered metformin, it is not plausible that they sustained the claimed injury.

theory of injury would require "a series of speculative calculations to ascertain whether, and in what amount, plaintiffs suffered a loss," when the reality is "that damages could have resulted from factors unrelated to the defendant's alleged acts of fraud." *McLaughlin v. American Tobacco Co.*, 522 F.3d 215, 230 (2d Cir. 2008) (citing *Anza*, 547 U.S. at 458-59).

The same principle applies with even greater force to RICO claims asserted by TPPs against drug manufacturers; as the Second Circuit has explained, a "price impact" theory has no place in such cases because the "market for prescription drugs is quite inelastic, meaning that the price of a medication rarely has significant impact on the demand for that medication." *UFCW Local 1776 v. Eli Lilly & Co.*, 620 F.3d 121, 125 (2d Cir. 2010). Indeed, a "drug company may even *increase* the price of a drug when it is expected that negative information will lower the demand," further highlighting the unsuitability of price-impact theories of injury in such cases. *Id.* The Eleventh Circuit has likewise expressly rejected a price-impact theory in a drug case, explaining that an allegation that a TPP "paid too much" for a drug is an impermissible "fraud on the market" theory that cannot establish injury or causation because the notion that there is a "market capable of efficiently digesting the truth [about a drug] and relaying it to [a TPP] in the form of a market price" is either too indirect or foreclosed by case law. *Se. Laborers Health & Welfare Fund v. Bayer Corp.*, 444 F. App'x 401, 405-10 & n.4 (11th Cir. 2011) (analyzing the proposed injury under state law and then adopting the same reasoning in rejecting the TPP's RICO claim).

For similar reasons, other courts of appeal have *repeatedly* rejected RICO claims that rest on the theory that a defendant's alleged fraud inflated prices. In one case involving the sale of polybutylene plumbing, for example, the Fifth Circuit rejected a theory that the allegedly fraudulent statements were "incorporated into the market price." *Summit Properties Inc. v. Hoechst Celanese Corp.*, 214 F.3d 556, 561 (5th Cir. 2000), *recognized as overruled on other grounds by Haley v. Merial, Ltd.*, 292 F.R.D. 339, 356-58 & n.11 (N.D. Miss. 2013). As the court explained, "[a]n efficient market is a critical element" of such a theory and is lacking in the context of mass-marketed products. *Id.* As a result, the Fifth Circuit observed, "*[n]o court* has accepted the use of this theory outside the context of securities fraud, and one circuit has expressly rejected its use in the context of a similar RICO case." *Id.* at 561 & n.24 (emphasis added) (citing *Appletree Square I v. W.R. Grace & Co.*, 29 F.3d 1283, 1287 (8th Cir. 1994)); see also *Appletree*, 29 F.3d at 1287 (rejecting the theory that an alleged fraud caused injury by inflating the price of a building).[7]

[7] These cases and the Eleventh Circuit's decision in *Southeast Laborers* were decided under the auspices of RICO's proximate-causation requirement rather than injury, but the concepts are closely related in this context, as evidenced in the Second Circuit's injury analysis in *McLaughlin*, which drew on its analysis of the price-inflation theory under the causation requirement. Compare 522 F.3d at 222-27 (concluding that it was not possible to establish loss causation based on a supposed "fraud on the market" given the inefficient market for consumer goods), with *id.* at 229-30 (citing similar considerations in explaining why the price-impact theory failed).

The Third Circuit did not even acknowledge this authority, relying instead on its statement in *In re Warfarin Sodium Antitrust Litigation*, 391 F.3d 516 (3d Cir. 2004) – an appeal involving the certifiability and fairness of a *class settlement* in an *antitrust* suit – that "'TPPs, like individual consumers, suffer direct economic harm when, as a result of a pharmaceutical company's alleged misrepresentations, they pay supracompetitive prices for brand drugs instead of purchasing lower-priced generic drugs.'" (App. 14a-15a (quoting *Warfarin*, 391 F.3d at 531) (alteration marks omitted).)

The logic of *Warfarin* makes no sense in the product liability context. In *Warfarin*, TPPs alleged that the defendant, DuPont, which manufactured a drug called Coumadin, violated § 2 of the Sherman Act by making false safety claims about the drug's generic equivalent (warfarin sodium), which had entered the market at a much lower price when Coumadin's patent expired. 391 F.3d at 528. According to the TPPs, these misrepresentations "permit[ed] DuPont to monopolize the market for warfarin sodium and charge supracompetitive prices for Coumadin . . . ." 391 F.3d at 528. In order to demonstrate that DuPont's misrepresentations and conduct had an anticompetitive effect, plaintiffs cited evidence that "more than 75% of prescriptions for sodium warfarin were still filled with Coumadin a year after [the competitor] introduced a generic version," even though the generic version had been approved by the FDA as the "bioequivalent and therapeutic equivalent to Coumadin." *Id.* at 522-23.[8] Accordingly, the TPPs argued that

[8] This rate was notable because "[g]enerally, about 40-70% of prescriptions for drugs available from multiple sources are filled

they were entitled to the difference in price between the two allegedly fungible products. See *id.* at 531. In the Third Circuit's view, the "same logic would apply here" – even though *Warfarin* "was an antitrust case" involving two fungible drugs – because "RICO's standing requirements were modeled on antitrust law." (See App. 14a-17a & n.32.)

The Third Circuit's analysis conflicts with this Court's precedent and basic logic. This Court expressly warned in *Anza* that courts should be wary of "blur[ring] the line between RICO and the antitrust laws," because antitrust theories of injury could entail "intricate, uncertain inquiries" when transplanted to the RICO context. 547 U.S. at 459-60 (highlighting the difficulty in ascertaining the causes and extent of an alleged drop in prices). After all, in the antitrust arena, consumers can be injured simply because they purchased a product "in a market where competition has been wrongfully restrained." *Warfarin*, 391 F.3d at 531. Thus, TPPs could plausibly allege that they would have paid for the cheaper of two *chemically-identical* drug products but for an antitrust violation.

Here, by contrast, the theory of injury is far more complicated because there is no chemically equivalent drug to Avandia. As such, it cannot be assumed that GSK's alleged fraud allowed it charge more for the drug than some theorized "market" price. To the contrary, the pricing of an innovative product with no equivalent counterpart is influenced by many factors. In the case of drugs, for example, a new product

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with less expensive generic products within one year of generic availability." *Warfarin*, 391 F.3d at 523.

might be more promising than older drugs, either generally or for specific patient populations. In such cases, the new drug is not in direct competition with other drugs, and its price will not be tied to theirs. Because there is no way to demonstrate that a TPP was financially injured under these circumstances, litigating such a theory of injury is barred under *Anza*. 547 U.S. at 460.

In short, the Third Circuit's decision is deeply in conflict with this Court's precedents and the decisions of other circuits. The Third Circuit's recognition of TPP injury where there is no allegation that the drug was ineffective or that it injured any of the TPPs' beneficiaries squarely conflicts with the Eleventh Circuit's decision in *Ironworkers*, as the Third Circuit tacitly acknowledged. Its adoption of an "inflated price" theory of injury has been rejected by the Second Circuit in another TPP case, repeatedly rejected in other RICO cases in other circuits, and conflicts with this Court's decision in *Anza*. And its reliance on antitrust precedents to support an inflated-price theory of injury separately conflicts with *Anza* because it ignores the Court's express warning not to conflate antitrust and RICO theories of injury. Absent review by this Court, the Third Circuit's decision paves the way for TPPs to establish RICO injury based solely on allegations of "overpayment" any time a scientific debate emerges over the safety and efficacy of a drug – a result that could produce a significant deterrent to research and development of new drugs and restrict patient access to beneficial medications. (See App. 14a.) For all of these reasons, the Court should grant review and reverse the decision below.

II. The Third Circuit's Causation Rulings Directly Conflict with Other Circuits and Ignore this Court's Cases Governing Basic Pleading Requirements.

The Third Circuit's resolution of the causation issues in this case also merits review. As noted previously, respondents proffered two theories of causation: (1) that GSK's alleged misrepresentations led doctors to write more Avandia prescriptions than they otherwise would have, causing respondents to reimburse more Avandia prescriptions; and (2) that respondents relied on the alleged misrepresentations in giving Avandia more favorable formulary placement than it would have otherwise received. The Third Circuit's acceptance of the first theory deepens a split between the First and Third Circuits on the one hand and the Second and Ninth Circuits on the other, over whether a theory of causation that depends on the individual decisions of thousands of prescribing doctors is too attenuated to satisfy proximate causation. And its acceptance of the second theory is inconsistent with this Court's rulings and those of various federal courts, including the Eleventh Circuit, because it condoned allegations of but-for causation that offer nothing more than "bare legal conclusions" and lack any "factual heft."

A. The Courts Of Appeals Are Now Squarely Divided Over Whether Individualized Prescribing Decisions Defeat Proximate Causation.

The Third Circuit's decision solidified a split over whether a TPP plausibly alleges causation under RICO by averring that a drug manufacturer's misrepresentations defrauded doctors, causing them to

write "excess prescriptions" for the medication. The majority of federal courts to consider the issue have held that the attenuated link between alleged misrepresentations made to doctors and any ultimate injury to TPPs is insufficiently *direct* to establish proximate causation. A small number of courts – including the Court of Appeals here – have disagreed, however, concluding that the alleged *foreseeability* of the injury to the TPPs suffices to establish proximate causation notwithstanding the lack of directness. The Court should intervene to resolve this split and clarify, consistent with the Court's prior rulings, that lack of directness defeats proximate causation even where harm to the plaintiff was allegedly foreseeable.

In *Holmes v. Securities Investor Protection Corporation*, 503 U.S. 258 (1992), this Court held that RICO's requirement that a private individual suing under the statute be injured "by reason of" a statutory violation is a "demand for some *direct* relation between the injury asserted and the injurious conduct alleged." *Id.* at 268 (emphasis added).

The Court reaffirmed this "direct relation" test for RICO proximate causation in *Anza*. See 547 U.S. at 461 (describing the proper inquiry as "whether the alleged violation led directly to the plaintiff's injuries"). The *Anza* ruling also expressly established that foreseeability does not satisfy proximate causation where directness is lacking, rejecting the Second Circuit's conclusion that, "because the [defendants] allegedly sought to gain a competitive advantage over [the plaintiff], it is immaterial whether they took an indirect route to accomplish their goal." *Id.* at 460. As this Court explained, that "rationale [did] not accord with *Holmes*," and a "RICO plaintiff cannot circumvent the proximate-cause requirement by

simply claiming that the defendant's aim was to increase market share at a competitor's expense." *Id.* at 461. Thus, "[w]hen a court evaluates a RICO claim for proximate causation, *the central question* it must ask is whether the alleged violation *led directly* to the plaintiff's injuries." *Id.* (emphases added).[9]

Consistent with the directness requirement emphasized in these decisions, most courts addressing TPP claims, like those here, that depend on an "excess prescriptions" or "quantity effect" theory of causation – i.e., that a drug manufacturer's alleged misrepresentations caused doctors to write more TPP-covered prescriptions – have rejected the claims as too attenuated to satisfy RICO's proximate-causation requirement. Indeed, both the Second and Ninth Circuits have rejected such theories on precisely this ground.

In *United Food & Commercial Workers Central Pennsylvania & Regional Health & Welfare Fund v. Amgen, Inc.*, 400 F. App'x 255 (9th Cir. 2010), the Ninth Circuit affirmed the dismissal of RICO and state consumer protection claims involving a defendant's allegedly fraudulent marketing of two prescription medications for off-label uses. *Id.* at 257. According to the Ninth Circuit, the plaintiffs "failed to plead a cognizable theory of proximate causation that links [the defendant's] alleged misconduct to

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[9] As a plurality of this Court recognized in *Hemi Group, LLC v. City of New York*, 559 U.S. 1 (2010), while the "concepts of direct relationship and foreseeability are of course two of the 'many shapes [proximate cause] took *at common law*,'" this Court's "precedents make clear that *in the RICO context*, the focus is on the directness of the relationship between the conduct and the harm." *Id.* at 12 (quoting *Holmes*, 503 U.S. at 268) (emphases added).

[the TPPs'] alleged injury." *Amgen*, 400 F. App'x at 257. In particular, "the complaint proffered an attenuated causal chain" involving physician prescription decisions. *Id.* In light of the multiple steps necessary to tie the defendant's alleged misconduct to the plaintiff's claimed injuries, the Ninth Circuit concluded that plaintiffs failed "to satisfy the Supreme Court's proximate causation requirement in the RICO context." *Id.* (citing *Hemi Grp.*, 559 U.S. at 9, and *Holmes*, 503 U.S. at 268, 271, 274).

Likewise, in *Lilly*, 620 F.3d at 134, the Second Circuit affirmed the denial of class certification in a RICO suit brought by TPPs alleging that fraudulent marketing of the drug Zyprexa had caused them to pay for prescriptions they otherwise would not have covered. According to the court, the "attenuated link between the alleged misrepresentations made to doctors and ultimate injury to the TPPs" made it impossible for the TPPs to establish proximate causation. This was so because the TPPs' "theory of liability rest[ed] on the independent actions of third and even fourth parties" that "play[ed] a role in the chain between [the manufacturer] and the TPPs." *Id.* (internal quotation marks and citation omitted); see also, *e.g.*, *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, 20 F. Supp. 3d 305, 323 (E.D.N.Y. 2014) (rejecting similar allegations in a putative class action; "[a]s recognized by the Second Circuit in *Zyprexa* . . . the prescribing decisions of physicians are based on so many factors as to defy any efforts to categorically attribute them to a particular cause"), *aff'd*, 806 F.3d 71 (2d Cir. 2015); *Emp'r Teamsters-Local Nos. 175/505 Health & Welfare Trust Fund v. Bristol Myers Squibb Co.*, 969 F. Supp. 2d 463, 475 (S.D. W. Va. 2013); *In re Yasmin*

& Yaz (Drospirenone) Mktg., Sales Practices & Prods. Liab. Litig., No. 3:09-md-02100-DRH-PMF, 2010 U.S. Dist. LEXIS 80758, at *23 (S.D. Ill. Aug. 5, 2010); *In re Epogen & Aranesp Off-Label Mktg. & Sales Practices Litig.,* No. 08-1934 PSG (AGRx), 2009 WL 1703285, at *6 (C.D. Cal. June 17, 2009), *aff'd*, 400 F. App'x 255 (9th Cir. 2010).

The Third Circuit did not address any of this authority in its proximate-causation analysis. Indeed, the court spent much of its proximate-causation analysis discussing respondents' *direct-reliance* theory rather than the excess-prescriptions theory – even though GSK only challenged proximate causation with respect to the latter theory. As a result, it barely addressed the proximate-cause argument GSK actually made.

In its short postscript addressing the excess-prescriptions theory, the Third Circuit said only that the "presence of intermediaries, doctors and patients" does not defeat proximate causation because the requisite directness is established where the plaintiffs are "the 'primary and intended victims of the scheme to defraud' and their injury was a 'foreseeable and natural consequence of the scheme,'" citing this Court's holding in *Bridge v. Phoenix Bond & Indemnity Company*, 553 U.S. 639 (2008). (App. 27a (quoting *Bridge*, 553 U.S. at 650, 658).) The court also mentioned in a footnote that the First Circuit had reached a similar conclusion in a case brought by TPPs alleging fraudulent marketing of the drug Neurontin. (See App. 28a n.75 (citing *In re Neurontin Mktg. and Sales Practices Litig.*, 712 F.3d 21, 37-38

(1st Cir. 2013)).)[10] But the minority view of proximate causation reflected in the *Neurontin* decision and embraced by the Court of Appeals in this case significantly over-reads *Bridge*. *Bridge* involved allegations that the defendants had committed mail fraud by falsely certifying compliance with a county rule imposing restrictions on bidders at tax lien sales. 553 U.S. at 642-44. The plaintiffs sued under RICO, alleging that the defendants had obtained a disproportionate share of tax sales by violating the rule. *Id.* at 644. The defendants argued that this Court's proximate-causation precedents defeated the claims because the alleged fraud was on the county, meaning that the plaintiffs could not have directly relied on the certifications of compliance. *Id.* at 653-54. This Court disagreed, explaining that there was a "sufficiently direct relationship" because: (1) the alleged injury was "a foreseeable and natural consequence of" the alleged scheme; (2) "no independent factors [could] account for [plaintiffs'] injury";

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[10] GSK acknowledges that the Court denied a petition for certiorari in *Neurontin*, but this case presents a far better vehicle for review because *Neurontin* involved allegations that the drug did not work at all and that no physicians would have prescribed it. See Brief in Opposition for Harden Respondents at 29-30, *Pfizer Inc. v. Harden Mfg. Corp.*, No. 13-289 (U.S. filed Nov. 4, 2013) (arguing that the allegation that Neurontin did not work at all for the uses at issue distinguished the case from others, like *Lilly*, that involved a "misrepresented drug [that was] still efficacious" because in cases involving effective drugs "it is much more difficult to determine whether the physician would have prescribed it"); see also *Neurontin*, 712 F.3d at 47 (specifically noting that the TPP plaintiff had "staked much of its case on proving that Neurontin was ineffective for the promoted off-label uses"). Moreover, the *Neurontin* petition, unlike this one, did not involve the additional issue of RICO injury that is presented in Part I of this petition.

(3) "there is no risk of duplicative recoveries by plaintiffs removed at different levels of injury from the violation"; and (4) "no more immediate victim is better situated to sue. Indeed . . . the [plaintiffs] and other losing bidders were the *only* parties injured by [defendants'] misrepresentations." *Id.* at 658.

The causal theory in this case is different in every critical respect. First, many "independent factors [could] account for [the TPPs' alleged] injury." As other courts have recognized, doctors receive information from numerous sources and may prescribe drugs for reasons unrelated to the drug manufacturer's alleged misrepresentations. *E.g.*, *Lilly*, 620 F.3d at 135. Moreover, there is a clear and substantial risk of "duplicative recoveries" because there are "more immediate victim[s] . . . better situated to sue" – i.e., those claiming to have actually sustained cardiovascular injuries as a result of ingesting Avandia. *E.g.*, *Se. Laborers Health & Welfare Fund v. Bayer Corp.*, 655 F. Supp. 2d 1270, 1284 (S.D. Fla. 2009) (explaining that the "proper parties to vindicate the law would be those persons physically injured by the deception," regardless of whether they could bring such claims under RICO), *aff'd*, 444 F. App'x 401 (11th Cir. 2011). To the extent any of respondents' beneficiaries bring and prevail on such claims, the TPPs could be made whole through liens, subrogation, or whatever other provisions govern such cases under the relevant plan documents. For all of these reasons, TPP cases like this one stand "in contrast to *Bridge*." *Hemi Grp.*, 559 U.S. at 15.

B. The Third Circuit's Resolution of Respondents' Direct-Reliance Allegations Contravened this Court's Precedents Governing Pleading Requirements.

Finally, the Court of Appeals contravened this Court's precedents by ignoring GSK's argument that respondents had failed to allege *facts* to support their conclusory allegations of direct reliance – i.e., that GSK's alleged misrepresentations caused them to make formulary decisions with respect to Avandia that they otherwise would not have made.

A RICO plaintiff must assert plausible allegations of but-for causation to make out a claim under the statute. *Holmes*, 503 U.S. at 265-66 (requiring that a defendant's alleged RICO violation be the "but for" cause of the plaintiff's injury). As a matter of basic pleading requirements, such a plausible allegation must include more than a mere conclusory assertion, without any factual detail, that the plaintiff relied on the defendant's alleged misrepresentations. As this Court made clear in *Bell Atlantic Corporation v. Twombly*, 550 U.S. 544, 555 (2007), and *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009), a plaintiff must plead sufficient "[f]actual allegations" to "raise a right to relief above the speculative level." *Twombly*, 550 U.S. at 555. This requirement ensures that defendants are not forced to finance speculative fishing expeditions in cases where plaintiffs lack a strong factual basis for their claims – a protection that is especially important in the context of complex suits like this one. See *id.* at 558-59. Thus, where a plaintiff provides only a "naked assertion" that a required element is satisfied, without "further factual enhancement," the allegations "stop[] short of the line

between possibility and plausibility of 'entitle[ment] to relief,'" and a complaint must be dismissed. *Twombly*, 550 U.S. at 557.

Here, respondents' allegations of but-for causation are nothing more than "naked assertion[s]" of "legal conclusions" that the "elements of a cause of action" are met. Respondents generally alleged in their complaints that "PBMs and pharmacy and therapeutic committees relied on the Defendants' misrepresentations of Avandia's safety when approving and/or placing Avandia on formularies"; that "[t]hird-party payors relied on the Defendants' misrepresentations of Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their" beneficiaries; and that "[b]ut for Defendants actions, third-party payors would not have paid for Avandia." (App. 141a-142a.) But respondents did not provide any "*factual enhancement*" to these allegations. Most critically, they did not identify the specific "misrepresentations of Avandia's safety" that *they* allegedly relied upon, or state how those alleged misrepresentations affected *their* formulary placement and reimbursement decisions. Indeed, the Third Circuit essentially acknowledged the absence of specific allegations concerning the TPPs' formulary decisions but deemed them irrelevant, saying only that their absence means that "we do not know" what decisions were made. (App. 25a-26a.)

The Third Circuit's conclusion that the TPPs' "[t]hreadbare recitals" sufficed not only contravenes this Court's precedents but also conflicts with the decisions of other federal courts in TPP cases – including the Eleventh Circuit – recognizing the need for plaintiffs to plead the factual details of reliance. In *Southeast Laborers Health and Welfare Fund v.*

Bayer Corp., 444 F. App'x 401 (11th Cir. 2011), for instance, the Eleventh Circuit affirmed the district court's dismissal of a TPP's RICO claim on causation grounds where the TPP "failed to allege facts plausibly demonstrating that [the TPP] would have independently determined that [the drug] was not 'medically necessary' if the [the drug manufacturer] had disclosed the allegedly suppressed material information." *Id.* at 410.[11] See also, *e.g.*, *Health Care Serv. Corp. v. Olivares*, No. 10-cv-221, 2011 WL 4591913, at *7 (E.D. Tex. Sept. 2, 2011), *adopted by* 2011 WL 4591915 (E.D. Tex. Sept. 30, 2011) (rejecting TPP's RICO and consumer-fraud claims based on allegations that drug manufacturer had caused it to cover prescriptions of various drugs by misrepresenting their safety and efficacy where the pleadings failed to include key facts; "although [the TPP] contends that [the drug manufacturers]' conduct caused [the TPP] to add [certain drugs] to its formulary, [the TPP] does not identify when it added those drugs to its formulary and under what circumstances those drugs were added"*); In re Actimmune Mktg. Litig.*, 614 F. Supp. 2d 1037, 1050, 1052 (N.D. Cal. 2009) (dismissing RICO claims by TPPs where they failed to "allege what *specific*" statements they relied on) (emphasis added); *Dist. 1199P*, 784 F. Supp. 2d at 525 (reasoning that "without sufficient allegations of direct reliance, [TPPs] have not properly alleged that [d]efendants' misrepresentations were the 'but for' cause of their injuries"). The Court of Appeals did

[11] Although the Eleventh Circuit used the words "proximate causation," 444 F. App'x at 409-10, its analysis focused on the insufficiency of the factual pleadings and sounded in but-for causation.

not even address this error in the district court's ruling.

As a result of the lower courts' rulings, GSK will be forced to incur the enormous expenses associated with discovery in this complex litigation, notwithstanding the glaring deficiencies in respondents' complaints, precisely the danger the Court sought to avoid in *Twombly*. See 550 U.S. at 558-59. This result is particularly troublesome because the omissions in respondents' complaints suggest that the facts needed to properly allege their claims simply do not exist. For this reason too, the Court should grant review and reverse the lower courts' holdings.

CONCLUSION

For the foregoing reasons, the Court should grant the petition for a writ of certiorari.

February 23, 2016

Respectfully submitted,

Nina M. Gussack
Anthony C.H. Vale
Yvonne M. McKenzie
PEPPER HAMILTON LLP
3000 Two Logan Square
Eighteenth & Arch Streets
Philadelphia, PA 19103
(215) 981-4000

John H. Beisner
Counsel of Record
Jessica D. Miller
Geoffrey M. Wyatt
SKADDEN, ARPS, SLATE,
MEAGHER & FLOM LLP
1440 New York Ave., NW
Washington, DC 20005
(202) 371-7000
john.beisner@skadden.com

Attorneys for Petitioner

APPENDIX

APPENDIX A — OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT, FILED OCTOBER 26, 2015

PRECEDENTIAL

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 14-1948

IN RE: AVANDIA MARKETING, SALES PRACTICES & PRODUCT LIABILITY LITIGATION

GlaxoSmithKline, LLC,

Appellant

On Appeal from the United States District Court for the Eastern District of Pennsylvania (D. C. Nos. 2-09-cv-00730, 2-10-cv-02475, 2-10-cv-05419, 2-07-md-01871) District Judge: Honorable Cynthia M. Rufe

Argued on November 18, 2014

Before: AMBRO, SCIRICA and ROTH, *Circuit Judges*.

(October 26, 2015, Opinion Filed)

OPINION

ROTH, *Circuit Judge*:

This interlocutory appeal involves claims brought against GlaxoSmithKline LLC (GSK) by third-party

payors (TPPs), based on GSK's alleged misrepresentation and concealment of the significant safety risks associated with use of Avandia, Avandamet, and Avandaryl (collectively, Avandia), Type II diabetes drugs. GSK argues that the District Court erred in finding that the TPPs adequately alleged the elements of standing under the Racketeer Influenced and Corrupt Organizations Act (RICO).[1] We agree with the District Court's analysis, finding standing, and therefore we will affirm.

I.

A.[2]

Plaintiffs, Allied Services Division Welfare Fund, UFCW Local 1776 and Participating Employers Health and Welfare Fund, and United Benefit Fund, are TPPs. They are union health and welfare funds and are suing GSK on behalf of themselves and other similarly situated TPPs. TPPs typically provide medical coverage, including prescription drug coverage, to their members and members' dependents.

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1. 18 U.S.C. § 1961 *et seq.*

2. These facts are taken from the Complaints and treated as true because, in reviewing a denial of a motion pursuant to Federal Rule of Civil Procedure 12(b)(6), we accept as true all well-pleaded allegations and construe the complaint in the light most favorable to the plaintiffs. *See Lewis v. Atlas Van Lines, Inc.*, 542 F.3d 403, 405 (3d Cir. 2008).

Appendix A

Whether a TPP will cover the cost of a member's prescription, in whole or in part, depends on whether that drug is listed in the TPP's "formulary." Pharmacy Benefit Managers (PBMs) prepare TPPs' formularies of drugs approved for use by the TPPs' members. The formularies are prepared by analyzing research regarding a drug's cost effectiveness, safety and efficacy. When a PBM determines that a drug offers advantages over a competing drug, it will give that drug preferred status on the formulary. A TPP will typically cover more of the cost of a particular drug when that drug has a higher preference status on the formulary. The greater coverage of cost by the TPP allows the member to pay a lower co-payment when prescribed that drug.

Type II diabetes is the most common form of diabetes and results from the body's failure to produce enough insulin or its inability to properly use insulin. Type II diabetes was first treated with oral medications, primarily metformin and sulfonylureas, or with injected insulin. In the 1990s, pharmaceutical companies began to develop a new form of Type II diabetes treatment known as thiazolidinediones (TZDs). On May 25, 1999, the Food and Drug Administration (FDA) approved Avandia, a TZD, for sale in the United States. GSK marketed Avandia as a more effective and safer alternative to the cheaper, existing Type II oral medications. In turn, TPPs included Avandia in their formularies and covered Avandia prescriptions at a favorable rate.

Soon after the FDA approved Avandia, concerns regarding its heart-related side effects began to surface.

For example, in 2001, the FDA requested that GSK add a warning to the prescription label regarding the increased risk of fluid retention resulting from Avandia use. Shortly thereafter, GSK's sales representatives denied the existence of this risk. As a result, the FDA instructed GSK to stop minimizing the risk of heart attacks and heart-related diseases in its marketing. In 2006, the FDA required GSK to update the warning to include new data about the potential increased occurrence of heart attack and heart-related chest pain in some Avandia patients.

In May 2007, Steven E. Nissen and Kathy Wolski published a paper in *The New England Journal of Medicine*, documenting the results of forty-two clinical trials of Avandia. The Nissen study concluded that, compared with the use of competing diabetes drugs, Avandia use was associated with a significant increase in the risk of myocardial infarction and a borderline-significant increase in the risk of death from heart-related diseases. According to the TPPs, GSK responded to the Nissen study with a marketing campaign designed to sway doctors and consumer confidence. This campaign included publishing full-page advertisements in more than a dozen newspapers and the release of promotional materials to prescribing physicians. Specifically, GSK challenged the Nissen study's methodology and conclusions and described the results of its own favorable study.

On May 23, 2007, the FDA recommended that GSK add a "black box" warning to Avandia's label to warn of the risk of congestive heart failure in connection with the use of Avandia. On August 14, 2007, GSK added the

warning, which stated that TZDs "cause or exacerbate congestive heart failure in some patients. . . . Avandia is not recommended in patients with symptomatic heart failure." Three months later, the FDA added a second black box warning, describing the Nissen study's results as showing "Avandia to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction."

In February 2010, the U.S. Senate Finance Committee released a report on Avandia. The Committee concluded that the "totality of the evidence suggests that GSK was aware of the possible cardiac risks associated with Avandia years before such evidence became public" and that GSK failed to notify the FDA and the public of these risks despite its duty to do so. The report also noted that GSK attempted to minimize or misrepresent those risks in order to contradict the Nissen study and to intimidate independent physicians.

Ultimately, on September 23, 2010, the FDA restricted access to Avandia in response to increasing evidence of its cardiovascular risks. Specifically, the FDA limited access to existing users and to new patients whose blood sugar could not be controlled with other medications and who had decided with their doctor not to take Actos, a competing TZD drug. Doctors were required to advise existing Avandia users of Avandia's cardiovascular risks before continuing to prescribe it.

Since its release, Avandia has been used on a regular basis by at least one million individuals in the United

States and has generated billions of dollars in revenue for GSK. A one-month supply of Avandia has sold for $90 to $220, with the TPP covering between $135 and $140 per prescription and the patient paying the balance. This was a dramatic increase in the cost of Type II diabetes treatment. Previously, the most prevalent oral drug therapy, metformin, cost approximately $45 to $55 for a one-month supply, with the TPP covering $40 to $50 of that amount. Although plaintiffs identify Actos as another alternative to Avandia, they do not provide the price which TPPs typically covered for Actos prescriptions.

B.

Plaintiffs bring this class action on behalf of themselves and other similarly situated TPPs that covered the cost of Avandia after May 25, 1999. They assert that GSK's failure to disclose Avandia's significant heart-related risks violated RICO based on predicate acts of mail fraud,[3] wire fraud,[4] tampering with witnesses,[5] and use of interstate facilities to conduct unlawful activity.[6] They also assert claims for unjust enrichment and violations of the Pennsylvania Unfair Trade Practices and Consumer Protection Law[7] and other states' consumer protection laws.

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3. *See* 18 U.S.C. § 1341.

4. *See id.* § 1343.

5. *See id.* § 1512.

6. *See id.* § 1952.

7. *See* 73 Pa. Cons. Stat. §§ 201-1-201-9.3.

Appendix A

Plaintiffs allege that GSK deliberately concealed the significant safety risks associated with the use of Avandia and continued to promote Avandia as a safer treatment for diabetes despite the known risks of heart attack and disease. Specifically, plaintiffs allege that GSK selectively manipulated data and scientific literature, made false and misleading statements in its 2007 advertising campaign, and intimidated physicians to publish false and misleading articles--all in order to increase Avandia sales. According to plaintiffs, TPPs and PBMs included Avandia in their formularies and covered Avandia at favorable rates in reliance on these misrepresentations by GSK. Plaintiffs allege that Avandia was worth less than the favorable rates at which they covered it (their "excess price" theory). Similarly, they allege that physicians relied on GSK's misrepresentations in deciding to prescribe Avandia and would have prescribed Avandia to fewer patients had GSK not concealed Avandia's risks (their "quantity effect" theory). Plaintiffs seek compensatory, punitive, and statutory damages for the financial harm they suffered as a result of GSK's conduct, and they seek injunctive relief to prevent GSK from continuing its allegedly unlawful activities.

On November 3, 2010, GSK moved to dismiss, in part, because plaintiffs failed to adequately allege standing under Section 1964(c) of RICO. The District Court rejected GSK's arguments, holding that plaintiffs plausibly alleged that they had suffered a concrete economic injury based on the substantial savings they would have experienced had they covered cheaper alternatives to Avandia. This was true regardless of whether any beneficiary who had ingested Avandia became ill.

The District Court also rejected GSK's argument that plaintiffs failed to adequately allege proximate causation. According to the District Court, it is sufficient that plaintiffs alleged that doctors relied upon GSK's misrepresentations in prescribing Avandia and that the TPPs themselves relied upon those misrepresentations in making formulary decisions. The District Court noted, however, that plaintiffs may have difficulty in proving causation at the next litigation stage because they did not restrict access to Avandia after the Nissen study publicized Avandia's heart-related risks. The District Court also rejected GSK's argument that prescribing doctors' independent actions broke the chain of causation. The District Court relied on *In re Neurontin Marketing and Sales Practices Litigation*,[8] in which the First Circuit Court of Appeals held that, where a TPP is a primary and intended victim and the injury is foreseeable, the doctor's independent actions do not break the causal chain.[9]

On February 19, 2014, the District Court certified its decision for interlocutory appeal under 28 U.S.C. § 1292(b). The certified questions are the following:

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8. 712 F.3d 21 (1st Cir. 2013).

9. The District Court also made a number of other findings, including that plaintiffs failed to adequately allege a claim for unjust enrichment. Because plaintiffs did not allege that Avandia injured their beneficiaries or failed to perform as advertised, the District Court held that they "received the benefit of their bargains" and therefore could not maintain a claim for unjust enrichment. This holding is not currently on appeal.

1) Did the Court err in its application of *Maio v. AETNA, Inc.*[10]

2) Did the TPPs sufficiently plead that Defendant's alleged misrepresentation about Avandia's safety caused their injuries, when the TPPs continued to include Avandia on their formularies and cover the cost of Avandia for their members after the alleged cardiovascular risks of Avandia were well-publicized, and

3) Does the independent judgment of doctors and decision-making of the physicians who wrote the prescriptions for Avandia render the causal chain too attenuated to state a claim?[11]

We granted permission to appeal on April 15, 2014.

II.[12]

We exercise plenary review over a district court's denial of a motion to dismiss for failure to state a claim

10. 221 F.3d 472 (3d Cir. 2000).

11. We do not address plaintiffs' state-law claims in this appeal because they are not explicitly addressed within the questions that have been certified to us.

12. The District Court had jurisdiction pursuant to 28 U.S.C. § 1331. We have appellate jurisdiction pursuant to 28 U.S.C. § 1292(b).

under Federal Rule of Civil Procedure 12(b)(6).[13] "A motion to dismiss pursuant to Rule 12(b)(6) may be granted only if, accepting all well pleaded allegations in the complaint as true, and viewing them in the light most favorable to plaintiff, plaintiff is not entitled to relief."[14] The facts alleged in the complaint must state a "plausible claim for relief."[15] "The issue is not whether a plaintiff will ultimately prevail but whether the claimant is entitled to offer evidence to support the claims."[16] We also exercise plenary review over a district court's legal determination that plaintiffs have standing to pursue a civil RICO action.[17]

III.

The issue on appeal is whether plaintiffs have adequately pled standing to pursue a civil action under Section 1964(c) of RICO. Section 1964(c) provides that:

> Any person injured in his business or property by reason of a violation of section 1962 of this

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13. *See Farber v. City of Paterson*, 440 F.3d 131, 134 (3d Cir. 2006).

14. *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1420 (3d Cir. 1997).

15. *See Ashcroft v. Iqbal*, 556 U.S. 662, 679, 129 S. Ct. 1937, 173 L. Ed. 2d 868 (2009).

16. *Maio*, 221 F.3d at 482 (quoting *In re Burlington*, 114 F.3d at 1420).

17. *See id.*

> chapter may sue therefor in any appropriate United States district court and shall recover threefold the damages he sustains and the cost of the suit, including a reasonable attorney's fee . . ..[18]

The language of § 1964(c) requires a RICO plaintiff to show that the plaintiff suffered an injury to business or property and that the plaintiff's injury was caused by the defendant's violation of 18 U.S.C. § 1962.[19] Section 1964(c)'s "limitation of RICO standing to persons 'injured in [their] business or property' has a 'restrictive significance, which helps to assure that RICO is not expanded to provide a federal cause of action and treble damages to every tort plaintiff.'"[20]

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18. 18 U.S.C. § 1964(c). Section 1962 prohibits, in part, "any person employed by or associated with any enterprise engaged in, or the activities of which affect, interstate or foreign commerce" from "conduct[ing] or participat[ing], directly or indirectly, in the conduct of such enterprise's affairs through a pattern of racketeering activity." *Id.* § 1962(c). A "racketeering activity" can consist of a variety of predicate offenses, including, as alleged in this case, mail fraud, wire fraud, tampering with witnesses, and use of interstate facilities to conduct unlawful activity, *see id.* § 1961(1), and a "pattern" of such activity requires at least two acts, *id.* § 1961(5).

19. *See Maio*, 221 F.3d at 483.

20. *Maio*, 221 F.3d at 483 (quoting *Steele v. Hospital Corp. of Am.*, 36 F.3d 69, 70 (9th Cir. 1994)) (internal citation omitted).

Appendix A

A.

We must first determine whether plaintiffs adequately alleged injury to business or property within the meaning of RICO. "'[A] showing of injury requires proof of a concrete financial loss, and not mere injury to a valuable intangible property interest.'"[21] This requirement "can be satisfied by allegations and proof of actual monetary loss, i.e., an out-of-pocket loss."[22]

GSK claims that the TPPs fail to assert a concrete injury, citing our decision in *Maio*. In that case, we considered whether health insurance beneficiaries could maintain a RICO claim for economic injury against their insurer, Aetna, based on alleged misrepresentations regarding the services included in their HMO plans.[23] The insured parties claimed that the insurer's failure to disclose restrictive internal policies caused them injury by causing them to "pa[y] too much in premiums for an 'inferior' health care product."[24] They alleged that the internal policies were designed to improve profitability at the expense of quality of care, whereas the insurer's marketing campaign represented that the purchased policy focused on quality of care.[25] The insured parties

21. *Id.* (quoting *Steele*, 36 F.3d at 70).

22. *Id.*

23. *See id.* at 483-84.

24. *Id.* at 484-85.

25. *Id.* at 474.

also claimed that the internal policies "restrict[ed] the physicians' ability to provide the high quality health care . . . promised."[26]

We rejected the plaintiffs' claims, finding that the insured parties suffered no cognizable injury. We construed the insured parties' property interests as the intangible "contractual right to receive benefits in the form of covered medical services," and found that the insured parties had suffered no injury absent allegations that they had received "inadequate, inferior delayed care, personal injuries resulting therefrom, or [the] denial of benefits due under the insurance arrangement.[27] Because the insured parties specifically disclaimed any contractual shortcoming on the part of the insurer, they "simply c[ould not] establish as a factual matter that they received anything less than what they bargained for."[28] Instead, the alleged economic harm was "contingent upon the impact of events in the future" -- namely, inadequate care produced by the insurer's internal policies.[29] We concluded that plaintiffs could not establish that they had suffered a tangible economic harm because their theory of injury was premised solely on the possibility that they *might* receive inadequate healthcare in the future.[30]

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26. *Id.* at 475.

27. *Id.* at 490.

28. *Id.* at 494.

29. *Id.* at 494-95.

30. *Id.* at 495.

GSK argues that here too, the TPPs' injury is predicated on the possibility that future events might occur -- namely, that the drugs purchased by the TPPs will prove to be unsafe or ineffective. However, because the TPPs do not allege that they received unsafe or ineffective prescriptions, GSK argues that they have received exactly what they bargained for and that they have not suffered a concrete injury.

The TPPs respond that their injury is one which has long been considered concrete: overpayment due to illegal or deceptive marketing practices. They cite our decision in *In re Warfarin Sodium Antitrust Litigation*,[31] in which TPPs alleged that DuPont violated antitrust law by disseminating false and misleading information about a cheaper generic drug, causing the TPPs to cover the cost of duPont's more expensive brand name drug.[32] We held that "TPPs, like individual consumers, suffer[] direct economic harm when, as a result of [a pharmaceutical company's] alleged misrepresentations, they pa[y] supracompetitive prices for [brand drugs] instead of

31. 391 F.3d 516 (3d Cir. 2004).

32. Although *Warfarin* was an antitrust case, it is applicable here because RICO's standing requirements were modeled on antitrust law. In drafting Section 1964(c), Congress "used the same words [as § 7 of the Sherman Act and § 4 of the Clayton Act], and we can only assume it intended them to have the same meaning that courts had already given them." *See Holmes*, 503 U.S. at 266-68; *see also Steamfitters Local Union No. 420 Welfare Fund v. Philip Morris, Inc.*, 171 F.3d 912, 921, 932 (3d Cir. 1999).

purchasing lower-priced generic [drugs]."[33] According to the TPPs, if allegedly anticompetitive behavior that leads to overpayment establishes a concrete injury, then so should allegedly fraudulent behavior that leads to overpayment.

We agree with the TPPs that *Warfarin* offers the closest analogy to the facts of this case and that GSK's reliance on *Maio* is distinguishable in one crucial respect: unlike the injury suffered by plaintiffs in *Maio*, the injury suffered by the TPPs here is *not* contingent on future events. The TPPs' damages do not depend on the effectiveness of the Avandia that they purchased, but rather on the inflationary effect that GSK's allegedly fraudulent behavior had on the price of Avandia. By contrast, the damages suffered by the plaintiffs in *Maio* were entirely dependent on the quality of the health care they received. Because the plaintiffs in that case did not allege that they had received inadequate care, their "theory of present economic loss require[d] a significant degree of factual speculation,"[34] and was thus insufficient to establish standing.

To further illustrate the point, suppose that the defendants in *Warfarin* had asserted that the TPPS had failed to establish standing because they had not alleged that the drugs they had purchased were ineffective. That argument would have been rejected by the court: the injury suffered by the TPPs in that case did not depend

33. *Warfarin*, 391 F.3d at 531.

34. *Maio*, 221 F.3d at 495.

on the drug's ineffectiveness but rather on the defendant's anticompetitive behavior. That same logic would apply here. The injury suffered by the TPPs in this case does not depend on Avandia's ineffectiveness, but rather on GSK's fraudulent behavior. As such, the TPPs' theory of economic loss does not require factual speculation. If we accept the plausible allegations in the complaint as true, the fraudulent behavior alleged in their complaint has already occurred, and its effect on the price of Avandia is not contingent on future events.

Reliance on our decisions in *In re Schering-Plough Corp. Intron/Temodar Consumer Class Action*,[35] and *Horvath v. Keystone Health Plan East, Inc.*,[36] is similarly misplaced. In *Schering-Plough*, TPPs alleged that Schering's off-label promotional activities of certain drugs caused them economic injury. Relying on *Maio*, the District Court held that the plaintiffs lacked standing to assert this injury because they failed to allege that any consumers or beneficiaries received inadequate drugs or suffered personal injuries.[37] On appeal, we affirmed the District Court on causation grounds. To the extent we agreed with the District Court's injury analysis in that case, we did so in *dictum*, not in binding precedent.[38]

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35. 678 F.3d 235 (3d Cir. 2012).

36. 333 F.3d 450 (3d Cir. 2003).

37. *See* No. 2:06-cv-5774, 2009 U.S. Dist. LEXIS 58900, 2009 WL 2043605, at *16 (D.N.J. July 10, 2009).

38. *See Schering-Plough*, 678 F.3d at 246.

Horvath, an ERISA case, is distinguishable on the same basis as *Maio*. In *Horvath*, as in *Maio*, the plaintiff alleged that she overpaid for the healthcare provided by an HMO due to the HMO's misleading statements.[39] But the plaintiff "d[id] not allege . . . that the care she received from the Keystone HMO was defective or substandard in any way."[40] Accordingly, we noted that the plaintiff's claims "rest not only on the troublesome assumption that a factfinder can accurately determine the amount her [employer] allegedly overpaid [the HMO], but also on the notion that the [employer] would have passed these savings on to its employees in the form of a higher salary or additional benefits.[41] We determined that such a claim was too speculative to establish standing.[42] In this case, however, if we accept the TPPs' plausible allegations as true -- as we are required to do at this stage -- then no speculation is required to determine whether they suffered an injury.

GSK advances one final argument for its position that the TPPs have not suffered a concrete injury. Relying on the Eleventh Circuit Court of Appeals' decision in *Ironworkers Local Union 68 v. AstraZeneca Pharm., LP.*,[43] GSK argues that TPPs can statistically

39. *Horvath*, 333 F.3d at 452.

40. *Id.* at 453.

41. *Id.* at 457.

42. *Id.*

43. 634 F.3d 1352 (11th Cir. 2011).

anticipate a certain level of fraud and pass this risk on to their beneficiaries in the form of higher premiums. In *Ironworkers*, a case with facts similar to these, the court found the plaintiff insurance companies suffered no injury because they "adjust[] their premiums upward to reflect the projected value of claims" for payment of "medically unnecessary or inappropriate prescriptions of formulary drugs" -- "even those caused by fraudulent marketing.[44] Although GSK says that the TPPs "presumably" adjusted their premiums in this way, we are not entitled to make such a presumption at the motion-to-dismiss stage. Furthermore, the argument lacks a limiting principle.[45]

B.

In addition to cognizable injury, a RICO plaintiff must satisfy RICO's proximate causation requirements. In evaluating the requirement for proximate cause in a RICO case, we cannot look only to the language of § 1964(c). It is too broad: "Any person injured in his business or property by reason of a violation of section 1962 of this chapter . . . shall recover . . .." The Supreme Court has been concerned about this breadth of language, which on its face might "be read to mean that a plaintiff is injured 'by reason of' a RICO violation, and therefore may recover, simply on

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44. *Id.* at 1364, 1368.

45. Were it "[t]aken to its ultimate conclusion . . a retailer would be unable to claim injury from shoplifting, or a bank from robbery, on the ground that their business models presumably accounted for such losses in pricing their products and services." Br. Amicus Curiae Third Party Payors at 10.

showing that the defendant violated § 1962, the plaintiff was injured, and the defendant's violation was a 'but for' cause of plaintiff's injury."[46]

The Court addressed this overbreadth concern in *Holmes v. Securities Investor Protection Corp.*[47] Noting that Congress had modeled the broad language of § 1964(c) on the language of the federal antitrust laws, the Court pointed out that historically the lower federal courts had read § 4 of the Clayton Act with the intent of adopting "the judicial gloss that avoided a simple literal interpretation . . .."[48] Thus, the Court had held in the antitrust case of *Associated General Contractors* that "the judicial remedy cannot encompass every conceivable harm that can be traced to alleged wrongdoing."[49]

The *Holmes* Court found the remedy for this overbreadth in the doctrine of "proximate cause." The Court specified that "we use 'proximate cause' to label generically the judicial tools used to limit a person's

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46. *Holmes v. Securities Investor Protection Corp.*, 503 U.S. 258, 265-66, 112 S. Ct. 1311, 117 L. Ed. 2d 532 (1992) (comparing *Associated General Contractors of California, Inc. v. California State Council of Carpenters*, 459 U.S. 519, 529, 103 S. Ct. 897, 74 L. Ed. 2d 723 (1983).

47. 503 U.S. 258, 112 S. Ct. 1311, 117 L. Ed. 2d 532 (1992).

48. *Id.* at 267-68 (quoting *Associated General Contractors*, 459 U.S. at 534.

49. *Associated General Contractors*, 459 U.S. at 537.

responsibility for the consequences of that person's acts."[50] Because of the common language of § 1964(c) and of § 4 of the Clayton Act, the Court in *Holmes* then discussed the elements of proximate cause developed in the common law and, in doing so, referred to *Associated General Contractors*.[51] Among the "many shapes" that the doctrine of proximate cause took at common law "was a demand for some direct relation between the injury asserted and the injurious conduct alleged. Thus, a plaintiff who complained of harm flowing merely from the misfortunes visited upon a third person by the defendant's acts was generally said to stand at too remote a distance to recover."[52]

The *Holmes* Court stated that there are three reasons behind the requirement of a directness of relationship between the injury and conduct alleged. First, the directness of the injury: indirect injuries make it difficult "to ascertain the amount of a plaintiff's damages attributable to the violation, as distinct from other, independent factors."[53] Second, the risk of multiple recoveries: indirect injuries may present such a risk and courts would have to adopt complicated rules apportioning damages to guard against this risk.[54] Third, the likelihood of vindication by others: the need to grapple with the

50. *Holmes*, 503 U.S. at 268.

51. 459 U.S. 519, 103 S. Ct. 897, 74 L. Ed. 2d 723.

52. *Holmes* at 268-69 (citing 1 J. Sutherland, Law of Damages 55-56 (1882)).

53. *Id.* at 269.

54. *Id.*

problems presented by indirect claims may be unjustified "since directly injured victims can generally be counted on to vindicate the law as private attorneys general."[55]

In *Holmes*, the Court concluded that the Securities Investor Protection Corporation (SIPC) had failed to satisfy the proximate cause requirement.[56] The SIPC, as a subrogee, alleged that the defendant engaged in a stock manipulation scheme, which caused two broker-dealers to become insolvent and, in turn, required that the SIPC reimburse the broker-dealers' customers' losses.[57] The Supreme Court held that, even if plaintiffs stood in the shoes of the customers, "the link is too remote between the stock manipulation alleged and the customers' harm, being purely contingent on the harm suffered by the broker-dealers."[58]

Since *Holmes*, the Court has found proximate cause lacking in RICO cases when the conduct directly causing the harm was distinct from the actions that gave rise to the fraud. In *Anza v. Ideal Steel Supply Corp.*,[59] plaintiff alleged that a competing business caused it harm by defrauding the State tax authority and using the proceeds

55. *Id.* at 269-70.

56. See *id.* at 261-63.

57. See *id.*

58. *Id.* at 271.

59. 547 U.S. 451, 126 S. Ct. 1991, 164 L. Ed. 2d 720 (2006).

to offer lower prices to attract more customers.[60] The Court held that the cause of plaintiff's harm was "a set of actions (offering lower prices) entirely distinct from the alleged RICO violation (defrauding the State.)."[61] A plurality of the justices reached a similar decision in *Hemi Group, LLC v. City of New York*,[62] where New York City alleged that out-of-state cigarette sellers failed to file Jenkins Act reports with the State, and asserted injury in the form of lost taxes from City residents.[63] The plurality concluded that causation was even more attenuated than in *Anza* because "the City's theory of liability rest[ed] not just on separate *actions*, but separate actions carried out by separate *parties*."[64] "Put simply, Hemi's obligation was to file the Jenkins Act reports with the State, not the City, and the City's harm was directly caused by the customers, not Hemi."[65]

In contrast, however, if there is a sufficiently direct relationship between the defendant's wrongful conduct and the plaintiffs' injury, the Court has held that a RICO plaintiff who did not directly rely on a defendant's misrepresentation can still establish proximate causation.[66]

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60. *Id.* at 457-58.

61. *Id.* at 458.

62. 559 U.S. 1, 130 S. Ct. 983, 175 L. Ed. 2d 943 (2010).

63. *Id.* at 4-5.

64. *Id.* at 11.

65. *Id.*

66. 553 U.S. 639, 657-58, 128 S. Ct. 2131, 170 L. Ed. 2d 1012 (2008).

In *Bridge v. Phoenix Bond & Indemnity Co.*, bidders at a county tax lien auction alleged that they were directly harmed by other bidders' fraudulent scheme to win more bids at the auction.[67] The defendants argued that the plaintiffs could not establish proximate causation because even though the county may have relied on defendants' misrepresentations, plaintiffs did not.[68] Rejecting this argument, the Court held that the "alleged injury--the loss of valuable liens--[was] the direct result of petitioners' fraud [because] . . . . [i]t was a foreseeable and natural consequence of petitioners' scheme to obtain more liens for themselves that other bidders would obtain fewer liens."[69]

Keeping in mind that at the motion-to-dismiss stage we must accept all plausible allegations in the complaint as true, we view the case before us as more akin to *Bridge* than to *Holmes, Anza*, or *Hemi*. The Court in *Holmes, Anza*, and *Hemi* was concerned that the conduct causing plaintiffs' injuries was different than the conduct allegedly constituting a RICO violation.[70] Each of those

67. *See id.* at 642.

68. *See id.* at 653.

69. *Id.* at 658.

70. *See, e.g., Holmes*, 503 U.S. at 272 ("[T]he link is too remote between the stock manipulation alleged and the customers' harm, being purely contingent on the harm suffered by the broker-dealers . . .. The broker-dealers simply cannot pay their bills, and only that intervening insolvency connects the conspirators' acts to the losses suffered by the nonpurchasing customers and general creditors."); *Anza*, 547 U.S. at 458 ("Ideal asserts it suffered its own harms when the Anzas failed to charge customers for the

cases featured plaintiffs alleging harm that was derivative of harm suffered by a more immediate victim of the RICO activity. Here, GSK focuses on the presence of intermediaries--physicians and patients--in the causal chain. But GSK does not argue that a doctor's decision to prescribe Avandia or a patient's decision to take Avandia caused plaintiffs' injuries. The conduct that allegedly caused plaintiffs' injuries is the same conduct forming the basis of the RICO scheme alleged in the complaint -- the misrepresentation of the heart-related risks of taking Avandia that caused TPPs and PBMs to place Avandia in the formulary. The injury alleged by the TPPs is an economic injury independent of any physical injury suffered by Avandia users.[71] And, as far as we can tell, prescribing physicians did not suffer RICO injury from GSK's marketing of Avandia.

Nor should there be difficulty in distinguishing between the amount of damages attributable to a

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applicable sales tax. The cause of Ideal's asserted harms, however, is a set of actions (offering lower prices) entirely distinct from the alleged RICO violation (defrauding the State)."); *Hemi*, 559 U.S. at 11 ("[T]he conduct directly responsible for the City's harm was the customers' failure to pay their taxes. And the conduct constituting the alleged fraud was Hemi's failure to file Jenkins Act reports. Thus, as in *Anza*, the conduct directly causing the harm was distinct from the conduct giving rise to the fraud.").

71. *See Warfarin*, 391 F.3d at 531 (holding that TPPs had standing to assert antitrust claims because they suffered "direct and independent harm" as a result of paying supracompetitive prices for the defendant's drug regardless of any injury suffered by the consumer plaintiffs).

defendant's violation and to other, independent factors. The amount of damages is either the difference between what Avandia coverage cost and the cost of coverage of cheaper, safer drugs and/or the overvaluation of Avandia caused by GSK's misrepresentations. This issue of damages, rather than demonstrating a lack of proximate causation, raises an issue of proof regarding the overall number of prescriptions (under the "quantity effect" theory) or amount of price inflation (under the "excess price" theory) attributable to GSK's actions. This is a question of damages and, more specifically, a question for another day.

GSK, however, claims that plaintiffs' theory of causation--that TPPs relied on GSK's misrepresentations when including Avandia on formularies--fails as a matter of law. According to GSK, plaintiffs cannot establish causation because they continued to cover Avandia prescriptions after its safety risks were publicly exposed in May 2007. But this argument is based on two faulty assumptions. GSK first asks us to assume, in the absence of contrary allegations, that plaintiffs did not change their coverage of Avandia in 2007.[72] At this stage, however, we do not know that this is true.

In addition, GSK's argument assumes that plaintiffs knew the full scope of GSK's alleged fraud based on the Nissen study. Other TPPs, however, may have chosen to

72. *See* Oral Arg. Tr. at 9:19-10:2 ("There's no allegation in the complaint [Plaintiffs] changed any behavior [in 2007]. And so I think the Court should assume that no change in behavior occurred.").

remove Avandia from their formularies in May 2007 simply out of an abundance of caution, not due to knowledge of Avandia's full scope of risks. In fact, GSK responded to the Nissen study with a marketing campaign, which plaintiffs allege was specifically designed to minimize the report's effects on the medical community. Furthermore, the FDA merely added black box warnings to Avandia in 2007 and did not restrict Avandia usage until September 2010, over three years after the Nissen study's release. Viewing these facts in the light most favorable to plaintiffs, we cannot conclude at this stage that Avandia's cardiovascular risks were fully known in May 2007.

GSK further argues that plaintiffs' claim, that doctors relied on GSK's misrepresentations when prescribing Avandia, fails because there are no allegations that alternative prescriptions would have been cheaper. As a preliminary matter, plaintiffs' injury is not entirely contingent on the existence of cheaper alternative drugs. Although these allegations are central to plaintiffs' "quantity effect" theory, they are less important to an "excess price" theory. Under that theory, plaintiffs may be able to show that Avandia cost too much regardless of whether cheaper drugs existed on the market.

In any event, plaintiffs identify metformin as a cheaper alternative drug, which they allege was the most prevalent oral drug therapy for Type II diabetes prior to Avandia and cost substantially less than Avandia. Despite GSK's contention, it was not necessary for plaintiffs to have included a price comparison between Avandia and Actos, another Type II diabetes drug. Although

metformin may belong to an older class of drugs, it is not entirely clear when -- or even if -- Actos was a more popular alternative to Avandia than metformin. Again, GSK seeks a dismissal as a matter of law when there is a factual dispute between plaintiffs and GSK on the existence of alternative therapies. It is sufficient that a plaintiff identify in the pleadings a specific alternative drug that doctors would have prescribed and that would have cost less.

Finally, GSK argues that the presence of intermediaries, doctors and patients, destroys proximate causation because they were the ones who ultimately decided whether to rely on GSK's misrepresentations. But *Bridge* precludes that argument. The plaintiffs in *Bridge* were the "primary and intended victims of the scheme to defraud" and their injury was a "foreseeable and natural consequence of [the] scheme," regardless of whether they relied on the misrepresentations.[73] The same is true here. Plaintiffs allege that drug manufacturers are well aware that TPPs cover the cost of their drugs and describe the alleged RICO scheme as consisting of "deliberately misrepresenting the safety of Avandia so that Plaintiff and members of the Class paid for this drug."[74] This fraudulent scheme could have been successful only if plaintiffs paid for Avandia, and this is the very injury that plaintiffs seek recovery for. We conclude therefore that plaintiffs' alleged

73. *See* 553 U.S. at 650, 658.

74. J.A.120, ¶ 184 (Allied Services Compl.); J.A.193, ¶ 178 (UFCW Local 1776 Compl.); J.A.265, ¶ 235 (United Benefit Compl.).

injury is sufficiently direct to satisfy the RICO proximate cause requirement at this stage.[75]

Nor does this decision conflict with our holding in *Steamfitters Local Union No. 420 Welfare Fund v. Philip Morris, Inc.*[76] There, we held that proximate causation was lacking where TPPs sued cigarette manufacturers based on alleged misrepresentations and sought damages for the money spent treating beneficiaries' smoking-related health conditions.[77] Analogizing to *Holmes*, we concluded that the smokers, like the broker-dealers there, were the "third party linking the plaintiffs and defendants."[78] In both cases, plaintiffs only "suffered a loss because of the harm that the defendants brought upon th[at] third party."[79] That is not what happened here. Although GSK identifies third parties, doctors and patients, within the causal chain, plaintiffs did not suffer economic harm because those third parties were injured.

To sum up, this case does not present any of the three fundamental causation concerns expressed in *Holmes*. At least for the purposes of this motion to dismiss, the injury is sufficiently direct. There is no risk of duplicative recovery here. And, no one is better suited to sue GSK for

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75. *See Neurontin*, 712 F.3d at 37-38.

76. 171 F.3d 912 (3d Cir. 1999).

77. *Id.* at 930.

78. *Id.* at 932.

79. *Id.*

its alleged fraud.[80] At this stage in the litigation, plaintiffs "need only put forth allegations that raise a reasonable expectation that discovery will reveal evidence" of proximate causation.[81] They have done that here.

IV.

Plaintiffs have plausibly alleged the elements of RICO standing, and GSK has not offered a valid justification for limiting the claims at this stage of the litigation. While many of these issues will resurface in the future, we will not opine on the likelihood of plaintiffs' success down the road. We simply hold that it would be premature to dismiss plaintiffs' well-pled RICO allegations at this juncture. Accordingly, we will affirm the judgment of the District Court.

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80. *See Bridge*, 553 U.S. at 658.

81. *See Fowler v. UPMC Shadyside*, 578 F.3d 203, 213 (3d Cir. 2009) (internal quotations omitted).

APPENDIX B — MEMORANDUM OPINION AND ORDER OF THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED OCTOBER 23, 2013

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF
PENNSYLVANIA

AVANDIA MDL 1871
2007-MD-1871
09-CV-730
10-CV-2475
10-CV-5419

In re: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT RELATES TO

Allied Services Division Welfare Fund,

v.

GSK

UFCW Local 1776 and Participating Employers Health and Welfare Fund,

v.

GSK

United Benefit Fund,

Appendix B

v.

GSK.

October 22, 2013, Decided
October 23, 2013, Filed

MEMORANDUM OPINION AND ORDER

RUFE, J.

Plaintiffs bring these actions against Defendant GlaxoSmithKline LLC ("GSK") alleging RICO violations, violations of state consumer protection laws, and unjust enrichment in GSK's marketing and sales of Avandia.[1] These actions have been filed in the Avandia Marketing, Sales Practices and Products Liability MDL. GSK has moved to dismiss the complaints for failure to state a claim. As similar factual and legal claims are raised in the three complaints, GSK has filed a single motion to dismiss the claims raised in the three cases. The Court, therefore, addresses the adequacy of the pleadings in each of the three complaints herein.

1. In Civ. A. No. 10-5419, only one complaint was filed [Doc. No. 1]. In Civ. A. No. 10-2475, the operative complaint is the First Amended Complaint [Doc. No. 7]. In Civ. A. No. 09-730, the operative complaint is the Second Amended Complaint [Doc. No. 17]. On September 24, 2013, Plaintiff Allied Services Division Welfare Fund filed a Motion for Leave to File a Third Amended Complaint, which GSK has opposed. As the Court has not yet ruled on that Motion, the Court considers only the viability of the allegations set forth in the Second Amended Complaint filed in Civ. A. No. 09-730 herein.

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I. Factual Background[2]

GSK, either directly or through related companies, produces, markets and distributes oral medications to treat Type II diabetes mellitus. These medications are sold under the brand names Avandia, Avandamet and Avandaryl (collectively "Avandia"). Plaintiffs are employee welfare benefit plans and employee benefit plans as defined by the Employee Retirement Income Security Act ("ERISA").[3] Plaintiffs provide medical coverage, including prescription drug coverage, to their members and their members' dependents and, along with other similarly-situated third-party payors ("TPPs"), have paid for Avandia since the Food and Drug Administration ("FDA") approved it for sale in the United States on May 25, 1999.[4]

The FDA approves drugs for sale when the manufacturer can establish, through well-designed, placebo-controlled clinical trials, that a drug is safe to use and effective (compared to a placebo) as a treatment for

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2. The facts set forth herein are taken from the operative complaints, and the allegations will be accepted as true for the purpose of resolving these motions to dismiss. Although the operative complaints are not identical, the alleged facts set forth in this Memorandum Opinion appear in each unless otherwise noted.

3. 29 U.S.C. §§ 1002(1), 1003(a).

4. Avandamet, which combines Avandia and metformin in one pill, was approved by the FDA on October 10, 2002. Avandaryl, which combines Avandia and glimepiride in one pill, was approved by the FDA on November 23, 2005.

all conditions listed or suggested on the drug's proposed label. The FDA also can direct additional research or conduct limited independent research on drug quality, safety, and effectiveness. Once the FDA approves a drug, its manufacturer or distributor can market the drug to doctors, pharmacy benefit managers, health insurance companies and plans, and state and federal agencies, but the information provided cannot be false or misleading.

TPPs generally have Pharmacy Benefit Managers ("PBMs") prepare a formulary, a list of drugs which are approved for coverage when prescribed to the TPP's beneficiaries. In preparing the formulary, the PBM examines research regarding a drug's safety and efficacy, and also assesses cost-effectiveness, for the TPP. If one drug has some advantage over other competing drugs, that drug can be given a priority status on the formulary, which means that a patient will pay a lower co-payment when his or her doctor prescribes that drug. Because PBMs rely on existing research on safety and efficacy, when a company acts, as Plaintiffs allege GSK did, to conceal material information about a drug's safety, the PBM will not have the information it needs to make an informed decision. Here, the TPPs opted to include Avandia on their formularies, sometimes at a higher preference level than competing drugs, and covered Avandia prescriptions at the favorable, formulary rate.

GSK marketed and promoted Avandia as a safe and effective treatment for Type II diabetes that would control blood sugar levels in individuals better than other established medications and thus would lower a

user's cardiovascular risk and improve overall health. Cardiovascular disease is the leading cause of death for individuals with Type II diabetes (more than 65% of diabetics will die of heart attack or stroke), so reduction of cardiovascular risk is a primary goal of any diabetes treatment.

Among other marketing tactics, many of which were directed at physicians or PBMs for TPPs, Plaintiffs allege that GSK employed "ghostwriters" to lend the appearance of independence and objectivity to scientific papers actually authored by GSK, focused on short-term studies so that significant side effects were unlikely to be revealed, and pressured a scientist into retracting statements recommending that clinical trials should be conducted to test the hypothesis that Avandia use was associated with increased heart attacks and heart-related diseases. Plaintiffs also allege that GSK knowingly made false statements to consumers, TPPs, doctors, and pharmacies, and concealed negative information regarding Avandia's cardiovascular risks.

TPPs and PBMs relied, in part, on GSK's representations about the safety and efficacy of Avandia, including promises of better cardiovascular outcomes compared with other diabetes drugs, when deciding whether and how to include Avandia on their formularies. Plaintiffs further allege that GSK knew or should have known that its misrepresentations would harm TPPs, as the TPPs paid a significant premium for a drug which they later learned was associated with serious health risks.

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Since at least 1999, GSK has been aware of, and the FDA has been monitoring, clinical trials and reports of heart-related adverse events associated with Avandia use. Early on, Plaintiffs allege, it was clear that certain adverse events, such as fluid retention, edema, and congestive heart failure, were associated with Avandia use. In 2001, the FDA asked GSK to add a warning to the prescription label, cautioning doctors that use of Avandia could cause fluid retention.[5] The FDA also issued a warning letter to GSK, instructing the company to stop denying or downplaying the risk of heart attacks and heart diseases in its marketing. In April 2006, the FDA required GSK to add a warning based upon data suggesting a potential increased incidence of heart attack and heart-related chest pain in some patients taking Avandia.

On May 21, 2007, Steven E. Nissen, M.D. and Kathy Wolski, M.P.H. published a paper in *The New England Journal of Medicine* documenting their meta-analysis of 42 clinical trials and other relevant published and unpublished studies of Avandia, all of which were trials or studies looking at the long-term effects of Avandia use (more than 24 weeks). The Nissen study reported that, although Avandia does lower blood sugar levels, Avandia is also associated with a statistically significant increase in the risk of myocardial infarction (specifically, a 43% increased risk) and a borderline-significant increase in the risk of death from heart-related diseases compared to competing diabetes medications. Other studies reached

5. Congestive heart failure is characterized by, *inter alia*, abnormal fluid retention, often resulting in edema in the legs and feet.

similar conclusions. Scientists have suggested possible mechanisms or contributing factors for this increased cardiac risk, noting in particular the elevated LDL cholesterol levels and apoB protein levels found in Avandia users, compared with those taking placebos.[6]

According to a 2007 Senate Report, GSK received a leaked draft of the Nissen study before it was published,[7] the results of which were shared with at least 40 GSK executives, including the CEO, the head of research, and the Vice President of Corporate Media Relations. Immediately after the Nissen study was published, GSK responded with a marketing campaign to increase consumer confidence in Avandia, including the publishing of full-page advertisements in more than a dozen United States newspapers on June 5, 2007, as well as the release of promotional materials directed at physician prescribers. The campaign focused on certain key messages. Despite acknowledging, in internal documents, that the results of the Nissen study were similar to the results of GSK's own findings, GSK publically challenged the methodology of and the conclusions reached by the Nissen study. GSK pointed to the company's own RECORD study,[8]

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6. Avandia's product labeling disclosed the association between Avandia use and higher LDL levels.

7. *The New England Journal of Medicine* sent Dr. Nissen's paper out to independent experts in the field for peer review prior to accepting the paper for publication. One of those experts violated the journal's policies by sharing that confidential pre-publication draft with GSK.

8. When Dr. Nissen's study was published, the RECORD study was incomplete and unpublished. GSK approached *The New England Journal of Medicine* about publishing an interim analysis

characterizing it as having employed a "scientifically rigorous way to examine the safety and benefits" of Avandia and as being reassuring with regard to heart-related risks. However, GSK knew that the RECORD study's results were completely compatible with the Nissen study's findings, that the RECORD study did not take into account mitigating factors such as the use of cholesterol-lowering medications with Avandia, and that the study was not designed with sufficient power to answer questions regarding cardiovascular risks.[9] In short, all three complaints allege that through its public statements and marketing efforts, GSK engaged in deceptive behavior with regard to the safety of Avandia, even after the Nissen study was published, and it took steps to avoid detection of their deceptive behavior.

On May 23, 2007, the FDA recommended that GSK add a "black box" warning to its product label to more prominently address the risk of congestive heart failure (not heart attack-- which was the risk at issue in the Nissen study) associated with the use of Avandia. In June

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of the RECORD data. The Journal sent the interim analysis to eight experts for peer review, and many of the reviewers were critical of the study's methods and conclusions. Nevertheless, *The New England Journal of Medicine* published the RECORD study on June 5, 2007, accompanied by an editorial criticizing the study's design, methods, and conclusions.

9. GSK also pointed to the DREAM and ADOPT studies, which had previously been conducted by GSK, to support their position that Avandia was safe. However, neither of these studies was designed to assess whether the use of Avandia by diabetics was associated with cardiovascular risks.

2007, the United States House of Representatives held a hearing to examine how the FDA had assessed the safety of Avandia. In response, two FDA advisory panels met to evaluate Avandia in July 2007. In November 2007, the FDA required GSK to add a black box warning regarding the possible increased risk of heart attacks and other ischemic events.

The complaint in Civil Action No. 10-5419 alleges that in the fall of 2007, the United States Department of Veteran's Affairs, followed by PBMs Prime Therapeutics and HealthTrans, and health insurers such as Kaiser Permanente and government providers, dropped Avandia from their formularies.

In February 2010, senior members of the United States Senate published a Senate Report that summarized a Senate investigation and concluded that GSK was aware of the possibility that Avandia use was correlated with increased cardiac risks years before the risks became publicly known, and had failed to timely notify the FDA and the public of the risk despite an arguable duty to do so. That report also noted that in order to contradict the findings of Dr. Nissen's study, GSK executives had engaged in certain practices designed to minimize or misrepresent findings that Avandia use was associated with greater cardiovascular risk. For example, GSK issued assurances that RECORD study's results contradicted the Nissen study, although GSK knew the RECORD study was not designed to answer questions about cardiovascular safety, and intimidated certain independent researchers in an attempt to prevent them from voicing concerns about Avandia's risks.

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In July 2010, an FDA advisory panel met to review scientific data on Avandia. Of the thirty-three panel members, eighteen felt there were significant safety concerns, twelve recommended that it be taken off the market, ten recommended that the black box warning should be enhanced and additional restrictions on use should be implemented, and seven members voted for enhanced warnings without restriction on prescriptions. Only three members voted for Avandia to continue to be sold with the existing warnings, and one member abstained. Around that time, the FDA placed on hold an ongoing study comparing Avandia and a competing drug, Actos (the TIDE study). Ultimately, in September 2010, the FDA announced significant restrictions on access to Avandia, allowing its continued use by patients already taking the drug only after their doctors reviewed with them statements describing the cardiovascular risks associated with Avandia,[10] and limiting new prescriptions to patients whose blood sugar was inadequately controlled with other medications and who decided, in consultation with their physician, not to take Actos. Around the same time, the European Medicines Agency suspended marketing authorization for Avandia in Europe, and advised physicians to transition patients to other treatment options.

Since its introduction in 1999, more than one million individuals in the United States have used Avandia on a

10. GSK is required to provide comprehensive risk information for dissemination to patients, and each patient's receipt and understanding of the materials must be documented in the patient's medical records.

regular basis. A monthly supply sold for between $90 and $220, with the TPPs typically paying between $135 and $140 per month per prescription, and patient co-pays covering the balance. In contrast, the typical cost for metformin, another medication used to treat Type II diabetes, was $45-55 for a monthly supply, with TPPs typically paying $40-50 per month per prescription. Although Plaintiffs also propose Actos as a safer alternative to Avandia, the complaints do not indicate the amount the TPPs typically pay for Actos prescriptions.

Plaintiffs seek to litigate their claims as class actions, filing on behalf of themselves and other health insurance companies, TPPs, health maintenance organizations (HMOs), health and welfare benefit plans, and other health benefit providers which paid for Avandia after May 25, 1999. Plaintiffs assert violations of RICO,[11] based on acts of mail fraud, wire fraud, tampering with witnesses, and use of interstate facilities to conduct unlawful activity. Plaintiffs also assert that GSK violated the Pennsylvania Unfair Trade Practices and Consumer Protection Law (UTPCPL),[12] and other state consumer protection and unfair and deceptive practices laws.[13] Finally, Plaintiffs assert claims for unjust enrichment. They seek both monetary damages and equitable relief.

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11. 18 U.S.C. § 1962(c)-(d).

12. 73 Pa. C.S.A. § 201-1 - 201-9.3.

13. The Complaint cites the applicable statute from each of the fifty states.

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II. Standard of review

Pursuant to Federal Rule of Civil Procedure 12(b)(6), dismissal of a complaint for failure to state a claim upon which relief can be granted is appropriate where a plaintiff's "plain statement" lacks enough substance to show that he is entitled to relief.[14] In determining whether a motion to dismiss should be granted, the court must consider only those facts alleged in the complaint, accepting the allegations as true and drawing all logical inferences in favor of the non-moving party.[15] Courts are not, however, bound to accept as true legal conclusions couched as factual allegations. [16] Something more than a mere *possibility* of a claim must be alleged; rather plaintiff must allege "enough facts to state a claim to relief that is plausible on its face."[17] The complaint must set forth "direct or inferential allegations respecting all the material elements necessary to sustain recovery under *some* viable legal theory."[18] The court has no duty to "conjure up unpleaded facts that might turn a frivolous

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14. *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 557, 127 S. Ct. 1955, 167 L. Ed. 2d 929 (2007).

15. *ALA, Inc. v. CCAIR, Inc.*, 29 F.3d 855, 859 (3d Cir. 1994); *Fay v. Muhlenberg Coll.*, No. 07-4516, 2008 U.S. Dist. LEXIS 5063, 2008 WL 205227, at *2 (E.D. Pa. Jan. 24, 2008).

16. *Twombly*, 550 U.S. at 555, 564.

17. *Id.* at 570.

18. *Id.* at 562 (quoting *Car Carriers, Inc. v. Ford Motor Co.*, 745 F.2d 1101, 1106 (7th Cir. 1984)) (internal quotation marks omitted).

. . . action into a substantial one."[19] Legal questions that depend upon a developed factual record are not properly the subject of a motion to dismiss.[20]

III. Discussion

GSK has filed a motion to dismiss each case, arguing generally that Plaintiffs have failed to establish causation, because they have failed to adequately allege a cognizable injury and proximate causation--a necessary element of each of Plaintiffs' claims. They further argue that Plaintiffs' RICO claims fail because Plaintiffs fail to allege a predicate act; that the Pennsylvania UTPCPL claim fails because the act does not allow consumer fraud claims based on the sale of a prescription drug; and that the unjust enrichment claims fail because they are predicated on invalid tort claims. Finally, GSK seeks dismissal of Plaintiffs' nationwide class allegations to the extent that they rely upon varying state consumer protection laws.

A. RICO

Plaintiffs allege two RICO violations: (1) the existence of a marketing enterprise which engaged in a pattern of racketeering activity;[21] and (2) a conspiracy related to that

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19. *Id.* (quoting *McGregor v. Indus. Excess Landfill, Inc.*, 856 F.2d 39, 42-43 (6th Cir. 1988)).

20. *See, e.g., TriState HVAC Equip., LLP v. Big Belly Solar, Inc.*, 836 F. Supp. 2d 274 (E.D. Pa. 2011).

21. The 18 U.S.C. § 1962(c) claim.

marketing and promotion enterprise.[22] To state a RICO claim, Plaintiffs must first establish statutory standing, by alleging: (1) that the Plaintiff suffered an injury to business or property; and (2) that the injury was caused by GSK's violations of 18 U.S.C. § 1962.[23] GSK argues that Plaintiffs' RICO claims must be dismissed for failure to allege facts demonstrating statutory standing, including injury and causation, as well as for failure to allege that GSK committed a predicate act (i.e. racketeering activities).

Statutory Standing

Injury: As noted in the factual summary above, the complaints include factual allegations supporting Plaintiffs' claim that GSK was misleading the public, as well as PBMs and TPPs, with regard to Avandia's safety. The complaints allege that GSK intended to mislead PBMs and TPPs, so that they would include and prioritize Avandia on their formularies and cover prescriptions for Avandia without restrictions. Moreover, it is alleged that the intervening acts of physician prescribers were not independent and unforeseeable to GSK; in fact, it is alleged, the marketing campaign was *designed* to mislead physicians, so as to increase the number of Avandia prescriptions written and covered by TPPs.[24] Plaintiffs

22. The 18 U.S.C. § 1962(d) claim.

23. *Maio v. Aetna, Inc.*, 221 F.3d 472, 483 (3d Cir. 2000).

24. The Court will discuss whether misrepresentations by GSK *caused* the TPPs to include Avandia on their formularies in the next section. In this section, it confines itself to an analysis of injury.

also allege that doctors are more likely to prescribe drugs which are included on a patient's insurer's formulary. Absent GSK's conduct, Plaintiffs allege, many patients would have been prescribed Metformin, another effective medication for diabetes treatment, which Plaintiffs claim is significantly cheaper and carries less risk than Avandia. The TPPs would then have covered the cost of prescriptions for a less expensive drug, at substantial savings to them.[25] Accordingly, Plaintiffs argue that they suffered a concrete economic injury, which is unaffected by whether any given patient who ingested Avandia became ill, and which may be redressed by economic damages.[26] The Court finds that Plaintiffs' claims sufficiently allege an economic injury at this pleading stage of the litigation.

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25. GSK argues that Plaintiffs have not alleged that they would have saved money had doctors prescribed alternative medications, pointing out that while some diabetes medications cost less than Avandia, others are priced similarly to Avandia, and moreover, doctors could prescribe two or more less expensive medications in combination, resulting in a monthly cost equivalent to or even greater than the cost of Avandia. While the Court recognizes that this may be true, that argument is more relevant to summary judgment or the calculation of damages; here, at the pleading stage, Plaintiffs' claims of injury are sufficient.

26. *In re Warfarin Sodium Antitrust Litig.*, 391 F3d 516, 531 (3d Cir. 2004); *Desiano v. Warner-Lambert Co.*, 326 F.3d 339 (2d Cir. 2003); *Am.. Fed'n of State County and Mun. Employees, District Council 47 Health and Welfare Fund v. Ortho-McNeil-Janssen Pharmaceuticals, Inc.*, No. 08-5904, 2010 U.S. Dist. LEXIS 23181, 2010 WL 891150, at *3 (E.D. Pa., March 11, 2010); *In re Neurontin Mktg. and Sales Practices Litig.*, 2011 U.S. Dist. LEXIS 99593, 2011 WL 3852254, at *54-57 (D. Mass. Aug. 31, 2011); *In re Neurontin Mktg. and Sales Practices Litig.*, 433 F. Supp. 2d 172, 185-86 (D. Mass. 2006).

Causation: To state a claim under RICO, Plaintiffs must plead not only "but-for" causation (factual cause), but proximate causation, which demands some direct relation between the injury asserted and the injurious conduct alleged.[27]

Plaintiffs allege that GSK's misrepresentations concerning Avandia's safety increased the number of prescriptions for Avandia written by doctors and filled by patients, as doctors would have prescribed other, safer medications to patients absent the alleged misconduct. As noted above, some of these safer medications, such as Metformin, are significantly less expensive than Avandia. Plaintiffs also argue that GSK's misrepresentations led TPPs to include and prioritize Avandia on their drug formularies without restrictions. Plaintiffs therefore paid for Avandia, which was not as safe as marketing materials suggested, rather than covering the cost of less risky and less costly alternatives which physicians would have otherwise prescribed, and that their injuries were foreseeable and natural consequences of GSK's scheme to mislead the public, including physicians and insurers, with regard to Avandia's safety.

GSK argues that Plaintiffs have failed to allege a "specific representation by GSK that caused it to pay for a prescription of Avandia."[28] Plaintiffs have put forth factual allegations which, if proved, would support a finding that

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27. *Holmes v. Sec. Investor Prot. Corp.*, 503 U.S. 258, 265-68, 112 S. Ct. 1311, 117 L. Ed. 2d 532 (1992).

28. Mem. of Law in Supp. of Def.'s Mot. to Dismiss at 9.

GSK deliberately *concealed* Avandia's cardiovascular risk, as well as issuing affirmatively misleading statements. For example, Plaintiffs allege facts suggesting that GSK manipulated scientific literature and available data, citing the United State Senate's finding that GSK had executed "an orchestrated plan to stifle opinion" by intimidation and that GSK's executives "focused on strategies to minimize findings that Avandia may increase cardiovascular risk." Although it is not clear from the Complaints the extent to which the alleged misrepresentations and concealments were directed at the TPPs or their PBMs, the Complaints allege that PBMs routinely rely upon existing scientific literature when making formulary decisions, and that they did rely upon such literature when making formulary decisions about Avandia. Therefore, Plaintiffs have adequately alleged that GSK misrepresented the safety of Avandia, and that these misrepresentations influenced the inclusion of Avandia on the formularies.

Defendant next argues that Plaintiffs cannot establish proximate cause because the company's research and marketing materials regarding the safety and efficacy of Avandia were directed at prescribing physicians, and not the insurers. However, the Court finds guidance in the First Circuit's decision in the Neurontin litigation, in which the court affirmed a jury verdict of liability against an insurance company and held that first-party reliance is not a necessary element of proximate cause in every private RICO claim.[29] Where misrepresentations are directed at

29. *In re Neurontin Mktg. and Sales Practices Litig.* 712 F.3d 21, 36-37 (1st Cir. 2013) (*citing Bridge v. Phoenix Bond & Indem. Co.*, 553 U.S. 639, 640, 128 S. Ct. 2131, 170 L. Ed. 2d 1012 (2008).

prescribing doctors, rather than TPPs, but a TPP, as payor, is a "primary and intended victim" and the injury to the insurer is foreseeable,[30] the doctor's independent actions do not break the causal chain.[31] Moreover, the First Circuit reasoned, the physicians to whom the pharmaceutical company made its misrepresentations never "paid anything toward a Neurontin prescription, so there is no risk of multiple recoveries due to a suit by another of those actors. [The TPP] is also in the best position to enforce the law because [the TPP] is the party that directly suffered economic injury from [defendant's] scheme."[32] Finally, the First Circuit noted that a finding of liability would have a deterrent effect on similar, wrongful conduct.[33]

The First Circuit also noted that some of the misrepresentations had been directed at the TPP's Drug Information Service ("DIS"), which functions similarly to the PBMs in this case, reviewing research and summarizing available evidence regarding safety and efficacy of medications to guide formulary decisions for TPPs. Because of the manufacturer's strategy, the

30. *Id.* at 37-39. The First Circuit wrote: "Pfizer has always known that, because of the structure of the American health care system, physicians would not be the ones paying for the drugs they prescribed. . . . Those payments came from Kaiser and other TPPs." *Id.* at 38-39.

31. *Id.*

32. *Id.*, at 37-38.

33. *Id.*, at 39-40.

court found that important negative study results were not publically available, and therefore the "[a] reasonable factfinder could readily conclude that misinformation received by the DIS would be widely disseminated, utilized, and relied upon throughout [plaintiff's] organization to cause but-for injury."[34] The appellate court found that the district court and the jury had correctly concluded that the manufacturer's publication strategies and other communications directly affected TPPs' decisions about the drug's placement on the formulary without restrictions, and the TPP's reliance on the drug manufacturer's intentional misrepresentations and omissions caused the TPP injury, because it reimbursed for Neurotin prescriptions rather than less costly alternatives.[35] The First Circuit concluded that the TPP had met both the direct relationship and functional tests for proximate causation which had been articulated in *Holmes* and its progeny.[36]

Similarly, in other TPP litigation, the Second Circuit found that the TPP's "quantity effect theory," which is the theory of injury Plaintiffs rely upon here, was potentially viable, although other theories of liability were not.[37] The Second Circuit described the chain of causation as follows: 1) TPPs place a drug on their formularies; 2) the

34. *Id.* at 40.

35. *Id.*, at 41..

36. *Id.*, at 38.

37. *UFCW Local 1776 v. Eli Lilly & Co.*, 620 F. 3d 121, 136 (2nd Cir. 2010).

manufacturer distributes misinformation about the drug; 3) physicians rely on that misinformation; and 4) TPPs pay for an excess number of prescriptions for that drug. Although the court noted that "even now, TPPs pay for Zyprexa and for the most part have not implemented close control or review of Zyprexa prescriptions"[38] the court found that the TPPs might be able to establish causation and therefore held that the theory was potentially viable. The Second Circuit remanded the case to the District Court for further consideration of whether the claims could survive a motion for summary judgment.

Turning to the facts before this Court, the Court must determine whether Plaintiffs have adequately pled that GSK's misrepresentations were the but-for and proximate cause of the alleged injury to Plaintiffs. Here, the TPPs have alleged that doctors relied upon GSK's misrepresentations, and also alleged that the TPPs themselves relied upon GSK's misrepresentations when making formulary decisions. "Defendant controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, [so] all Class members . . . were obligated to rely on Defendant's representations about Avandia. Further, Defendant perpetuated this reliance by . . . suppress[ing] the dissemination of any critical information about Avandia."[39] Although Plaintiffs argue that "had the truth about the significant, life-threatening health risks associated with Avandia been known, Plaintiffs would not have paid for this dangerous

38. *Id.*

39. Civ. A. No. 09-730, Compl. ¶191.

drug,"[40] GSK argues that Plaintiffs have pled no facts from which the Court can infer that Plaintiffs would have made different coverage decisions regarding Avandia if GSK had provided more or different information about the risks. In support of this argument, GSK points out that Plaintiffs have not alleged that they removed Avandia from their formularies or limited coverage for Avandia after the Nissen study was published in 2007. Although alternative diabetes drugs were available, including those which Plaintiffs indicate could have been covered at lower cost--Metformin and the sulfonylureas--Plaintiffs continued to cover Avandia as a formulary drug.[41] Therefore, GSK argues, Plaintiffs' allegations that they would not have included Avandia on their formularies if GSK had not concealed the risks are not plausible.

The Court recognizes the logic of this argument, but finds that Plaintiffs may be able to prove that GSK's earlier misrepresentations regarding Avandia's risks were a proximate cause of formulary and coverage decisions made prior to 2007, as well as prescribing physicians' decisions prior to 2007, notwithstanding their failure to remove Avandia from their formularies after Dr. Nissen's study was published. At this stage in the litigation, the

40. Resp. to Def.'s Mot. to Dismiss, filed by Allied Services and UFCW, at 19.

41. In its complaint, United Benefit Fund alleges that other TPPs, including the United States Department of Veteran's Affairs, Kaiser Permanente, and the County of Santa Clara, as well as two PBMs, Prime Therapeutic and HealthTrans, dropped Avandia from their formularies in 2007, following the publication of Dr. Nissen's study.

Court finds that Plaintiffs have alleged sufficient facts to survive a motion to dismiss. However, because the named TPPs did not act to remove Avandia from their formularies or even restrict their coverage of Avandia in light of research published and widely publicized in 2007, whereas other TPPs did take such actions, the Court notes the potential difficulty in proving causation in the next stage of the litigation.[42]

The Court thus finds that Plaintiffs have alleged sufficient facts regarding the causal relationship between GSK's concealment of the drug's true safety profile and Plaintiffs' injuries to satisfy the causation requirements of RICO at this stage in the litigation. The Court sees the alleged chain of causation as follows: 1) the manufacturer distributes misinformation about the drug; 2) TPPs rely upon that misinformation and place Avandia on their formularies; 3) physicians rely upon that misinformation (and possibly formulary status) and prescribe the drug; and 4) TPPs pay for an excess number of prescriptions for that drug. As the Complaints sufficiently plead causation and injury, the Court finds that the TPPs have statutory standing to assert RICO claims against GSK.

Elements of a RICO Claim

In addition to establishing statutory standing, to state a RICO claim under § 1962(c), Plaintiffs must allege that: (1) an enterprise that engaged in interstate commerce existed; (2) GSK was associated with that enterprise;

42. *UFCW*, 620 F.3d at 134.

(3) GSK participated in the affairs of the enterprise; and (4) GSK participated in a pattern of racketeering activity (i.e. at least two racketeering acts).[43] GSK argues that Plaintiffs have failed to adequately allege two or more predicate acts of racketeering, as defined by § 1961. Plaintiffs allege that GSK both acted on its own and with non-employees, including scientists who agreed to be ghost-writers for GSK-conducted research, in its efforts to mislead the public with regard to the safety of Avandia.[44] They further argue that they have adequately alleged that GSK engaged in the following predicate "racketeering activities": mail fraud, wire fraud, use of interstate facilities to conduct unlawful conduct, and witness tampering.

When fraud is the predicate act, a plaintiff must satisfy the heightened pleading standard of Federal Rule of Civil Procedure 9(b).[45] "To satisfy this standard, the plaintiff must plead or allege the date, time and place of the alleged fraud or otherwise inject precision or some measure of substantiation into a fraud allegation."[46] To state a claim for mail fraud, Plaintiff must plead, with

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43. *Sedima S.P.R.L. v. Imrex Co.*, 473 U.S. 479, 496, 105 S. Ct. 3275, 87 L. Ed. 2d 346 (1985).

44. Defendant does not contest Plaintiffs' allegations regarding the existence of an enterprise.

45. *Warden v. McLelland*, 288 F.3d 105, 114 (3d Cir. 2002).

46. *District 1199P Health and Welfare Plan v. Janssen, L.P.*, No. 06-3044, 2008 U.S. Dist. LEXIS 103526, 2008 WL 5413105, at *10. (D.N.J. Dec. 23, 2008) (citing *Lum v. Bank of America*, 361 F.3d 217, 223-24 (3d Cir. 2004)).

specificity, the use of a mailing through the United States Postal Service or interstate use of a wire in furtherance of a scheme to defraud.[47] Here, among other allegations, Plaintiffs allege that GSK orchestrated a plan to stifle the opinion of Dr. Buse, who, in 1999, wrote to Defendant regarding his research indicating that Avandia had the potential to increase heart-attacks and heart-related diseases, and received several telephone calls and a letter in response which threatened legal action against him if he publicized such findings. Under pressure from GSK, Dr. Buse signed a retraction letter prepared by GSK. Similarly, in February 2010, Defendant allegedly sent a letter to the editor of *European Heart Journal*, urging him not to publish Dr. Nissen's editorial on the cardiovascular risks of Avandia. Plaintiffs note that these attempts to suppress the voices of scientists were just one part of GSK's elaborate scheme to conceal the true risks of Avandia use. That scheme also included the issuance of press releases, televised advertisements, and the nationwide distribution of marketing materials to prescribing doctors and TPPs, all involving the use of the mail and interstate wires. Plaintiff pleads all of these actions in sufficient detail to survive a motion to dismiss.

Plaintiffs also argue that GSK violated the witness tampering act, 18 U.S.C. § 1512. As noted above, Plaintiffs allege that Defendant intimidated certain scientists, including Dr. Buse, to prevent them from publishing research which might reveal the true risks of Avandia use. Defendant argues that Plaintiffs have not alleged

47. 2008 U.S. Dist. LEXIS 103526, [WL] at *11.

that such tampering had any impact on an official federal proceeding or investigation, as required under the statute.[48] However, as Plaintiffs allege in their complaint, the FDA, a government agency, was engaged in continuing oversight of Avandia, which included periodic reviews and proceedings regarding the safety and efficacy of Avandia. Therefore, if Defendant intimidated Dr. Buse to suppress his research on the risks of Avandia, Plaintiffs may be able to establish that the intimidation did interfere with FDA proceedings. The allegations are sufficient at this point in the proceedings.

Plaintiffs argue that GSK also used interstate facilities to engage in unlawful conduct, in violation of 18 U.S.C. § 1952, but fail to allege any unlawful conduct as defined by that statute.[49] Therefore, Plaintiffs have failed to state a claim under 18 U.S.C. § 1952.

B. State Consumer Protection Act Claims

Standing to Assert Claims Under the Laws of Other States

The parties agree that each Plaintiff has standing to assert claims under the consumer protection laws of the state in which it is located. Allied Services may raise

48. 18 U.S.C. §§ 1512, 1515.

49. See 18 U.S.C. §1952(b), defining unlawful conduct to include illegal gambling, sale of liquor, prostitution, narcotics sales, use of extortion, bribes, or arson, or any indictable act. This section does not apply to civil RICO claims.

claims under the law of Illinois, UFCW may bring claims under the laws of Pennsylvania, and United Benefit Funds may assert claims under the laws of New York.

However, the complaints assert claims under the consumer protection laws of every state. GSK argues that a TPP lacks standing to assert claims under the laws of states other than the state in which it is located, and therefore those claims should be dismissed. Allied Services and UFCW agree that a TPP has standing to proceed *only* under the consumer protection law of the state in which that TPP is based, and indicate that the complaints merely include claims under the laws of the other states in the event that the Court certifies a nationwide class of TPPs.[50] Because other members of the proposed class may have viable claims under the laws of other states, the Court will not dismiss those claims at this time.

United Benefit Fund, in contrast, argues that a TPP can also assert claims under the law of the states where their members resided and made reimbursed drug purchases. However, although United Benefit Fund's complaint alleges that it represents approximately 2,500 members, and no discovery from GSK is needed to learn where those members purchased Avandia, United Benefit Fund's complaint does not allege that a single member filled a prescription for Avandia outside of New York. Accordingly, United Benefit Fund may only assert a claim under New York law.

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50. Doc. No. 23 at 25.

United Benefit Fund also argues that it has standing to sue GSK under Pennsylvania's UTPCPL, despite being a citizen of New York, on the grounds that GSK is a "Pennsylvania merchant"[51] whose wrongful actions were orchestrated in and emanated from Pennsylvania. However, the UTPCLP was enacted to protect Pennsylvania consumers, and United Benefit Fund cites to no authority for the proposition that Pennsylvania law should apply when wrongdoing emanating from Pennsylvania affects non-residents.[52] Accordingly, the Court finds United Benefit Fund, a New York-based company, lacks standing to assert claims on its own behalf except under the consumer protection laws of New York State.[53]

For the reasons above, the Court finds that each TPP has standing to sue only under the consumer protection act of the state in which the TPP is located.

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51. In *Johnson v. SmithKline Beecham Corp*, 724 F.3d 337, 349 (3d Cir. 2013), the Third Circuit held that GSK is a citizen of Delaware for purposes of diversity jurisdiction. However, it is undisputed that GSK's headquarters is in Pennsylvania. For the purpose of this motion, the Court will accept as true the allegation that GSK's wrongful actions emanated from Pennsylvania.

52. *See Baker v. Family Credit Counseling Corp.*, 440 F.Supp.2d 392, 414 (E.D. Pa. 2006) (noting that states have a strong interest in applying their own consumer protection laws to their own citizens, and refusing to apply the UTPCPL to non-residents of Pennsylvania).

53. *In re Wellbutrin XL Antitrust Litig.*, 260 F.R.D. 143, 156-57 (E.D. Pa. 2009).

Appendix B

Elements of Consumer Protection Act Claims

1. UFCW

Plaintiff UFCW is located in Pennsylvania, and asserts claims under Pennsylvania's UTPCPL on behalf of UFCW and other Pennsylvania-based TPPs. GSK argues that UFCW has not adequately alleged that GSK committed unfair or deceptive acts or practices under Pennsylvania's UTPCPL, as it has not adequately alleged exposure to a misrepresentation, injury, justifiable reliance, or causation.[54]

54. GSK also argues that the UTPCPL does not apply to the sale of prescription drugs, because of the learned intermediary doctrine, relying on cases in which the plaintiffs were patients who used prescription drugs, and those drugs had been prescribed by physicians who had been adequately warned about the risks. However, here, Plaintiffs are TPPs who allege that they themselves relied on misinformation GSK provided. Unlike patients, whose doctors would weigh many factors before prescribing a medication for them, including factors unique to each patient as wells as disclosed risks, PBMs would not weigh patient-specific information, but rather would focus only on general factors, such as the available safety and efficacy information, in deciding whether to include a drug on a TPP's formulary. Plaintiffs allege that GSK intended the TPPs to be misled by the research and marketing materials and to rely on those misrepresentations when making formulary decisions. That is, providing misinformation to induce the TPPs to include Avandia on their formularies was part of GSK's scheme. Based upon these allegations, the Court does not find that UTPCPL claims are *necessarily* barred by the learned intermediary doctrine. However, upon a proper motion, this challenge can be asserted again once the parties have developed a complete factual record.

Appendix B

UFCW has alleged that GSK deliberately concealed information about the increased cardiovascular risks associated with Avandia use, and provided misinformation about its safety, knowing that the information it provided would be considered by the TPPs and the PBMs they work with as they determined whether they would cover the costs of Avandia for their members. It is further alleged that GSK did so in order to increase sales and profits. The factual allegations include details about the people involved and the methods used to deceive the public, as well as facts from which the Court can infer that Plaintiffs were intentionally exposed to the misrepresentations; for example, it was alleged that GSK marketed Avandia directly to the PBMs, and that GSK knew that the PBMs would rely upon the reported results of GSK's own research when making formulary decisions. UFCW also alleges financial consequences: Once it decided to include Avandia on its formulary, it was required to pay for members' prescriptions for Avandia despite the availability of cheaper and safer alternatives. Plaintiffs adequately allege that they relied upon GSK's misrepresentations about Avandia's safety in deciding to place Avandia on their formularies, as they allege that they were reliant upon studies and marketing materials which had been impacted by GSK's alleged scheme to suppress publication of information about risks associated with Avandia use. They also allege that the decision to put Avandia on their formulary, based on this alleged misinformation, caused financial losses. Therefore, the Court finds that UCFW has adequately stated a claim under Pennsylvania law.

2. Allied Services

Allied Services is based in Illinois, and asserts a claim on its own behalf and on behalf of other Illinois-based TPPs under the Illinois Consumer Fraud Act.[55] To state a under this Act, Allied Services must allege that (1) GSK engaged in an unfair and/or deceptive act or practice; (2) GSK intended TPPs to rely on that act or practice;[56] (3) the act or practice impacted on trade or commerce; and (4) the act or practice was the proximate cause of an actual injury to Plaintiff.[57] For the reasons set forth above, the Court finds that Allied Services has alleged that GSK engaged in deceptive practices, that GSK intended the TPPs to rely on those practices. For the reasons set forth in its discussion of RICO claims, the Court also finds that the allegations of proximate causation are adequate as to the Illinois Consumer Fraud Act.

3. United Benefit Fund

United Benefit Fund is based in New York. To state a claim under New York's Consumer Protection Act[58] a plaintiff must allege "that the defendant engaged in

55. 815 Ill. Comp. Stat. §§ 505/1 - 505/12.

56. Actual reliance is not an element of the claim. *Connick v. Suzuki Motor Co., Ltd.*, 174 Ill. 2d 482, 675 N.E.2d 584, 221 Ill. Dec. 389 (Ill. 1996).

57. *Zekman v. Direct Am. Marketers, Inc.*, 182 Ill. 2d 359, 695 N.E.2d 853, 860-61, 231 Ill. Dec. 80 (Ill. 1998).

58. N.Y. Gen. Bus. Law § 349, et seq.

a material deceptive act or practice that caused actual . . . harm."[59] While the plaintiff need not allege justifiable reliance, it must plead that the deceptive act or practice was the cause of the alleged harm. [60] Again, for the reasons set forth above, the Court finds that the allegations of proximate causation are adequate under New York law, and the claims brought under the New York Consumer Protection Act will not be dismissed.

C. Unjust Enrichment[61]

Finally, GSK argues that Plaintiffs' unjust enrichment claims must be dismissed. Unjust enrichment is an equitable concept most commonly invoked in the context of quasi-contractual relationships in which one party is

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59. *Oswego Laborers' Local 214 Pension Fund v. Marine Midland Bank, N.A.*, 85 N.Y. 2d 20, 26, 647 N.E.2d 741, 623 N.Y.S.2d 529 (N.Y. 1995).

60. *Id.*

61. The briefs filed by United Benefit Fund ask the Court to apply Pennsylvania law, the law of the forum, with regard to its unjust enrichment claims. Allied Services Division Welfare Fund's briefs include both the Pennsylvania and Illinois standards for pleading unjust enrichment. The two standards are substantially similar, and therefore the Court need not engage in a choice of law analysis. *See HPI Health Care Services, Inc. v. Mt. Vernon Hosp., Inc.*, 131 Ill. 2d 145, 545 N.E. 2d 672, 679, 137 Ill. Dec. 19 (Ill. 1989) ("To state a cause of action based on a theory of unjust enrichment, a plaintiff must allege that the defendant has unjustly retained a benefit to the plaintiff's detriment, and that defendant's retention of the benefit violates the fundamental principles of justice, equity, and good conscience.")

enriched, the enriched party knew about and accepted the benefit, and the conferral of that benefit without recovery or compensation would be unjust.[62] GSK argues that Plaintiffs have not adequately alleged that they received anything less than what they paid for (i.e. a drug which treated diabetes by effectively controlling blood sugar).

To state an unjust enrichment claim under Pennsylvania law, Plaintiffs must allege: 1) a benefit conferred on one party by another; 2) appreciation of the benefit by the recipient; 3) acceptance and retention of the benefit under circumstances that would make it inequitable for the recipient to retain the benefit without providing compensation.[63] Plaintiffs allege that it conferred a benefit on GSK by paying for or reimbursing the cost of Avandia prescriptions for its members, which payment was appreciated, accepted, and retained by GSK. Plaintiff further argues that because GSK hid the dangers of Avandia, GSK's retention of those payments is unjust. However, Plaintiffs have failed to allege: 1) that Avandia injured a single one of its beneficiaries; 2) that Avandia failed to perform as advertised for its members;[64]

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62. *Steamfitters Local Union No. 420 Welfare Fund v. Philip Morris, Inc.*, 171 F.3d 912, 936 (3d Cir. 1999); *In re Actiq Sales and Mktg. Practices Litig.*, 790 F. Supp. 2d 313, 329 (E.D. Pa. 2011)

63. *Allegheny Gen. Hosp. v. Phillip Morris, Inc.*, 228 F.3d 429, 447 (3d Cir. 2000); *Am. Fed'n. of State County and Mun. Employees, Inc.*, 2010 U.S. Dist. LEXIS 23181, 2010 WL 891150, at *7.

64. Plaintiffs do not dispute GSK's claim that Avandia effectively lowers blood sugar in Type 2 diabetes.

or 3) that their beneficiaries were advised to or did discard purchased Avandia medication when they learned of the risks.[65] Therefore, based on the allegations before the Court, it appears that Plaintiffs have received the benefit of their bargains. Accordingly, the Court finds that they have failed to state a claim for unjust enrichment under Pennsylvania law.[66]

IV. Conclusion

For the foregoing reasons, the Court will dismiss Plaintiffs' unjust enrichment claims, but Plaintiffs will be allowed to proceed on their RICO claims and on claims asserted under the state consumer protection laws of the state in which the TPP operates. An appropriate Order follows.

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65. *Cf Am. Fed'n. of State County and Mun. Employees*, 2010 U.S. Dist. LEXIS 23181, 2010 WL 891150.

66. *District 1199P*, 2008 U.S. Dist. LEXIS 103526, 2008 WL 5413105 (addressing the issue of injury in the RICO context).

APPENDIX C — CORRECTED ORDER OF THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED FEBRUARY 19, 2014

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

AVANDIA MDL 1871
2007-MD-1871
09-CV-730
10-CV-2475
10-CV-5419

In re: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT RELATES TO

Allied Services Division Welfare Fund,

v.

GSK UFCW Local 1776 and Participating Employers Health and Welfare Fund,

v.

GSK United Benefit Fund,

v.

GSK

Appendix C

CORRECTED ORDER

AND NOW, this 18th day of February 2014, upon consideration of Defendant's Motion to Amend October 22, 2013 Order[1] to Conform to Memorandum Opinion [MDL 1871 Doc. No. 3669], the Court hereby enters this **CORRECTED ORDER** implementing the ruling set forth in the Court's October 22, 2013 Memorandum Opinion (MDL 1871, Doc. No. 3618).

Upon consideration of Defendant's Motion to Dismiss the claims of the above named Plaintiffs, and all responses, replies, sur-replies, and supplemental authority submitted, and for the reasons set forth in the Court's October 22, 2013 Memorandum Opinion, it is hereby **ORDERED** that:

1. The Motion to Dismiss the claims of Allied Services Division Welfare Fund [Case No. 09-730, Doc. No. 19] is **DENIED** in substantial part. Having found that Allied Services Division Welfare Fund has failed to state a claim for unjust enrichment under Pennsylvania law, claims for unjust enrichment are dismissed without prejudice.

2. The Motion to Dismiss the claims of UFCW Local 1776 [Case No. 10-2475, Doc. No. 16] is **DENIED** in substantial part. Having found that UFCW Local 1776 has failed to state a claim for unjust enrichment under Pennsylvania law, claims for unjust enrichment are dismissed without prejudice.

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1. The relevant Memorandum Opinion and Order were signed by the Court on October 22, 2013 but docketed on October 23, 2013. See MDL 1871, Doc. No. 3618 and 3619. The Court will refer to these using the October 22, 2013 date.

3. The Motion to Dismiss the claims of United Benefit Fund [Case No. 10-5419, Doc. No. 6] is **DENIED** in substantial part. However, having found that United Benefit Fund lacks standing to assert a claim on its own behalf under Pennsylvania's UTPCLP, its UTPCLP claim asserted on its own behalf is **DISMISSED**. Having found that United Benefit Fund has failed to state a claim on its own behalf under the consumer protection laws of any state except New York, those state law claims are **DISMISSED** without prejudice. Having found that UTPCLP has failed to state a claim for unjust enrichment under Pennsylvania law, claims for unjust enrichment are dismissed without prejudice.

4. To the extent that the Motions ask the Court to strike the class allegations contained in the complaints, the Court finds a ruling on the viability of the class allegations would be premature, and accordingly **DENIES** the motions to strike class allegations without prejudice.

It is so **ORDERED**:

BY THE COURT:

s/_____
CYNTHIA M. RUFE, J.

APPENDIX D — ORDER OF THE UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED FEBRUARY 19, 2014

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

AVANDIA MDL 1871
2007-MD-1871
09-CV-730
10-CV-2475
10-CV-5419

In re: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT RELATES TO

Allied Services Division Welfare Fund,

v.

GSK UFCW Local 1776 and Participating Employers Health and Welfare Fund,

v.

GSK United Benefit Fund v. GSK

Appendix D

ORDER

On October 22, 2013, this Court issued a Memorandum Opinion and Order in the above captioned cases, denying in substantial part Defendant's Motion to Dismiss the claims set forth in the operative complaints.[1] Defendant has moved the Court to certify its October 22, 2013 Memorandum Opinion and Order for interlocutory appeal. This motion is opposed.

Under 28 U.S.C. § 1292(b), the Court may, at its discretion, certify an issue for interlocutory appeal when its opinion and order involved a controlling issue of law as to which there is substantial ground for difference of opinion, and where an immediate appeal may materially advance the termination of the litigation. While such certification should be used "sparingly and in exceptional circumstances"[2] the Court finds that certification for interlocutory appeal is appropriate here. Resolving the Motion to Dismiss required the Court to consider divergent rulings reached by different appellate circuits and district courts on controlling issues of law. The Court finds that immediate appeal may materially advance the termination of this litigation, as resolution of these unsettled issues oflaw in Defendant's favor would avoid

1. In Civ. A. No. 09-730, the operative complaint is the Second Amended Complaint [Doc. No. 17]. In Civ. A. No. 10-2475, the operative complaint is the First Amended Complaint [Doc. No. 7]. In Civ. A. No. 10-5419, only one Complaint was filed [Doc. No. 1].

2. *Burella v. City of Philadelphia*, No. 00cv884, 2010 WL 235110, *4 (E.D. Pa. Jan. 14, 2010).

the necessity of litigating these complex, class action lawsuits, and resolution in Plaintiffs' favor is likely to decrease motion practice and clarify the legal standards so that the parties understand what factual evidence they must develop for trial.

Accordingly, the Court will certify its October 22, 2013 Order, as amended by separate order entered this date,[3] for interlocutory appeal, so that the Third Circuit may address the following controlling questions of law: 1) Did the Court err in its application of *Maio v. AETNA*?[4] 2) Did the TPPs sufficiently plead that Defendant's alleged misrepresentation about Avandia's safety caused their injuries, when the TPPs continued to include Avandia on their formularies and cover the cost of Avandia for their members after the alleged cardiovascular risks of Avandia were well-publicized? and 3) Does the independent judgment and decision-making of the physicians who wrote the prescriptions for Avandia render the causal chain too attenuated to state a claim?

For the reasons set forth herein, it is hereby **ORDERED** that Defendant's Motion to Certify an Interlocutory Appeal under 28 U.S.C. §1292(b) [Doc. No. 3669] is **GRANTED**.

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3. The Court's October 22, 2013 Memorandum Opinion [MDL 1871, Doc. No. 3618] indicated that the Court would grant the Motion to Dismiss as to Plaintiffs' unjust enrichment claims, but the Order [MDL 1871, Doc. No. 3619] did not reflect that ruling. Accordingly, the Court has entered a corrected Order this date, dismissing the unjust enrichment claims asserted in the operative complaints.

4. 221F.3d472 (3d Cir. 2000).

It is so **ORDERED**.

BY THE COURT:

/s/
CYNTHIA M. RUFE, J.

APPENDIX E — ORDER OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT, FILED APRIL 15, 2014

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 14-8018

IN RE: AV ANDIA MARKETING, SALES PRACTICES & PROCDUCTS LIABILITY LITIGATION GLAXOSMITHKLINE, LLC,

Petitioner.

(D.N.J. Nos. 2-09-c.v.-00730,2-10-cv-02475, 2-10-cv-05419)

Present: AMBRO, CHAGARES and V ANASKIE, *Circuit Judges*

1. Petition for Permission to Appeal under 28 U.S.C. Section 1292(b) filed by Petitioner GlaxoSmithKline LLC.

2. Response filed by Respondent Allied Services Division Welfare Fund to Petition for Permission to Appeal under 28 U.S.C. Section 1292(b).

Respectfully,

Clerk/JK

Appendix E

ORDER

The foregoing Petition for permission to file an interlocutory appeal under 28 U.S.C. Section 1292(b) is granted.

By the Court,

s/ Thomas L. Ambro, Circuit Judge

Dated: April 15, 2014

Appendix E

OFFICE OF THE CLERK

UNITED STATES COURT OF APPEALS
21400 UNITED STATES COURTHOUSE
601 MARKET STREET
PHILADELPHIA, PA 19106-1790
Website: www.ca3.uscourts.gov
April 15, 2014

Michael Kunz
United States District Court for the Eastern District of Pennsylvania, Room 2609
James A. Byrne United States Courthouse, 601 Market Street
Philadelphia, PA 19106

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

NOTICE

GRANT OF PERMISSION FOR LEAVE TO APPEAL

The Court of Appeals has granted a petition for leave to appeal in this matter.

The $505.00 docketing and filing fee must be paid in the district court within 14 days after the entry of the order granting permission for leave to appeal, unless the petitioner is the United States government. Fed. R. App. P. 5. In addition, a cost bond must be filed if one is required under Fed. R. App. P. 7.

Appendix E

A notice of appeal does not need to be filed as a copy of the Court's order granting permission for leave to appeal which has been forwarded to the district court will serve as the notice of appeal.

The entry date of the order granting permission to appeal serves as the date of the filing of the notice of appeal for calculating time under the Federal Rules of Appellate Procedure. **Petitioner should notify the Court of Appeals in writing that the filing fee has been paid**.

Upon receipt of the notice from petitioner, the appeal will be opened on the general docket. All future filings regarding the appeal will be entered under the new docket number.

Very truly yours,

/s/ Marcia M. Waldron

APPENDIX F — SUR PETITION FOR REHEARING OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT, FILED NOVEMBER 25, 2015

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 14-1948

IN RE: AVANDIA MARKETING SALES PRACTICES & PRODUCT LIABILITY LITIGATION
GlaxoSmithKline, LLC,

Appellant

(E.D. Pa. Nos. 2-09-cv-00730, 2-10-cv-02475, 2-10-cv-05419 & 2-07-md-01871))

SUR PETITION FOR REHEARING

Present: McKEE, *Chief Judge*, AMBRO, FUENTES, SMITH, FISHER, CHAGARES, JORDAN, GREENAWAY, JR., VANASKIE, SHWARTZ, *SCIRICA and *ROTH, *Circuit Judges*

The petition for rehearing filed by **appellant** in the above-entitled case having been submitted to the judges who participated in the decision of this Court and to all the other available circuit judges of the circuit in regular active service, and no judge who concurred in the decision

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* The Honorable Anthony J. Scirica and Jane R. Roth votes are limited to panel rehearing only.

having asked for rehearing, and a majority of the judges of the circuit in regular service not having voted for rehearing, the petition for rehearing by the panel and the Court en banc, is denied.

BY THE COURT,

s/ Jane R. Roth
Circuit Judge

Dated: November 25, 2015
JK/cc: All Counsel of Record

APPENDIX G — CLASS ACTION COMPLAINT, *UNITED BENEFIT FUND V. GLAXOSMITHKLINE*, UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED OCTOBER 14, 2010

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

Case No. ____

UNITED BENEFIT FUND
7415 Metropolitan Ave.
Middle Village, Queens, NY 11379

on behalf of itself and others similarly situated;

Plaintiff

v.

GLAXOSMITHKLINE LLC
formerly SMITHKLINE BEECHAM
CORPORATION d/b/a GLAXOSMITHKLINE
One Franklin Plaza
Philadelphia, PA

Defendant.

CIVIL ACTION
CLASS ACTION COMPLAINT

JURY DEMAND REQUESTED

Appendix G

CLASS ACTION COMPLAINT

Plaintiff United Benefit Fund (referred to herein as "UBF" or "Plaintiff"), on behalf of itself and all others similarly situated, alleges the following against Defendant GlaxoSmithKline LLC, formerly SmithKline Beecham Corporation d/b/a GlaxoSmithKline ("Defendant" or "GSK"), based upon personal knowledge when in regards to itself and upon the information and belief and the investigation and research of counsel:

NATURE OF THE ACTION

1. Plaintiff and the Class members are "employee welfare benefit plans" and "employee benefit plans" as defined in the Employee Retirement Income Security Act (ERISA), 29 USC §§ 1002(1) and 1003(a) that paid for part or all of its participants purchases of the prescription drugs Avandia® (generically referred to as rosiglitazone maleate), Avandamet® (a combination of rosiglitazone maleate and metformin) and Avandaryl® (a combination of rosiglitazone maleate and glimepiride) (collectively, "Avandia" or "the Avandia drugs").

2. Avandia is one of two thiazolidinediones ("TZD" or glitazones) that, on May 25, 1999, was approved by the Food and Drug Administration ("FDA") as an oral antidiabetic agent which acts primarily by increasing cell insulin sensitivity. TZDs lower the blood sugar levels of persons with diabetes. Avandia is recommended and prescribed for the management of Type II diabetes mellitus, also known as non-insulin-dependent diabetes

mellitus ("NIDDM") or adult-onset diabetes. Millions of individuals in the United States have used Avandia to treat their Type II diabetes.

3. GSK has promoted the idea that the lowering of blood sugar levels demonstrates that Avandia enhances the transport of sugar from the blood to cells thereby improving cell health and the overall health of the patient. Thus, GSK claims that blood sugar level control is a valid "surrogate", which reflects the broader efficacy of Avandia.[1] Unfortunately, in this instance, GSK's surrogate is an extremely poor indicator that Avandia provides any health benefit.

4. Although Avandia lowers blood sugar levels, it does not enhance the health of persons with diabetes. The drug actually *increases one's chance of heart attack by over 40%. See* Psaty B, Editorial: "The Record on Rosiglitazone and the Risk of Myocardial Infarction." *New England Journal of Medicine* 357:15 July 2007: 67-69 (emphasis added).

5. Avandia users can also develop coronary artery disease ("CAD"), macular edema, bone fractures in

1. P. Gaede, et al. "Lowering of blood sugar levels has not, in itself, been proven to provide a health benefit for persons with diabetes." "Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes." *New England Journal of Medicine* February 7, 2008; and "For Safety, NHLBI Changes Intensive Blood Sugar Treatment Strategy in Clinical Trial of Diabetes and Cardiovascular Disease." *National Institutes of Health* press release regarding ACCORD trial dated February 6, 2008.

women, and/or liver failure. Hence, while use of Avandia may lower the blood sugar levels of a person with diabetes, it does so at great risks.

6. According to a February 25, 2010 report from The Institute for Safe Medication Practices, more than 1,000 reports of patient deaths associated with Avandia were received in the first three quarters of 2009, more than any other drug monitored.

7. GSK has concealed, and continues to conceal these very real risks which have been known to GSK since at least 1999, when Avandia was approved for sale.

8. To increase the sales of Avandia, Defendant embarked on a comprehensive and carefully-orchestrated scheme to promote Avandia's safety, efficacy and effectiveness through a fraudulent and deceptive marketing program. In addition to the thousands of people who died or suffered serious injury as a result of their use of Avandia, third-party payors such as Plaintiff and others similarly situated, who paid for the drug, also fell victim to Defendant's wrongful scheme to promote and market the Avandia Drugs.

9. Defendant (a) deliberately misrepresented the scientific, medical and clinical data concerning the safety, efficacy, effectiveness, and superiority of Avandia over comparable drugs; (b) suppressed or mischaracterized negative studies relating to the drug; and (c) caused false and misleading presentations concerning Avandia's safety, efficacy and lack of purported side effects to be made to

physicians and those paying for Avandia, including third-party payors such as UBF.

10. In June 2007, prompted by studies of Avandia that showed an increasing risk of heart attacks and heart-related disease from the drug, the House Committee on Oversight and Government Relations held a hearing to examine how the FDA had assessed the safety of Avandia. It was revealed that a senior FDA scientist had recommended a black box warning for Avandia as early as February 2006, but the FDA allegedly removed that scientist from work on Avandia because she voiced concerns about the safety of the drug.

11. Similarly, on Februrary 18, 2010, after another extensive review of Defendant's internal documents, senior Senate members concluded that Defendant was aware of the possible cardiac risks associated with Avandia years before the evidence became public; Defendant had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner; Defendant intimidated independent physicians and strategized ways to minimize findings that Avandia may increase cardiovascular risk; and Defendant schemed to downplay findings that alternative drugs might reduce cardiovascular risk.

12. Thus, although Defendant had longstanding knowledge of the dangers associated with Avandia, including significant heart attack or heart-disease related risks, Defendant engaged, and continues to engage, in a nationwide, uniform marketing campaign involving misstatements regarding Avandia's safety and efficacy,

deliberately concealing these dangers in order to promote its drug.

13. Further, Defendant concealed and failed to properly and adequately disclose adverse events to Plaintiff and the Class.

14. Defendant also made and continues to make misrepresentations regarding Avandia's safety and efficacy as compared to older medications, including sulfonylureas and metformin, to the healthcare community, consumers, third-party payors, and others, with the goal of increasing sales and market share of Avandia so as to increase GSK's profits.

15. The financial success of Defendant's scheme depended in large part upon targeting third-party payors and insurers and convincing them to add Avandia to their formularies. Avandia was a much more expensive medication (approximately twenty-two times as expensive) than older, available drugs that were often more effective, and more tolerable than Avandia. The average monthly prescription cost for older diabetes drugs like metformin varied from $4 to $100. The cost for Avandia varied from $90 to $220.

16. The cost of Avandia has an enormous impact on third-party payors, including Plaintiff and the Class members.

17. Furthermore, Defendant set out to persuade Plaintiff and the healthcare community, including third-

party payors to favor Avandia over alternative treatments that were cheaper, safer and/or more efficacious than Avandia.[2] As such, Plaintiff and other class members paid for Avandia in quantities far exceeding its warranted use, and these payments (and resulting revenues for Defendant) were the direct result of GSK's fraudulent scheme.

18. From the time of their releases until approximately May of 2007, the Avandia drugs proved to be blockbusters for Defendant. More than 6,000,000 people worldwide have taken these drugs to control blood sugar since the first Avandia drug came on the market in 1999. Since its introduction, Avandia has been used on a regular basis by at least one million individuals in the United States.

19. Defendant's unlawful scheme to inflate sales of Avandia was extraordinarily successful, with U.S. sales soaring to approximately $1.8 billion in 2005 and approximately $2.36 billion in 2006. Even in 2007, when serious health risks were revealed concerning Avandia, sales only declined to approximately $1.55 billion. And sales have remained steady since, topping $658 million in 2009, making it a hugely successful drug for GSK.

20. Finally, on or about September 23, 2010, in a highly unusual coordinated announcement, drug regulators in Europe and the United States announced that Avandia

2. Drug manufacturers also attempt to keep harmful drugs on formularies by "bundling" the harmful drug with other drugs which locks in customers, increases drug prices, and increases profits.

would no longer be widely available. Avandia sales are suspended entirely in Europe. Patients in the United States will only be allowed to access the medicine if they and their doctors attest that they have tried every medication used to treat Type Two Diabetes and that the patients have been made aware of the drug's substantial risks to the heart. Dr. Steven Nissen, a Cleveland Clinic cardiologist whose studies highlighted the heart attack risk associated with Avandia, said that the decision brought an end to "one of the worst drug safety tragedies in our lifetime."

21. This is a proposed nationwide class action on behalf of third party payors such as Plaintiff, that have paid for part or all of the purchase price of the Avandia Drugs, as a consequence of Defendant's violation of the applicable state statutes set forth herein.

22. Plaintiff and the Class seek compensatory damages as a result of their payments for Avandia and the amounts by which Defendant was unjustly enriched, as well as punitive or statutory damages to the extent allowable under applicable state statutes.

PARTIES

23. Plaintiff, UBF, is a citizen of the State of New York, and has its principal place of business at 7415 Metropolitan Ave., Middle Village, Queens, New York 11379. As an "employee benefit plan" as defined in ERISA, UBF is a legal entity entitled to bring suit in its own name pursuant to 29 USC § 1132(d). UBF is a not-for-profit-trust,

sponsored by and administered by a Board of Trustees, established and maintained to provide comprehensive health care benefits to participant-workers, who are employed under various collective bargaining agreements, and to their dependents.

24. UBF represents approximately 2,500 members.

25. UBF has paid all or part of the cost of its participants' purchases of Avandia during the Class Period, as defined herein. Pursuant to its plan, Plaintiff, through a pharmacy benefit manager ("PBM") and a third-party administrator, purchased prescription drugs for its participants and provided coverage for medical testing and visits to physicians. Plan participants each have a prescription drug plan identification card which he/she presents at a participating pharmacy. The pharmacy collects a co-payment from the participant and bills UBF (through a prescription benefit manager) for the remaining cost of Avandia purchases. Avandia prescriptions would have been restricted or priced differently if the FDA, Plaintiff's PBM and/or prescribers had truthful and complete information about the safety and efficacy of Avandia. Plaintiff and the Class have been injured as a result of the unlawful conduct of Defendant as alleged herein.

26. Defendant GlaxoSmithKline LLC (GSK LLC), formerly SmithKline Beecham Corporation d/b/a GlaxoSmithKline has its principal place of business and address at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania. GSK designed, produced,

marketed and promoted the drugs Avandia, Avandamet and Avandaryl in Pennsylvania and nationwide. At all relevant times, GSK acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting in the course and scope of their actual and apparent authority, agency, duties or employment.

27. Upon information and belief, Defendant GlaxoSmithKline LLC (GSK LLC), formerly SmithKline Beecham Corporation d/b/a GlaxoSmithKline, purports to be a limited liability corporation organized and existing under the laws of the State of Delaware but which maintains its principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania.

28. Upon information and belief, Defendant GlaxoSmithKline was and still is a business entity organized under the laws of Pennsylvania that maintained and maintains a principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania.

29. Upon information and belief, Defendant SmithKline Beecham Corporation was and still is a business entity organized under the laws of Pennsylvania that maintained and maintains a principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania.

30. Upon information and belief, Defendant GlaxoSmithKline LLC (GSK LLC), formerly SmithKline Beecham Corporation d/b/a GlaxoSmithKline was and still is a business entity organized under the laws of Pennsylvania that maintained and maintains a principal

place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania.

31. Upon information and belief, Defendant SmithKline Beecham d/b/a GlaxoSmithKline, was and still is a business entity organized under the laws of Pennsylvania that maintained and maintains a principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania.

32. Defendant designed, produced, marketed and promoted Avandia, Avandamet and Avandaryl Pennsylvania and nationwide. Defendant has manufacturing sites in Pittsburgh, Pennsylvania, Clifton, New Jersey and Parsippany, New Jersey. At all relevant times, GSK acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting through the course and scope of their actual and apparent authority, agency, duties or employment.

JURISDICTION AND VENUE

33. This Court has subject matter jurisdiction over this action pursuant to the Class Action Fairness Act of 2005, 28 U.S.C. § 1332(d)(2) because at least one member of the Class is of diverse citizenship from Defendant; there are more than 100 class members nationwide; and the aggregate amount in controversy exceeds $5,000,000.

34. This Court has personal jurisdiction over the parties because Plaintiff has consented to the jurisdiction of this Court, and Defendant is a resident or has agents

and representatives in this State. Defendant is authorized to do business and in fact does business in this state, and Defendant has sufficient minimum contacts with this state and otherwise intentionally avails itself of the markets in this state through the distribution, promotion, marketing and sale of its products in this state, to render the exercise of jurisdiction by this Court permissible under traditional notions of fair play and substantial justice. The Avandia related marketing and sales directives eminated from Defendant's headquarters in Pennsylania and Defendant designed and distributed their research studies from its home office here.

35. Venue is proper in this District under 28 U.S.C. § 1391. The claims asserted in this Complaint arise, in part, within this District. A subsantial part of the events and conduct giving rise to the violations of law complained of herein occurred or emanated from this District. Defendant resides in the State. Defendant also conducts business with consumers in this District and has caused injury to residents in this state.

FACTUAL ALLEGATIONS

A. FDA Regulations for Marketing and Promotion in the United States

36. Pursuant to the Federal Food, Drug and Cosmetic Act ("FDCA"), new pharmaceutical drugs may not be marketed in the United States until FDA determines that the drug is "safe for use" and effective for all "conditions prescribed, recommended, or suggested" on a drug's label. *See* 21 C.F.R. 99.103; *see also* 21 C.F.R. §201.5.

37. The indications and dosages approved by the FDA are set forth in the drug's labeling, the content of which is also approved by the FDA.

38. A manufacturer's, statement that a drug is "effective" or "works" or "has been proven to . . ." is understood to mean that well-controlled clinical studies support the use. To make such a statement without such clinical trial proof is misleading. Further, failure to inform physicians that no placebo-controlled clinical trials support a representation of drug efficacy is a violation of a pharmaceutical company's obligation to disclose the necessary information. *See*, 21 C.F.R. § 99.205.

39. In any other circumstance, a manufacturer cannot disseminate information regarding a drug to health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, or federal and state government agencies unless such information is fair and balanced and the manufacturer meets the following conditions:

- The information concerns a drug that has been approved, licensed and cleared for marketing by the FDA;

- The information is in the form of an unabridged copy of a peer-reviewed scientific or medical journal article or reprint, or an unabridged reference publication that pertains to a clinical investigation involving the drug and that is considered scientifically sound by experts who

are qualified to evaluate the product's safety or effectiveness;

- The information does not pose a significant risk to the public health;
- The information is not false or misleading; and
- The information is not derived from clinical research conducted by another manufacturer, unless permission is received from that manufacturer.

See, 21 C.F.R. § 201.6(a); *see also*, 21 U.S.C. §§ 360aaa; 360aaa-1.

40. With regard to the second practice – manufacturer's involvement in CME programs – the FDA's examination of these practices led to the publication of an agency enforcement policy in 1997 entitled, "Guidance for Industry: Industry-Supported Scientific and Educational Activities." 62 Fed. Reg. 64,074, 64,093, 1997 WL 740420 (F.R.) (1997). This guidance document states that CME programs must be truly *independent* of the drug companies, and sets forth a number of factors that the FDA will consider in determining whether a program is "free from the supporting company's influence and bias." *Id*.

41. Sections 502(a) and 201(n) of the FDCA (21 U.S.C. §§ 352(a), 321(n)) require Defendant to fully and accurately disclose information in Defendant's possession relating to the efficacy of Avandia, as well as information relating to

adverse events associated with Avandia use, including but not limited to cardiovascular events. These disclosures must appear in the Avandia Package Insert ("Avandia PI"), other labeling, and promotional materials.

42. Sections 502(a) and 201(n) of the FDCA (21 U.S.C. §§ 352(a) and 321(n)) prohibit Defendant from claiming efficacy or minimizing risks of adverse events, and from making misleading claims that Avandia is safer or more effective than other available medications.

43. Defendant violated Sections 502(a) and 201(n) of the FDCA (21 U.S.C. §§ 352(a) and 321(n)) by omitting information concerning risks and benefits from the Avandia PI and other labeling, and by utilizing and/or distributing promotional materials that were false and misleading regarding Avandia's efficacy and effectiveness.

44. Furthermore, Defendant minimized the risks of these serious adverse events, failed to advise consumers and physicians to monitor patients for these adverse events, and otherwise falsely claimed that Avandia was safer and more efficacious than other medications available on the market. Thus, the information disseminated by Defendant was not fair and balanced.

B. Avandia's Factual Background

1. Diabetes and Cardiovascular Risk

45. Type II diabetes is a serious and life threatening disease that affects approximately 18 to 20 million

Americans. Type II diabetes is a medical condition where the patient becomes resistant to his/her endogenous insulin. Insulin is necessary to enable the transport of sugar (generated from food and drink) from the blood into the cells. Without insulin, sugar builds up in the bloodstream and the cells are starved for energy. This can cause tissue breakdown which in turn can lead to kidney failure, blindness, amputations, heart attacks and stroke. When a patient's insulin resistance results in a fasting blood glucose in excess of 126 mg/dl for two consecutive days, the subject patient is classified as having Type II diabetes.

46. Cardiovascular disease is the leading cause of death for persons with Type II diabetes and more than 65 percent of persons with diabetes will die from a heart attack or stroke. *See* http://www.diabetes.org/type-2-diabetes/well-being/heart-disease-and-stroke.jsp. Thus, the primary goal of any diabetes treatment should be the reduction of this cardiovascular risk. *See* Scott M. Grundy, et al. "Diabetes and Cardiovascular Disease, A Statement for Healthcare Professionals From the American Heart Association." *Circulation* 1999; 100: 1134-1146.

47. Type II diabetic patients have a wide array of pharmaceutical treatment options available to them including, but not limited to, insulin, alpha-glucosidase inhibitors, biguanieds, meglitinides, sulfonylureas and thiazolidinediones.

Appendix G

2. TZDs and Treatment of Type II Diabetes

48. TZDs, also referred to as "Insulin Sensitizers," are a class of drug which includes Avandia, Actos® (pioglitazone) and Actosplus met (pioglitazone and metformin). First manufactured in the 1990s, and considered a new treatment for Type II diabetes, TZDs are a novel class of insulin-sensitizing agents which work in part by increasing cell sensitivity to insulin. TZDs lower blood sugar levels, and enable the body to more effectively use insulin by reducing insulin resistance in the body.

49. As a TZD approved on May 25, 1999, Avandia is prescribed for the management of Type II diabetes mellitus or NIDDM.

50. Avandamet was approved by the FDA on October 10, 2002 as a combination of Avandia and metformin in one single pill; Avandamet is indicated to treat Type II diabetes.

51. Avandaryl was approved by the FDA on November 23, 2005 as a combination of Avandia and glimepiride in one single pill; Avandaryl is indicated to treat Type II diabetes.

52. Despite the fact that Avandia lowers blood glucose levels in Type II diabetes patients, at least 42 studies have shown that use of Avandia dramatically increases the risk of cardiovascular events in Type II diabetes patients.

53. One potential contributing factor may be the adverse effect of Avandia on serum lipids. Studies of Avandia users illustrate an increase in LDL cholesterol, as compared with a placebo. In fact, Avandia's product labeling states that Avandia increases LDL cholesterol.

54. Elevated levels of LDL cholesterol are associated with an increase in adverse cardiovascular outcomes. Thus, an increase in LDL cholesterol of the magnitude observed in Avandia may have contributed to adverse cardiovascular outcomes.

55. One researcher has indicated:

> [R]osiglitazone [Avandia] was approved on the basis of its ability to improve glycemic control, a surrogate endpoint. Because high glucose levels increase the risk of vascular disease, a glucose-lowering drug is presumed to reduce the risk of major adverse health outcomes such as myocardial infarction [heart attack]. **Rosiglitazone however, appears to be associated with an increase rather than a decrease in the risk of myocardial infarction [heart attack]**.[3]

56. Nevertheless, Defendant downplayed the significance of the increase in LDL by characterizing the

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3. *See* Psaty Bruce M., et al., Editorial: "The Record on Rosiglitazone and the Risk of Myocardial Infarction." *New England Journal of Medicine* 357: 67-69 (5 July 2007) number 1 (emphasis added) Avandia users can develop CAD.

LDL attributed to Avandia as "fluffy" or non-atherogenic LDL, which would not increase the risk of cardiovascular events.

57. Defendant also assured physicians that these studies only illustrate a very slight increase in LDL levels, and continued to promote Avandia as a superior and effective drug for diabetic patients.

58. Moreover, studies illustrate Avandia increases apoB levels as well as LDL particle numbers. *See* Linda von Wartburg. "Updated: Analysis Associates Avandia With Greater Risk of Heart Attack," Diabetes Health May 31, 2007. *See* http://www.diabeteshealth.com/read/2007/05/31/5204/updated-analysis-associates-avandia-with-greater-risk-of-heart-attack/.

59. ApoB is the structural protein for the low-, intermediate- and very low-density lipoproteins (LDL, IDL and VLDL, respectively) ("bad" cholesterol). In general, apoB-containing lipoproteins carry lipid from the liver (apoB-100) and gut (apoB-48) to the sites of utilization. Apo AI is the active ingredient in HDL (high-density lipoprotein), helping to transport excess cholesterol from cell surfaces to lipoprotein particles for its transfer to the liver and has anti-inflammatory and anti-oxidant properties which contributes to its cardioprotective role.

60. Additionally, the activity and mass of lipoprotein-associated phospholipase A2, an inflammatory enzyme

expressed in atherosclerotic plaques, shows continuous associations with risk of coronary heart disease.[4]

61. Monitoring apoB levels, along with other lipids tests such as LDL cholesterol, helps to determine an individual's risk of developing cardiovascular disease.

62. Several large-scale population studies confirmed that measurements of apo AI and B could be taken with a high degree of accuracy and precision[5] and are more accurate that those of direct HDL-C and direct LDL-C.

63. Furthermore, at least one "study indicates that apoB may be a better predicator of cardiovascular disease risk" than "bad" cholesterol. Steve Haffner, M.D. "ApoB: better marker for heart disease than

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4. D. Sennik. "Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies." *Lancet* 375: 2010: 1536 – 44.

5. P.S. Bachorik, K.L. Lovejoy, M.D. Carroll, C.L. Johnson. "Apolipoprotein B and AI distributions in the United States, 1988–1991: results of the National Health and Nutrition Examination Survey III (NHANES III)." *Clin Chem*: 43: 1997: 2364–78; I. Jungner, S.M. Marcovina, G. Walldius, I. Holme, W. Kolar, E. Steiner. "Apolipoprotein B and A-I values in 147,576 Swedish males and females, standardized according to the World Health Organization-International Federation of Clinical Chemistry First International Reference Materials." *Clin Chem*: 44: 1998: 1641–9; J.H. Contois, J.R. McNamara, C.J. Lammi-Keefe, P.W.F. Wilson, T. Massov T, E.J. Schaeffer. "Reference intervals for plasma apolipoprotein A-I determined with a standardized commercial immunoturbidimetric assay: results from the Framingham Offspring Study." *Clin Chem*: 42: 1996: 507–14.

"bad" cholesterol," *See* http://www.americanheart.org/presenter.jhtml?identifier=3022935.

64. Although diabetes causes an increase in apoB, further increases in apoB levels and decreases in apo AI levels contributes to long-term cardiovascular complications in diabetics.

65. Despite these facts, Defendant failed to mention Avandia's propensity to increase apoB levels and the associated cardiovascular risks on its labels.

66. One Cleveland Clinic physician described the absurdity of GSK's position regarding the benefits of Avandia as follows:

> The majority of patients who have diabetes eventually die of cardiovascular events. If the ultimate goal is to reduce deaths from cardiovascular events, prescribing a drug that increases the incidence of stroke and myocardial infarction in a significant number of patients doesn't make sense. **A patient doesn't care about blood sugar if he or she is having a heart attack.**

Michael A. Lincoff. "Diabetes Drugs in the Spotlight." *Cleveland Clinic Cardiac Consult* Winter 3 (2007) (emphasis added).

B. Defendant's Knowledge of Avandia's Safety Risks and Defendant's Deliberate Decision to Disseminate False and Misleading Scientific, Medical and Clinical Data Regarding Avandia's Efficacy and Effectiveness

67. Defendant knows, and has known, that the FDA prohibits drug manufacturers from promoting and marketing drugs for uses for which it has not been proven to be efficacious, and/or safe.

68. Defendant knows, and has known, that Avandia is not efficacious and is associated with numerous safety risks. Nevertheless, the fraudulent scheme devised by Defendant not only misrepresented the scientific data regarding Avandia, but also the source and authors of the data and related publications.

1. Pre-Approval Signals of Avandia's Risks

69. Prior to approval, Avandia underwent a FDA Medical Officer Review (MOR). Avandia's MOR was completed on April 16, 1999. Even at this early stage, GSK was alerted to the cardiovascular risks associated with its drug. The reviewing officer stated as follows: "The major issues regarding safety of rosiglitazone relate to hepatitis, edema, anemia and the heart." *See* Robert Misbin, MD. "Medical Officer's Review of New Drug Application." April 16, 1999 at 26.

70. Regarding one study, the MOR stated: "Safety: The only safety issue noted in this study is that 6 patients

on 4 mg bid had cardiac events including two myocardial infarctions." *Id.* Additionally, under the Safety/Cardiac Abnormalities section of the review, the reviewer stated as follows:

> Acute myocardial infarctions occurred in 22 patients (0.5%) of patients on [Avandia] and was fatal in six. This result would appear somewhat higher than in other treatment arms . . . .

Id. at 28.

71. Given these early signals of cardiovascular risk, the reviewing officer stated that, as a condition for approval, the company needed to conduct a post-marketing study to better assess this risk. *Id*. at 41.

72. Rather than complying with the reviewing officer's mandate, GSK refused to undertake the study because it was too expensive. As support for its decision to forego performing the study, Defendant stated, "given the scope, complexity, and expense of such trials, [GSK] is not currently in a position to make any commitment about a long term outcomes trial." Letter to Jena Weber from Clare Kahn, re: NDA 21-071 – Request for Revised Annotated Labeling and Outline of Phase IV Commitments dated May 5, 1999.

73. With this, the first chance to protect consumers was, at best, ignored.

Appendix G

2. Early Post-Approval Signals of Avandia's Risks

74. Since approval in 1999, the FDA has been monitoring controlled clinical trials and post-marketing reports related to Avandia which have revealed several heart-related adverse events (e.g. fluid retention, edema, and congestive heart failure ("CHF")).

75. For example, almost immediately after its 1999 approval, Avandia's cardiac safety profile was questioned. In the year of its release, John Buse, M.D., Ph.D, a world-famous endocrinologist and a former president of the American Diabetes Association, opined that Avandia may carry cardiovascular risks. At the time Dr. Buse discovered his findings and reported them to GSK, he was an investigator for a GSK study on Avandia.

76. GSK reacted to these criticisms by threatening Dr. Buse with a lawsuit. *See* Dr. Buse's testimony before the Committee on Oversight and Government Reform on June 6, 2007.

77. On or around June 28, 1999, in response to GSK's pressure, Dr. Buse sent a three-page letter to Dr. Tadataka Yamada, GSK's Chairman of Research and Development. In the letter, Dr. Buse wrote, "I may disagree with GSK's interpretation of that data [but] I am not for sale…. Please call off the dogs. I cannot remain civilized much longer under this kind of heat."

78. On March 15, 2000, Dr. Buse followed up with a letter to Dr. Jane Henney, Commissioner of the FDA, stating

that he was concerned GSK had "overstated the safety of [Avandia] with respect to cardiovascular issues" because studies reflected a "worrisome trend in cardiovascular deaths and severe adverse events" associated with the drug. Dr. Buse letter to Dr. Jane Henney, FDA re: Citizen's Petition to Immediately Require Class Labeling for the Diabetes Drugs Troglitazone (Rezulin), Rosiglitazone (Avandia) and Pioglitazone (Actos)" dated March 15, 2000.

79. GSK's attempt to silence Dr. Buse was the subject of a congressional inquiry. In November 2007, the U.S. Senate Committee on Finance issued a Staff Report which called GSK's response to Dr. Buse's concerns "extremely serious" and stated that it revealed an "orchestrated plan to stifle the opinion" of a professor of medicine who specializes in diabetes. Committee Staff Report to the Chairman and Ranking Member, Committee on Finance, United States Senate, "The Intimidation of Dr. John Buse and the Diabetes Drug Avandia" dated November 2007.

80. The Committee Staff Report noted that GSK's campaign to silence Dr. Buse involved "executives at the highest levels of GSK," including then and current Chief Executive Officer Jean-Pierre Garnier. *Id.* The Committee remained concerned that GSK had not altered its corporate culture in the years since the attacks on Dr. Buse (1999-2000) because "GSK's behavior since the Committee first brought these allegations to light has been less than stellar. Instead of acknowledging the misdeed to investors, apologizing to patients, and pledging to change corporate behavior, GSK launched a public relations campaign of denial." *Id.*

81. Additionally, a November 19, 2008 *Wall Street Journal* article noted that Dr. Mary Money of Hagerstown, Maryland, observed problems with Avandia shortly after it entered the market in 1999 and attempted to warn GSK in 2000. According to the article, Dr. Money linked Avandia to congestive heart failure when a patient had begun taking Avandia two weeks earlier, and an echocardiogram showed high pressure in the arteries of the lungs.

82. GSK rejected Dr. Money's warning and tried to make her stop talking about it with other doctors and hospitals, according to documents and interviews. GSK defends its effort, which it says was an attempt to correct "inaccuracies."

83. In February 2002, GSK submitted a supplemental New Drug Application (sNDA) seeking approval for the use of Avandia in combination with insulin. In response to this application, the FDA asked the company to submit additional information on adverse events from follow-up trials it had performed. Upon review of the information submitted, the FDA noted that results showed that "approximately 10% of patients treated with rosiglitazone and insulin experienced **cardiac AEs** [adverse events] across the trials to date." Memorandum from the FDA re: NDA review issues and recommended action, dated February 26, 2003 (emphasis added).

84. Additionally, the FDA memorandum noted that, given the earlier signals, an increase in cardiovascular risk was not unexpected. It stated:

> [W]hile the signal of increased risk for edema, CHF [congestive heart failure], and other CV [cardiovascular] adverse events persists in these follow up trials (indeed, there was no expectation that it was a fluke of the earlier trials and would disappear in subsequent studies), a strategy of careful patient selection (e.g., no history of cardiac compromise), judicious titration, and monitoring may obviate some of the fluid-related AEs of the combination.

85. After reviewing GSK's application, the FDA's Medical Team Leader stated "there was a marked increase in total adverse cardiac events, serious adverse cardiac events, and adverse cardiac events leading to withdrawal in patients on insulin and Avandia combination therapy when compared to insulin alone (14% vs. <5% respectively)." Memorandum from the Medical Team Leader to the Division Director at the FDA re: Team Leader Recommendation.

86. Based on this information, the FDA's Medical Team Leader recommended **against** approving GSK's application for combination therapy with insulin, stating, "although the sponsor has shown that Avandia is effective in providing better glucose control when added to insulin, the safety information that emerged from the studies is quite troublesome." *Id.* In addition to recommending against approval, the Medical Team Leader also recommended that the company consider sending a letter to medical doctors warning them of the dangers associated with combining Avandia and insulin therapies.

87. The data also showed that Avandia study subjects and users experienced improvement of symptoms upon cessation of Avandia consumption. The same memorandum also stated that "[t]his case series suggests [CHF] may be occurring in individuals without previously diagnosed disease."

88. Despite these concerns and over the Medical Team Leader's objections, GSK secured FDA approval for use of Avandia with insulin. GSK had ignored another signal.

89. The FDA then requested that Defendant make a change to Avandia's prescribing label to warn doctors that the drug could cause fluid retention. In most cases, CHF is a process that occurs over time, when an underlying condition damages the heart or makes it work excessively hard, weakening the organ. CHF is characterized by, among other symptoms, abnormal fluid retention, which usually results in swelling (edema) in the feet and legs.

90. However, shortly after this regulatory request, GSK's sales representatives denied the existence of serious risks associated with Avandia during oral presentations at a medical convention. The FDA sent a "Warning Letter" to GSK instructing the company to, among other things, order its sales representatives and marketers to stop denying or minimizing the risks of heart attacks and heart-related diseases in patients.

91. Defendant's concealment was also discussed in a June 1, 2007 article published by *Bloomberg News* which stated that, in 2005, Defendant performed a review and

found that Avandia raised the risk of heart attacks by 31%. Defendant gave the review to the FDA and, while including the information on its website, Defendant buried the information amid information concerning more than 2,000 studies.

92. According to that same article, Defendant stated that the heart-risk studies, including Defendant's own, are flawed and GSK did not believe it was obligated, or legally required, to highlight every study done on its drugs. As Jean-Pierre Garnier, the Chief Exeutive Officer of GlaxoSmithKline PLC, told reporters at the company's annual meeting on May 23, 2007 in London, "Why would you publicize it [?]. . . We don't publicize every submission we make to the Food and Drug Administration."

3. Pre-2007 FDA Hearing Studies Confirming Defendant's Knowledge of Avandia's Risks

93. More early signals known to GSK concerning Avandia's cardiovascular risks were also revealed, confirmed and made public.

94. A 12-week study from March 2006 (and only uncovered recently) entitled, "A 12-Week Randomized, Double-Blind, Local Multicenter, Placebo-Controlled Study To Evaluate The Efficacy, Safety And Tolerability Of Rosiglitazone (BRL 49653C) When Administered Once Daily To Patients With Type-2 Diabetes Mellitus (T2DM) Who Are Inadequately Controlled On At Least Half Maximal Dose of Usual Sulphonylurea," revealed adverse events in 98% of those patients taking Avandia.

This study was conducted to evaluate the safety and efficacy of Avandia in combination with sulphonylurea in subjects with Type II diabetes, and to determine if the combination has an additive effect. The study reported an approximate 24% increase in LDL and 10% decrease in HDL levels after 12 weeks.

95. In April 2006, the FDA required labeling for Avandia to be updated to include new data in the WARNINGS section about a potential increase in heart attack and heart-related chest pain in some patients. This change was based on the results of a controlled clinical trial in patients with existing CHF. A higher number of heart attacks or angina was observed in patients treated with Avandia compared to those treated with a placebo. Angina is chest pain or discomfort that occurs when an area of the heart muscle does not receive enough oxygen-rich blood. In most cases, the lack of blood supply is due to a narrowing of the coronary arteries as a result of arterosclerosis.

96. Within the next year, Steven E. Nissen, M.D., and Kathy Wolski, M.P.H., tabulated and compiled a meta-analysis[6] using published literature, the FDA website and a clinical-trials registry maintained by Defendant. Drs. Nissen and Wolski used 116 potentially relevant studies, and 42 trials comprising approximately 28,000 people who took Avandia and that met the inclusion criteria, including

6. Meta-analysis is the systematic method of evaluating statistical data based on the results of several independent studies of the same problem. *See* http://medical-dictionary.thefreedictionary.com/meta-analysis.

a study that was more than 24 weeks in duration that used a randomized control group not receiving Avandia.

97. The study, entitled *Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes* (the "Nissen Study"), was published on May 21, 2007 in the *New England Journal of Medicine*. It revealed that Avandia was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from heart attacks and heart-related diseases. Specifically, the meta-analysis revealed a **43% higher risk of heart attack** for those taking Avandia compared to people taking other diabetes drugs or no diabetes medication: people taking Avandia suffered such adverse events at a rate of 1.99%, as opposed to 1.51% for other patients.

98. Instead of providing a responsible and reasoned response to this study, GSK took steps to encourage aggressive prescribing and dispensation of Avandia for persons to whom it posed grave health dangers. *See infra.*

99. Based in part on the Nissen Study, on May 21, 2007 the FDA issued a new safety alert that addressed potential safety issues stemming from the pooled analysis of previously completely controlled clinical trials demonstrating a potentially significant increase in the risk of heart attack and heart-related diseases in patients treated with Avandia.

100. On May 23, 2007, consistent with recommendations made by senior FDA staff at an internal regulatory briefing

held the prior month, the FDA issued letters to Defendant requesting that Avandia's product labeling include a black box warning to more prominently address the risks of heart failure associated with the use of Avandia. Although this risk was already contained in the WARNINGS section of the Avandia PI, the FDA decided to make this request because, despite the existing warnings, these drugs were being prescribed to patients with significant heart failure.

101. Right on the heels of these studies and FDA pronouncements, Defendant engaged in a massive publication and advertising campaign designed to bolster consumer confidence in Avandia.

102. For example, on and around June 5, 2007, GSK published full-page advertisements in more than a dozen major U.S. newspapers touting Avandia in an attempt to reassure patients of the safety of Avandia.

103. This advertising and promotional campaign consisted of advertisements, promotional literature for doctors and other health care providers, and other direct to consumer promotional materials to be provided by Defendant to potential users of Avandia.

4. Congressional, Regulatory and Industry Reaction

104. On June 6, 2007, sparked by the publication of the Nissen Study, the House Committee on Oversight and Government Relations held a hearing to examine how the FDA had assessed the safety of Avandia.

105. During the hearing, the FDA announced that a meeting would be held on July 30, 2007 to discuss the risk of heart attacks and heart-related diseases associated with thiazolidinediones, with a focus on Avandia.

106. Further, U.S. Senator Chuck Grassley revealed, in a statement published in late July 2007, that a senior FDA scientist had recommended a black box warning for Avandia in February 2006. However, the FDA allegedly removed that scientist, Rosemary Johann-Liang, from work on Avandia after she voiced concerns about the safety of the drug.

107. According to Senator Grassley's statement, the FDA did not act on the recommendations from Dr. Johann-Liang. The statement did not say why the FDA took no action on the advice.

108. On July 30, 2007, the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA convened in Gaithersburg, Maryland (the "July 30th Hearing") to discuss the myocardial ischemic risk associated with rosiglitazone treatment in patients with Type II diabetes mellitus. Both the FDA and GSK made presentations at this hearing.

109. The joint committee consisted of 24 experts in cardiovascular disease, epidemiology, biostatistics, and endocrinology. Approximately ten indivduals presented testimony during the all-day hearing.

Appendix G

a. FDA's Dr. David Graham Calls for Avandia Removal

110. David J. Graham, M.D., M.P.H. of the FDA Office of Surveillance and Epidemiology presented the following results of the FDA's meta-analysis of Avandia data at the July 30th Hearing:

- FDA meta-analysis shows a 20% to 68% increased cardiovascular risk with six to twelve months of Avandia use compared to non-use;

- Avandia increased risk of ischemic heart disease by 40% compared with comparator drugs and by 70% compared with placebo;

- Compared to pioglitazone (Actos), Avandia increases the risk of a cardiovascular event over three and half times;

- The data indicates that since its introduction to the market Avandia use caused between 66,000 and 205,000 cardiovascular events that otherwise would not have occurred.

111. At the July 30th Hearing, Dr. Graham concluded that Avandia should be pulled from the market.

112. Referring to a host of cardiovascular adverse events including heart attacks, Dr. Graham stated "[t]here is no evidence, none whatsoever, to support the benefits of rosiglitazone with these outcomes." Best case

scenario for GSK, Dr. Graham said, was that Avandia was responsible for 40,000 excessive cardiovascular events in 6.5 years since 1999. Dr. Graham put the real number at 80,000 excess cases. Transcript from the FDA Advisory Committee Hearing, dated July 30, 2007 at 229, 231.

b. Public Citizen Calls for Avandia Removal

113. Sidney Wolfe, M.D., Elizabeth Barbehenn Ph.D. and Ben Wolpaw, members of Public Citizen's Health Research Group ("Public Citizen"), also presented testimony at the July 30th Hearing.

114. Public Citizen revealed many of the early signals of Avandia's significant cardiac adverse effects including a 1999 FDA pharmacology review of animal toxicity in rosiglitazone use and anticipated potential human toxicities. As a result, the FDA pharmacologist recommended not to approve rosiglitazone for the proposed indication for long-term human use.

115. Additionally, Public Citizen stated that due to the ubiquitous nature of Peroxisome proliferator-activated receptor (PPAR gamma), the receptor which Avandia acts upon and is expressed in many tissues, it was hardly surprising Avandia was causing patients so many significant kinds of damage (e.g., cardiac, liver, bone, bone marrow).

116. Public Citizen demonstrated that when Avandia binds to the PPAR gamma receptors, those receptors react and bind to DNA, initiating gene expression. The

effect is to lower plasma glucose, but it also causes the cardiac cells to produce and store fat. This results in the cells becoming fatty and dying off. Myocardial contraction is disrupted, and the development of heart failure appears to occur.

117. The members of Public Citizen also stated that the increased risk of ischemic heart disease, including myocardial infarctions, justified the removal of the drug from the market.

c. GSK's DREAM and ADOPT Studies

118. During the hearing, in response to those opposing Avandia continuation on the market, GSK presented the results of two industry-sponsored studies, DREAM and ADOPT, claiming these studies did not suggest a large cardiovascular risk. However, as the FDA pointed out, neither study adequately addressed the cardiovascular risk issue.

119. The DREAM study endeavored to determine whether use of Avandia *before a patient was diagnosed with diabetes* would prevent the onset of the disease. H.C. Gerstein, et al. "DREAM (Diabetes Reduction Assessment with Ramipril and rosiglitazone Medication) Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomized controlled trial." *Lancet* 368: 2006:1096-105. Hence, the study population *did not have diabetes.*

120. The Advisory Committee recognized this weakness in GSK's presentation:

> [T]he committee expressed concern that these trials [DREAM and ADOPT] do not study the patients of interest, and in fact, excluded the patients that we are concerned about [*i.e., persons with diabetes*]; **therefore lack of a signal for the outcomes in these trials may not necessarily inform decisions regarding risk for Avandia.**

Summary Minutes of the Joint Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, July 30, 2007 (emphasis added).

121. Dr. Nissen later noted that, even with this relatively healthier *pre-diabetes* patient population, DREAM reflected increased cardiovascular risks. He wrote as follows:

> In DREAM, despite a substantial delay in onset of diabetes, rosiglitazone resulted in a **37% increase in adverse cardiovascular events**, a finding that very nearly reached conventional levels of significance. This trend virtually precludes the possibility of an overall benefit and suggests an unexpected mechanism for harm.

Nissen SE. "The DREAM trial." *Lancet* 368: 2006: 2049 (emphasis added).

122. In fact, Dr. Nissen questioned the entire basis of the DREAM study in that it was designed, not to treat diabetes, but to treat "pre-diabetes" — a non-existent illness.

> In the absence of evidence of actual health benefits, the public health rationale for the use of a drug to treat a precondition and thereby to prevent the onset of a related condition that would, normally and simply, mark the beginning of drug treatment is not clear. **The DREAM study represents an effort to medicalize a predisease state.**

Id. (emphasis added).

123. The ADOPT study, also relied upon by GSK at the July 30th Hearing also failed to support its position. Again, the Committee noted that the study did not provide valuable information to test the cardiovascular safety of Avandia as it was not designed to record cardiovascular outcomes. As one researcher noted:

> The manufacturer did not make a serious effort to verify the presumed health benefits of rosiglitazone in a timely fashion. In ADOPT…. [cardiovascular] events were not identified or recorded in a systemic fashion, and heart failure was the only outcome that was reviewed and adjudicated at the end of the trial. Nonetheless… rosiglitazone in ADOPT was associated with a higher risk of cardiovascular events [than the comparator drug].

Psaty B, Editorial: "The Record on Rosiglitazone and the Risk of Myocardial Infarction." *New England Journal of Medicine*, 357:15 July 2007: 67-69.

124. At the July 30th Hearing, the advisory committee made the non-binding recommendation, based on a 22 to 1 vote, that Avandia should remain on the market. However, the committee also voted 20 to 3 in agreement that available data shows that the cardiovascular risk associated with Avandia is greater than with other available therapies for the treatment of Type II diabetes.

125. The advisory committee also overwhelmingly urged that the FDA require GSK to apply a "black box warning" for Avandia – the strictest warning the FDA can issue.

126. Clifford J. Rosen, M.D., chairman of the committee and an osteoporosis and endocrinology expert at the Maine Center for Osteoporosis, stated that "there was enough concern on the advisory committee that virtually everybody felt there was risk." Dr. Rosen predicted that "there's going to be changes in the way [Avandia] is promoted … and certainly in how physicians use this drug."

127. On August 14, 2007, the FDA issued a press release indicating that GSK had agreed to strengthen Avandia's label to add a "black box label" concerning the risk of heart failure. The FDA stated that "The upgraded warning emphasizes that [Avandia] may cause or worsen heart failure in certain patients."

128. Further, the FDA advisory panel is scheduled to hold another hearing in July 2010 to consider the results of new Avandia studies.

5. Post-FDA Hearing Studies and Petitions for Avandia Removal

129. The September 12, 2007 issue of the Journal of American Medical Association ("JAMA") published a study that found that Avandia doubled the risks of heart failure and raised the risks of heart attack by 42% (the "JAMA Study"). S. Singh, et al. "Long Term Risk of Cardiovascular Events with Rosiglitazone." *Journal of the American Medical Association* 298: 2007: 189-1195.

130. The JAMA Study, which consisted of a *third* meta-analysis, confirmed both the Nissen analysis and the FDA's results showing a **42% increase** in myocardial infarction associated with Avandia use. The study concluded, "rosiglitazone significantly increased the risk of myocardial infarction."

131. Sonal Singh, M.D., a professor and board-certified Internal Medicine at the Wake Forest School of Medicine, was the co-author of the JAMA Study. Dr. Singh stated: "If you use Avandia to treat patients with Type 2 diabetes their chance of getting heart failure due to Avandia is one in 30 and their risk of getting a heart attack is one in 220. All due to the drug."

132. Subsequent studies have supported these three meta-analyses. For example, a Canadian study described

as "independent" and "not funded by industry, and … huge" examined "real-life data" for nearly 160,000 patients and reached similar conclusions reflecting a **40% increase** of heart attack risk in Avandia users. Lipscombe, et al. "Thiazolidinediones and Cardiovascular Outcomes in Older Patients with Diabetes." *Journal of the American Medical Association* 298: 2007: 2634-2643.

133. The lead author stated as follows:

> Our larger, well-designed population-based study provides more convincing evidence that [Avandia] is associated with in increased risk of cardiac events and deaths among elderly patients with diabetes. Moreover, the magnitude of association between TZDs and adverse outcomes, was consistent with risks reported elsewhere.
>
> Current treatment with TZD monotherapy was associated with a significantly increased risk of congestive heart failure . . . acute myocardial infarction . . . and death . . . compared with other oral hypoglycemic agent combination therapies. . . The increased risk of congestive heart failure, acute myocardial infarction, and mortality associated with TZD use appeared limited to rosiglitazone [Avandia]. *Id.*

134. On September 29, 2007, a study published in the medical journal *Lancet* found that patients with a history of heart disease and heart failure have as high as a **72%** increased risk of heart failure while taking Avandia.

135. The study was conducted by pooling data from seven different clinical trials to study the risks of Avandia and Actos, another diabetes drug. Researchers from the Lahey Clinic in Massachusetts included more than 20,000 patients who, during the study, were given either Actos or Avandia to treat Type II diabetes.

136. In addition to its deleterious effects on the heart, Avandia can cause blindness and doubles the risks of bone fractures in women.

137. On October 17, 2007, the U.S. Department of Veterans Affairs ("VA") announced that after its own review, it concluded that, for some patients, rosiglitazone may not afford the same margin of safety as alternative drug therapies.

138. The VA stated that Avandia would be available for patients already using it, if they decided to continue; however, the VA urged doctors to inform patients about Avandia's risks and benefits. The VA also stated that it "will not provide it [Avandia] to patients for whom it is not currently prescribed." Thus, the VA effectively dropped Avandia from its formulary for new patients.

139. Shortly after, the VA's decision to limit Avandia, two U.S. pharmacy benefit managers, Prime Therapeutics and HealthTrans, dropping Avandia from their national formularies after a thorough analysis of the clinical literature examining Avandia's safety and efficacy. This was reported by Reuters in a December 6, 2007 article.

140. Other health insurers like Kaiser Permanente and governments including the County of Santa Clara have also removed Avandia from their formularies.

141. Remarkably, despite the overwhelming evidence, GSK continued to deny that there was evidence of an increased heart risk with Avandia. For example, in December 2007, instead of admitting that Avandia posed a risk to its users and warning the public of its dangers, GSK published the following statement:

> Across multiple sources of data, there is no consistent or systematic evidence that rosiglitazone increases the risk of myocardial ischemic events or deaths in comparison to other anti-diabetic agents.

Press Release: "GlaxoSmithKline responds to JAMA article on the ICES thiazolidinediones and cardiovascular outcomes in older patients with diabetes," dated December 11, 2007.

142. In October 2008, Public Citizen petitioned the FDA to immediately ban Avandia based on the clear evidence of increased risk of heart attacks, heart failure, bone fractures, anemia and macular (retinal) edema with vision loss. The petition also stated that the evidence for Avandia's toxicities is compounded by the accompanying lack of evidence of any clinical benefit, compared to other approved drugs for diabetes, such as metformin, insulin and sulfonylureas.

143. Moreover, a June 5, 2009 *Forbes* article describes GSK's failed attempt to dismiss charges that Avandia raises the risk of heart attacks. Unveiling results of a large 4,447-patient study called RECORD, GSK attempted to combat the Nissen Study by showing that there is no difference in the rates at which patients were hospitalized for or killed by heart disease whether they were on a drug combination that contained Avandia or not. However, the RECORD study ignored a key fact: 40% of patients analyzed in the study were not taking Avandia at the study's end. GSK's study also had another problem – patients on Avandia took 10% more cholesterol-lowering drugs, which reduces the rate of heart attack and makes the trial worthless or questionable at best.

144. Also, some doctors examined the results and believed that the study actually showed slightly more heart problems with Avandia - a bad sign even if the difference was so small that it could have occurred by chance alone. "This study, which was designed to show the benefit of rosiglitazone (Avandia), if anything shows the opposite," said Dr. David Nathan, M.D., chief of diabetes care at Massachusetts General Hospital. Dr. Nathan has no role in the study nor financial ties to any diabetes drug maker.

145. Furthermore, a May 6, 2009 study also showed Avandia increases apoB levels, increases LDL particle numbers, and the increased apoB levels' association with cardiovascular risks in Type II diabetes. *See* Seth S. Martin, *et al*., "Apolipoprotein B but not LDL Cholesterol is Associated with Coronary Artery Calcification in Type

2 Diabetic Whites." *The American Diabetes Association* 58: 2009: 1887-1892. *See* http://diabetes.diabetesjournals.org/content/58/8/1887.abstract. Defendant failed to warn patients and doctors of the increased apoB levels contributing to cardiovascular events.

146. Despite knowledge of the widespread health dangers of Avandia, Defendant failed to effectively warn consumers about the use of this drug as compared to other competing formulations which posed much lesser health risks.

6. January 2010 Senate Staff Report Reveals Defendant Knew about Avandia's Cardiovascular Risks for Years But Failed to Warn Patients and the FDA

147. Triggered by the May 2007 study published in the *New England Journal of Medicine*, in January 2010, the U.S. Senate Staff Committee on Finance published the "Staff Report on GlaxoSmithKline and the Diabetes Drug Avandia." ("Senate Report on Avandia"). The staff report was developed by the U.S. Senate Committee on Finance who reviewed documents provided by Defendant, the FDA, and others and conducted numerous interviews and phone calls with Defendant, the FDA, and an anonymous whistleblower.

148. The staff report reveals,

> . . . the reviewed evidence suggests that **GSK knew for several years prior to this study that**

> **there were possible cardiac risks associated with Avandia**. As a result, **it can be argued that GSK had a duty to warn patients and the FDA of the Company's concerns**. Instead, **GSK executives attempted to intimidate independent physicians, focused on strategies to minimize or misrepresent findings that Avandia may increase cardiovascular risk**, and **sought ways to downplay findings that a competing drug might reduce cardiovascular risk**.

Sen. Max Baucus and Sen. Chuck Grassley, Staff Rep. On GlaxoSmithKline and the Diabetes Drug Avandia, S. PRT. 111-41, 111th Cong. 2d Sess., at 1 (2010) (emphasis added).

149. The Senate Report on Avandia revealed that in December 2007, Dr. Steve Haffner, a professor of medicine at the University of Texas Health Sciences Center, San Antonio, and a consultant for Defendant, leaked to Defendant the draft *New England Journal of Medicine* Nissen study critical of Avandia. Dr. Haffner was entrusted with a confidential copy of the manuscript draft because he was peer-reviewing the study. The leaked manuscript was widely disseminated within the company, and allowed Defendant to launch a public relations plan to protect Avandia, a multi-billion dollar product.

150. Furthermore, the Senate Report on Avandia revealed Defendant was aware since at least 2004 that the RECORD trial was statistically inadequate, or "underpowered" to answer questions regarding

cardiovascular safety and the report states that "inconclusive" results could be favorable to GSK and the marketing strategy for Avandia.

151. According to the Senate Report on Avandia, experts were advising Defendant since 2004 about the possible biological mechanisms related to why Avandia may cause an increased risk for heart attacks. However, Defendant appeared eager to design studies to prove that Avandia was safer than its competitor Actos.

152. Furthermore, in late 2005, Defendant published a draft retrospective analysis of cardiovascular events in Avandia clinical trials discussing the underlying cause for the increase in ischemia. In the analysis that examined myocardial ischemia, the authors mention a "hypothesis that small degrees of fluid retention may be an important contributor to the development of worsening myocardial ischemia in high risk patients."

153. According to the Senate Report on Avandia, after Defendant reviewed the evidence found in this analysis, it appears that Defendant was aware of the potential cardiovascular risks associated with Avandia in late 2004 or early 2005.

154. Additionally, in 2005, Defendant ordered an "observational" trial study that was conducted in two parts: the first part in 2005 and the second in 2006. The results of these studies support the further investigation of the cardiovascular risks associated with Avandia.

155. According to a February 22, 2010 *New York Times* article, one internal e-mail message from the Senate Report found that Defendant's statistician stated that "there is no statistical reason for disregarding the findings" of Dr. Nissen's study. In another email, Dr. Moncef Slaoui, head of research at GlaxoSmithKline, wrote that federal drug regulators, Dr. Nissen and the company's own researchers all seemed to agree that studies of the drug showed that it substantially increased the risks of death and heart attacks, also known as ischemic events: "F.D.A., Nissen and G.S.K. all come to comparable conclusions regarding increased risk for ischemic events, ranging from 30 percent to 43 percent!"

156. On February 22, 2010, less than a month after the Senate released its scathing Senate Report, the FDA announced that it was still reviewing safety data on Avandia and that conclusions will likely be released around a public meeting scheduled for July 2010.

157. Rather than acknowledge the wrongdoing exposed in the Senate Report, GSK instead criticized the Senate Report stating the report "mischaracterizes and distorts" the company's record. In a February 2010 press release posted on its website, Defendant condemned the highly critical Senate Report that has reignited the debate around its troubled product.

7. February 18, 2010 Baucus-Grassley Letter to the FDA Commissioner on the Avandia TIDE study

158. After reviewing internal GSK documents, in a February 18, 2010 letter from senior Senate members Max Baucus and Chuck Grassley to Margeret A. Hamburg, Commissioner of the FDA ("Baucus-Grassley letter"), the Senators concluded: 1) Defendant was aware of the possible cardiac risks associated with Avandia years before such evidence became public; 2) Defendant had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner; 3) Defendant's executives intimidated independent physicians and strategized ways to minimize findings that Avandia may increase cardiovascular risk; and 4) Defendant sought ways to downplay findings that Actos might reduce cardiovascular risk.

159. The Baucus-Grassley letter also revealed that in 2007, the FDA requested Defendant perform a cardiovascular safety trial, called TIDE (Thiazolidinedione Intervention With Vitamin D Evaluation), comparing Avandia to other diabetes treatments such as Actos.

160. An October 2008 analysis by FDA safety officials raised concerns regarding the TIDE study, stating there is no evidence that Avandia confers any unique health benefits over Actos, and there is strong evidence that Avandia confers an increased risk of [heart attacks] and heart failure compared to Actos. The safety officer wrote that because of cardiovascular concerns with Avandia "the safety of the study itself cannot be assured, and is not acceptable."

161. According to an April 19, 2010 *Wall Street Journal* article, the FDA is weighing whether to halt the TIDE safety study which involves thousands of patients taking Avandia, a decision that could also determine whether the drug stays on the U.S. market. Some scientists inside and outside the FDA have stated it is unethical to compare a drug with known cardiac risks with a seemingly safer alternative. They also say Avandia should be pulled from the market.

162. Public Citizen's primary spokesperson, Dr. Sidney Wolfe, told Congress on April 28, 2010 that the TIDE study comparing Avandia with Actos should be stopped without delay, and the group continued to advocate for Avandia's removal from the market.

D. Alternatives to Avandia

1. Actos

163. Physicians are free to prescribe to their patients approved drugs as they see fit to treat any condition or symptom. The medical community generally encourages physicians to prescribe the safest, most effective and cost-efficient treatment. Research and studies have illustrated that physicians can prescribe safer and/or equally effective alternatives to treat the conditions for which Defendant has promoted Avandia.

164. Another prescription medication for Type II diabetes mellitus is Actos, a drug manufactured and promoted by Takeda Pharmaceuticals North America.

165. On March 15, 2000, Dr. Buse wrote to Dr. Jane Henney, former FDA Commissioner of Food and Drugs, and stated that "the frequency of mild and serious adverse events that I have seen with troglitazone [Rezulin®] and pioglitazone is comparable to or less than the number I have observed with other antidiabetic agents." Dr. Buse letter to Dr. Jane Henney, FDA re: Citizen's Petition to Immediately Require Class Labeling for the Diabetes Drugs Troglitazone (Rezulin), Rosiglitazone (Avandia) and Pioglitazone (Actos)" dated March 15, 2000. Rezulin was withdrawn from the U.S. market on March 21, 2000.

166. In his letter, Dr. Buse strongly suggested that Actos is one of the "most effective, safe and beneficial drugs in its class" and that Avandia "may be associated with less beneficial cardiac effects or even adverse cardiac outcomes." Dr. Buse stated he found that only Avandia had been associated with increased cardiac weight, which is another negative cardiac effect.

167. A European clinical trial called PROactive (Prospective Pioglitazone Clinical Trial in Macrovascular Events) has assessed the effects of Actos on mortality and morbidity associated with cardiovascular disease progression in patients with Type II diabetes.

168. The trial examined whether the observed effects of Avandia represent a "class effect" of thiazolidinediones. The study suggested that Actos consistently improved components of diabetic dyslipidemia, another cardiovascular disease risk factor, which is characterized by low HDL ("good") cholesterol levels and high triglycerides.

169. Additionally, a June 23, 2007 *Bloomberg* article discussed a study finding Actos may lower the risk of heart attack and death by 44 percent in diabetic patients with kidney disease. The findings, from a subgroup of patients enrolled in a previous study, were reported at the June 23, 2007 meeting of the America Diabetes Association in Chicago. In a separate study, Actos reduced inflammation and blood clots more than a placebo.

170. Furthermore, a February 20, 2010 *New York Times* article discusses FDA reports with claims that if every diabetic now taking Avandia were instead given Actos, about 500 heart attacks and 300 cases of heart failure would be averted each month.

171. A June 18, 2007 *USA Today* article discusses an increased number of physcians discontinuing Avandia prescriptions and are instead prescribing Actos as an alternative diabetes medication. "Before the [*The New England Journal of Medicine*] posted the study May 21, U.S. doctors were writing about 240,000 prescriptions [of Avandia] per week, Glaxo spokeswoman Alice Hunt says. That has dropped to about 215,000 to 220,000 per week. Glaxo estimates the number of people taking Avandia has dropped from about 1 million to 900,000 in the USA." Additionally, new prescriptions for Avandia had dropped 40% as a result of Dr. Nissen's study. New prescriptions are defined as the first prescription a doctor writes for a patient even if the patient might already have been taking Avandia under a different doctor's care. "Prior to Nissen's study, U.S. doctors wrote about 80,000 new Avandia prescriptions weekly; that number has dropped

to about 55,000, Hunt says." The *USA Today* article explains that physicians are switching patients to Actos as an alternative.

172. A May 2009 Canadian study conducted by David N. Juurlink and published in *British Medical Journal* and entitled "Adverse cardiovascular events during treatment with piolitazone and rosiglitazone: population based cohort study" compared the risk of acute myocardial infarction, heart failure and death with Type II diabetes treated with Avandia and Actos in 39,736 patients aged 66 years and older between 2002 and 2008.

173. The study concluded that among older patients with diabetes, Actos is associated with a significantly lower risk of heart failure and death than Avandia and given that Avandia lacks a distinct clinical advantage over Actos, continued use of Avandia may not be justified.

174. A Johns Hopkins study published in 2009 in the *British Medical Journal* reviewed 40 randomized, controlled trials involving cardiac risks of older and newer diabetes drugs and found that metformin hydrochloride was the only drug associated with a decreased risk of cardiovascular mortality compared with any other oral diabetes agent or placebo. "The only diabetes drug with increased cardiovascular risk was rosiglitazone (Avandia), for which the increased risk was 1.68, falling just short of statistical significance," Dr. Wolfe said. "Pioglitazone (Actos) had neither increased nor decreased cardiovascular risk in the six randomized trials that comprised the study.

175. Thus, Actos has fewer cardiac risks than Avandia and may prove to be a safer alternative to Avandia for the treatment of Type II diabetes mellitus.

176. However, physicians have been misled by Defendant to believe that Avandia is superior in its effectiveness and safety to other equally effective and safer alternatives like Actos. As a result of Defendant's widespread misleading marketing and promotion of Avandia's superior safety and effectiveness over safer and equally effective alternative drugs like Actos, many physicians are less inclined to prescribe patients these antidiabetic alternatives.

2. Avandia Is No Better Than Cheaper Alternatives at Preventing Heart Attacks, Strokes or Deaths

177. A study published in the *Annals of Internal Medicine* in September 2007 concluded that when compared "with newer, more expensive agents [like Avandia], older agents (second-generation sulfonylureas and metformin) have similar or superior effects on glycemic [blood sugar] control, lipids, and other intermediate endpoints."

178. A June 8, 2009 *Wall Street Journal* article describes a diabetes study sponsored by the National Institutes of Health and several drug companies. The five-year study of 2,368 diabetics was an effort to answer: 1) whether aggressively reopening clogged arteries with stents or bypass surgery work better than inexpensive pills such as beta blockers and other generic heart drugs, and 2) whether diabetes drugs such as Avandia help the

body use insulin more efficiently than injecting insulin. The study revealed that aggressive use of expensive diabetes drugs like Avandia performed no better in preventing deaths, heart attacks or strokes than cheaper treatments such as insulin.

179. A February 2010 study published in the journal for the American Diabetes Association, *Diabetes Care*, found that Avandia increases diabetic's heart attack risk by 30% compared with the older diabetes drug sulfonylurea. When compared with metformin, Avandia increases a diabetic's heart attack risk **by 120%**.

E. <u>Defendant's Publication Misrepresents Avandia's Safety, Efficacy and Effectiveness and Suppresses Unfavorable Avandia Information</u>

180. Defendant knew or should have known that Avandia was unsafe as compared to other diabetes medications. Despite having knowledge of the increased risk of heart problems related to use of its product, Defendant intentionally, negligently and/or willfully misrepresented the safety and efficacy of Avandia and omitted relevant information showing adverse effects of Avandia, including an increased risk of death or illness due to heart disease or heart attack.

181. Defendant knew or should have known that Plaintiff and the Class would be injured as a result of its misrepresentations and omissions. As a result of Defendant's omissions and deliberate misrepresentations related to critical information regarding the serious health risks associated with Avandia, Plaintiff and the Class:

- Paid in part or in full for more prescriptions of Avandia than they otherwise would have paid for and/or

- paid for Avandia that would have been sold at a lower price had market forces been allowed to operate unfettered by Defendant's violations and/or

- paid for a more effective and/or cheaper alternative medication.

182. From its product launch to the present, Defendant engaged in wide-spread deceptive statements and conduct, and pervasive false and misleading marketing, advertising and promotion of Avandia. Defendant deceived physicians, consumers and third party payors such as Plaintiff regarding the comparative efficacy of Avandia to other medications designed to control Type II diabetes mellitus. Defendant failed to warn – and affirmatively misled – physicians, consumers and others in the medical community regarding Avandia's association with increased risk of heart attacks and heart-related diseases.

183. Defendant also represented that patients could stay on Avandia longer than the older drugs. Additionally, Defendant represented that, unlike the older diabetes drugs, Avandia had the additional benefit of *lowering* diabetics' cardiovascular risks.

184. Despite being on notice of the potential for deadly heart attacks and heart-related diseases, Defendant

opted for the bare minima of narrowly-tailored clinical trials, of limited duration, such that little to no side effects were likely to be revealed. Thus, instead of conducting true scientific research in good faith to legitimately test the efficacy and safety of Avandia, Defendant focused on creating studies specifically designed to enhance commercial value.

185. Defendant was required to provide fair and balanced information whenever they engaged in promotional activities. Promotional activities encompass not only written material but all presentations. Defendant knew whenever it was required to provide fair and balanced information, it was required to provide any negative as well as positive information about their drug.

186. In today's health care market, physicians face extreme time constraints in determining which drugs and treatments are best. Physicians, consumers and third-party payors use a variety of trusted sources including independent studies for such information. Many of these sources are directly controlled or heavily influenced by pharmaceutical manufacturers such as Defendant. All of these sources contain susceptibilities that have been exploited by Defendant and other pharmaceutical manufacturers.

187. Among the tactics employed by Defendant were plans to create studies designed to illustrate Avandia's allegedly superior profile to both (a) placebo and (b) comparable medications designed to control Type II diabetes mellitus while providing funding to engage "key

opinion" and "thought" leaders in publication-worthy trials.

188. Upon information and belief, Defendant's scheme was carried out by: making false statements to consumers, physicians and pharmacies concerning the efficacy and safety of Avandia; and training Defendant's employees to conceal negative information regarding Avandia to avoid detection of their activities by Plaintiff and the Refund and California Medical Monitoring Classes.

189. Upon information and belief, Defendant sought out, and provided incentives and funding to, doctors and researchers prior to their respective launches to develop deceptive and misleading medical literature for use in marketing.

1. Misrepresentations in Medical Publications

190. FDA regulations and industry standards prohibit Defendant from misrepresenting scientific evidence that supports (or fails to support) claims that their respective drug is safe and effective for a specific condition. Thus, anecdotal evidence of a drug's usefulness for a given condition could not be presented as the equivalent of the findings of a well-designed clinical trial. Failure to comply with these standards violates Defendant's legal duty to provide accurate and non-misleading information.

191. Nevertheless, despite scientifically sound and reliable studies that identify Avandia's adverse effect of increased heart attack and heart-related disease, and

the FDA's stringent regulations and recommendations to Defendant regarding the black box labeling of Avandia's adverse side effects, Defendant continued and continues to mislead and deceive consumers by placing full page advertisements in newspapers nationwide.

192. The ads, which appeared in newspapers such as *The New York Times*, *The Washington Post*, *USA Today* and *The Wall Street Journal*, were in the form of a letter to Avandia patients signed by Ronald Krall, GSK's chief medical officer. Therein, Defendant states that they have "conducted an unprecedented number of clinical trials in order to continuously evaluate the safety of Avandia, including its impact on the cardiovasculary system." Defendant claims that the response from the "well-informed" experts and researchers has been "enouraging." Yet despite these "encouraging" studies, the ad warns that Avandia can cause fluid retention, which "can make some heart problems worse or lead to heart failure."

193. Another example of Defendant's attempt to conceal criticisms of Avandia occurred in early on February 21, 2010, when the Editor-in-Chief of the *European Heart Journal* received a letter from Dr. Moncef Slaoui, the chairman of research and development of Defendant, to cease publication of Steven Nissen's editorial on the cardiovascular effects of Avandia. Dr. Slaoui urged the journal not to publish in print an online editorial by Steven Nissen accompanying an analysis on the cardiovascular effects of rosiglitazone reporting an increased incidence of congestive heart failure in the RECORD trial.

194. Defendant deceived consumers and members of the medical community by overemphasizing controlled and misleading favorable studies, while failing to disclose studies illustrating Avandia's dangerous side effects. Defendant continues to expose vulnerable patients with Type II diabetes to an increased risk of heart attack and heart-related diseases.

2. Defendant's Funding for Studies and Payments to Doctors

195. According to a February 23, 2010 Heart.org article and study presented at the American College of Preventive Medicine Preventive Medicine 2010 annual meeting, an analysis of authors who published reports on Avandia shows that those authors with ties to industry were more likely to conclude that Avandia did not increase myocardial ischemia risk as compared with authors with no industry ties.

196. Among the 202 papers that were evaluated, among authors who concluded Avandia does not increase risk of myocardial ischemia, 91% had financial relationships with antihyperglycemic agent manufacturers and 86% had relationships with Defendant. Among authors of articles representing unfavorable reviews of Avandia, only 25% had financial relationships with antihyperglycemic agent manufacturers and 18% had relationships with Defendant.

197. A June 5, 2007 *The Bulletin* article reveals that Dr. Anne E. Peters, a diabetes expert who operates a clinic for Los Angeles County and who is affiliated with

the University of Southern California medical school, had previously received money from Defendant as a speaker on behalf of Avandia.

198. According to the article, Dr. Peters resigned from that position when she enumerated her concerns about the drug's risks. Dr. Peters said that five years ago, she removed Avandia from the formulary (the list of preferred drugs) maintained by the Los Angeles Clinic. That meant that patients would receive Actos instead of Avandia. "The Avandia people, it was just so surprising, they asked me what I wanted to keep Avandia on the formulary." "Dr. Peters said that she asked the company to establish a database at the clinic that would track the outcomes of patients on both drugs. When she asked for the database, which would have cost several thousand dollars, she said a company representative replied: 'That's all you want? Other doctors ask to go to the Caribbean.'" Dr. Peters said, "They wanted to do everything but approve my request."

199. Further, Avandia's pre-marketing clinical trials were specifically designed to produce positive results and do not support the assertion that the medication is less likely to cause dangerous heart-related diseases. Manufacturers like Defendant fund clinical trials, where the manufacturers create and control the research design. In a 2001 study published in NEJM, researchers found that more than two-thirds of the academic institutions accepted research contracts that prohibit researchers from changing the research design of sponsors like Defendant. Half of the medical centers allowed commercial sponsors to "draft manuscripts reporting the research results, with

the investigators' role limited to review and suggestions for revision."

200. In "Ensuring Integrity in Industry-Sponsored Research," published in the March 2010 *Journal of American Medical Association*, editorial authors, Catherine D. DeAngelis, MD, MPH and Phil B. Fontanarosa, MD, MBA, criticized industry-sponsored drug research for such products as Avandia. Specifically, the authors describes Defendant's dissemination of the Avandia study as "inappropriate conduct surrounding an industry-sponsored clinical trial of rosiglitazone and reveals a situation in which concerns about preserving market share apparently trumped concerns about the potential for causing patient harm.".

201. Additionally, in "Setting the RECORD Straight," published in March 2010 *Journal of the American Medical Association*, Steven E. Nissen, MD states that although Defendant's final RECORD article reports that external statistical confirmation was obtained, the extent and depth of these confirmatory analyses still remain uncertain. Furthermore, Nissen explains, as illustrated by the problems with the RECORD trial, absence of independent access to all of the data in the trial may allow physician-scientists to be manipulated by the sponsor, resulting in a manuscript that does not provide the most accurate assessment of the risks and benefits of the therapy. Nissen adds that the requirement of independent outside statistical confirmation of trial results is an essential step and should be universally mandated and would significantly improve the quality of reporting of industry-sponsored clinical trials.

202. According to an April 12, 2010 *New York Times* article, as a response to critics who say the payments to doctors can overly influence how the doctors practice medicine and prescribe drugs like Avandia, pharmaceutical companies like Defendant are now operating databases that disclose payments to doctors who act as consultants or speakers.

203. Defendant's omissions of, and deliberate misrepresentations related to, critical information regarding the serious health risks associated with Avandia have increased the risk of of disease based on exposure to Avandia and caused financial harm to Plaintiff and the Classes and the sale of Avandia without adequate warning, and based upon false representations regarding its safety, is in violation of various consumer protection statutes in states across the country and the common law.

F. <u>Concealment of Defendant's Conduct and Tolling of Statute of Limitations</u>

204. The applicable statute of limitations regarding the claims of Plaintiff and the Class has been tolled by Defendant's concealment of its unlawful, deceit, as alleged in detail throughout this Complaint.

205. As evidenced by the allegations in this Complaint, Defendant has employed and continues to employ practices and techniques of secrecy in order to avoid detection of, and to conceal, their deceptive and conspiratorial behavior regarding the safety and efficacy of Avandia as well as Avandia's risks associated with heart attacks and heart-related diseases.

206. Defendant successfully concealed from Plaintiff and the Class facts sufficient to excite suspicion of claims against Defendant arising from its deception.

207. Despite taking on the responsibility to reveal this information to the general public, Defendant has kept such information hidden.

208. As such, Plaintiff and the Class were not effectively alerted to the existence and scope of this industry-wide smokescreen and were not on notice of their potential claims until shortly prior to the filing of this Complaint.

209. Plaintiff and the Class could not have acquired such knowledge through the exercise of reasonable diligence.

210. Through its public statements, marketing and advertising, Defendant's self-concealing scheme and affirmative conduct to perpetuate its scheme deprived Plaintiff and the Class members of actual or presumptive knowledge of facts sufficient to put them on notice as to their potential claims.

G. <u>Injury to Plaintiff and the Class</u>

211. Defendant's deceptive and misleading marketing scheme increased the number of prescriptions of Avandia written and filled during the Class Period. Because Defendants withheld material information about the true safety and efficacy of Avandia, the prescribing

physicians did not have the knowledge necessary to make informed decisions regarding Avandia prescriptions. Plaintiff and the Class, unaware of Defendant's scheme, paid for these prescriptions. Although more effective, safer, and less expensive alternatives are available, Defendant's promotion and marketing of Avandia's safety and effectiveness has been highly successful, resulting in Defendants receiving billions of dollars in profits, representing ill-gotten gains to which Defendants were not entitled.

212. Plaintiff and similarly-situated Class members bear the ultimate responsibility of paying for their Avandia prescriptions.

213. PBMs prepare a "formulary," which is a list of the drugs that are approved for coverage by their third-party payor clients, such as Plaintiff and Class members. In order for a drug to be listed on the formulary, it must be assessed by the PBM for clinical safety, efficacy, and cost effectiveness. Further, where a PBM finds that a drug has an advantage over competing drugs, that drug is given a preferred status on its formulary.

214. The level of preference on the formulary corresponds with the amount that a plan participant must contribute as a co-payment when purchasing a drug the higher the preference, the lower the co-payment, the more likely that the drug will be purchased by a prescription plan's beneficiary in lieu of a cheaper or more cost effective alternative, and vice versa. As such, the higher a drug's preference on the formulary, the more likely it is for a

doctor to prescribe that drug. This system is well known to pharmaceutical manufacturers, including Defendants.

215. Due to the large number of drugs purchased through third-party payors, it is vital to a drug manufacturer's economic interests to have its product listed on as many formularies as possible.

216. By directly and falsely promoting Avandia as safe and effective for Type II diabetes and training its sales forces and representatives to avoid alerting the FDA to its activities and to dismiss any safety concerns raised by physicians, Defendant influenced PBMs to place Avandia on their formularies and higher in preference on those formularies.

217. Defendants falsely promoted Avandia as safe and effective directly to PBMs in order to get Avandia placed on, or placed more favorably than its competitor drugs on the PBM formularies.

218. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors relied on the Defendant's misrepresentations of Avandia's safety. Physicians relied on the Defendant's misrepresentations of Avandia's safety in prescribing the drug for their patients. Patients relied on the Defendant's misrepresentations of Avandia' s safety in purchasing the drug. PBMs and pharmacy and therapeutic committees relied on Defendant's misrepresentations regarding Avandia's safety when approving and/or placing Avandia on formularies. Third-party payors relied on the

Defendant's misrepresentations regarding Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their members.

219. Therefore, Defendant's failure to adequately inform consumers, third-party payors and those in the medical community that the use of Avandia dangerously increases the risk of heart attacks and heart-related diseases, and its false and misleading promotion of Avandia's efficacy over competing less expensive antidiabetic drugs, caused patients and third-party payors to pay for Avandia, which is neither safer nor more effective than other less expensive antidiabetic drugs.

220. But for Defendant's actions, third-party payors would not have paid for Avandia but would instead have paid for safer, equally efficacious drugs like metformin and/or sulfonyureas.

CLASS ACTION ALLEGATIONS

221. Plaintiff brings this suit as a Class action pursuant to Rule 23(b)(2) and (b)(3) of the Federal Rules of Civil Procedure, on behalf of a Class consisting of:

> All health insurance companies, third-party administrators, health maintenance organizations, self-funded health and welfare benefit plans, third-party payors and any other health benefit provider, in the United States of America and its territories, which paid or incurred costs for the drug Avandia,

> for purposes other than resale, since May 25, 1999. Excluded from the Class are employees of Defendant, including its officers or directors, and the Court to which this case is assigned.

222. The proposed Class is sufficiently numerous, as thousands of members of the Class were induced to pay for Avandia through Defendant's scheme. The Class members are so numerous and dispersed throughout the United States that joinder of all members is impracticable. The Class is composed of thousands of third-party payors, and the disposition of their claims in a Class action will benefit both the parties and the Court. It is estimated that in 2007, at least half a million individuals nationwide received prescriptions for Avandia. Defendant sells millions of doses of Avandia in the United States every year, and thus the Class is sufficiently numerous to make joinder impracticable, if not outright impossible. The Class members can be identified by, inter alia, records maintained by Defendant, pharmacies, and PBMs.

223. Common questions of law and fact exist as to all members of the Class and predominate over any questions affecting solely individual members of the Class. Among the questions of law and fact common to the Class members are:

a. whether Defendant misrepresented the safety and efficacy of Avandia, to the financial detriment of the Class;

b. whether Defendant engaged in a conspiracy to promote the sale of Avandia while at the same time suppressing any adverse information regarding Avandia;

c. whether Defendant's acts and omissions violate, inter alia, the Pennsylvania Unfair Trade Practices and State Consumer Protection Laws;

d. whether Defendant made material misrepresentations of fact, or omitted material facts regarding the increased risk of heart attacks and heart-related diseases associated with Avandia, which material misrepresentations or omissions operated as a fraud and deceit upon the Class;

e. whether Plaintiff and the Class paid more for Avandia than for other safer and equally or more efficacious drugs that were available at a cheaper price;

f. whether persons who took Avandia are at increased risk of severe and permanent injuries, including liver damage and/or failure, cardiac damage and visual impairment and damage;

g. whether, in marketing and selling Avandia, Defendant failed to disclose the dangers and risks to the health of persons ingesting the drug;

h. whether Defendant failed to warn adequately of the adverse effects of Avandia;

i. whether Defendant misrepresented in its advertisements, promotional materials and other materials, among other things, the safety, potential side effects and convenience of Avandia;

j. whether Defendant knew or should have known that the ingestion of Avandia leads to serious adverse health effects;

k. whether Defendant adequately tested Avandia prior to selling it;

l. whether Defendant manufactured, marketed, distributed and sold Avandia notwithstanding its knowledge of the drug's dangerous nature;

m. whether Defendant knowingly omitted, suppressed and/or concealed material facts about the unsafe and defective nature of Avandia from government regulators, the medical community and/or the consuming public;

n. whether the Class has been damaged, and if so, the extent of such damages and/or the nature of the equitable relief, statutory damages, or punitive damages to which the Class is entitled;

o. whether Defendant was and is unjustly enriched by its acts and omissions, at the expense of the Class;

p. the amount of attorneys' fees, prejudgment interest, and costs of the suit to which the Class is entitled;

q. whether Defendants engaged in conduct that violates federal RICO statutes in promoting the sales of and suppressing adverse information about Avandia; and

r. whether Defendant engaged in a conspiracy to promote the sales of and suppress adverse information about Avandia in violation of federal RICO statutes.

224. Plaintiff's claims are typical of the claims of the members of the Class because Plaintiff and the Class sustained damages arising out of the Defendant's wrongful conduct as detailed herein. Specifically, Plaintiff, having expended substantial sums for the purchase of Avandia, assert claims that are typical of the claims of the entire Class, and will fairly and adequately represent and protect the interest of the Class.

225. Plaintiff will fairly and adequately protect the interests of the Class members and has retained counsel competent and experienced in class action lawsuits.

226. Plaintiff has no interests antagonistic to or in conflict with those of the Class members and therefore should be adequate as representatives for the Class members.

227. A Class action is superior to other available methods for the fair and efficient adjudication of this controversy since joinder of all members of the Class is impracticable. Furthermore, because the damages

suffered by individual members of the Class may in some instances be relatively small, the expense and burden of individual litigation make it impossible for such Class members individually to redress the wrongs done to them. Also, the adjudication of this controversy through a Class action will avoid the possibility of inconsistent and possibly conflicting adjudications of the claims asserted herein. There will be no difficulty in the management of this action as a Class action.

CAUSES OF ACTION

First Cause of Action

Violation of 18 U.S.C. § 1962(C)
Avandia Promotion Enterprise

228. Plaintiff and the Class incorporate by reference all preceeding paragraphs as if fully set forth herein.

229. Defendant is a "person" within the meaning of 18 U.S.C. §1961(3) who conducted the affairs of the enterprise, the Avandia Promotion Enterprise, through a pattern of racketeering activity in violation of 18 U.S.C. § 1962(c).

230. The Avandia Promotion Enterprise is an association-in-fact within the meaning of 18 U.S.C. § 1961(4), consisting of Defendant, including its employees, agents and external consultants like Sir Colin Dollery and Dr. Stephen Haffner, co-promoters Bristol-Myers Squibb, and other as yet unknown consultants, marketing firms

and distribution agents employed by Defendant to promote Avandia. All entities are persons within the meaning of 18 U.S.C. §1961(3) and acted to enable Defendant to fraudulently market Avandia as scientifically proven as safe and effective. The Avandia Promotion Enterprise is an organization that functioned as an ongoing organization and continuing unit. The Avandia Promotion Enterprise was created and/or used as a tool to effectuate a pattern of racketeering activity. Each of these entities, including Defendant, is a "person" distinct from the Avandia Promotion Enterprise.

231. Defendant, in concert with other participants in the Avandia Promotion Enterprise, created and maintained systematic links for a common purpose— to aid in marketing Avandia as safe for its intended uses, while suppressing evidence to the contrary and improperly inducing physicians to prescribe Avandia. Each of the participants in the Avandia Promotion Enterprise received substantial revenue from the scheme to promote Avandia as safe for its intended uses. Such revenue was exponentially greater than it would have been if Avandia was marketed appropriately and the true safety risks of Avandia had been disclosed. All participants of the Avandia Promotion Enterprise were aware of Defendant's control over the activities of the Avandia Promotion Enterprise in promoting Avandia. Furthermore, each portion of the enterprise benefited from the existence of the other parts.

232. The Avandia Promotion Enterprise engaged in and affected interstate commerce, because, inter

alia, it marketed, promoted, sold, or provided Avandia to thousands of individuals and entities throughout the United States.

233. Defendant exerted control over the Avandia Promotion Enterprise and management of the affairs of the Avandia Promotion Enterprise.

234. Defendant conducted and participated in the affairs of the Avandia Promotion Enterprise through patterns of racketeering activity, including acts indictable under 18 U.S.C. §§ 1341 (mail fraud); 1343 (wire fraud); 1512 (tampering with witnesses); and 1952 (use of interstate facilities to conduct unlawful activity).

235. Defendant's fraudulent scheme consisted of, inter alia: deliberately misrepresenting the safety of Avandia so that Plaintiff and members of the Class paid for this drug to treat symptoms for which it was not scientifically proven to be safe and effective and actively concealing and causing others to conceal, information about the safety of Avandia.

236. Defendant's use of the mail and wires to perpetuate its fraud involved thousands of communications, including, but not limited to:

a. communications with and among the enterprise participants that misrepresented the safety and risks of Avandia amongst themselves and others;

b. communications with patients and Class Members, including Plaintiffs, inducing payments for Avandia by misrepresenting the safety and risks of Avandia;

c. receiving the proceeds in the course of and resulting from Defendant's improper scheme;

d. transmittal and receipt of monies from governmental health organizations and programs, including without limitation Medicare and Medicaid; and

e. transmittal and receipt of payments in exchange for, directly or indirectly, activities in furtherance of the Avandia Promotion Enterprise.

237. At all times during the fraudulent scheme, Defendant's and the Fraud Participants had a legal and ethical obligation of candor to and honest dealing with public and private payors, physicians and the medical community.

238. The conduct of the Avandia Promotion Enterprise described above constitutes "racketeering activity" within the meaning of 18 U.S.C. § 1961(1). Defendant's decisions and activity in connection with the Avandia Promotion Enterprise to routinely conduct its transactions in such a manner constitutes a "pattern of racketeering activity" within the meaning of 18 U.S.C. § 1961(5).

239. The above described racketeering activities amounted to a common course of conduct intended to deceive and harm Plaintiff and the Class. Each such

racketeering activity was related, had similar purposes, involved similar or the same participants, and methods of commission, and had similar results affecting the same or similar victims, including Plaintiff and members of the Class. Defendant's racketeering activities were part of their ongoing business and constitute a continuing threat to the property of Plaintiffs and the Class.

240. Plaintiff and members of the Class have been injured in their property by reason of these violations in that Plaintiff and members of the Class paid hundreds of millions of dollars for Avandia that they would not have paid had Defendant not engaged in this pattern of racketeering activity.

241. The injuries to Plaintiff and members of the Class were directly and proximately caused by Defendant's racketeering activity.

242. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors, including Plaintiff and the Class, directly relied on the racketeering activities of the Defendant's and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the representations as to the efficacy and safety of Avandia as promoted by Defendant. Because Defendant controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendant's representations about Avandia. Further, Defendant perpetuated this reliance

by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

243. By virtue of these violations of 18 U.S.C, § 1962(c), Defendants are liable to Plaintiff and the Class for three times the damages sustained, plus the costs of this suit, including reasonable attorneys' fees.

244. By reason of the foregoing, and as a direct and proximate result of Defendant's fraudulent misrepresentations, Plaintiff and the Class have suffered damages. Plaintiff and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

245. By reason of the foregoing, Plaintiff and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts.

Second Cause of Action

Violation of 18 U.S.C. § 1962 (d) -RICO Conspiracy

246. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

247. Section 1962(d) of RICO provides that it "shall be unlawful for any person to conspire to violate any of the provision of subsection (a), (b), or (c) of this section."

248. Defendant has violated § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c). The object of this conspiracy

has been and is to conduct or participate in, directly or indirectly, the conduct of the affairs of the Avandia Promotion Enterprise described previously through a pattern of racketeering activity. The corporate defendants conspired with, inter alia, publicists, sales representatives, medical professionals, academics and other intermediaries to promote Avandia and suppress information about the harms known to result from Avandia use.

249. Defendant's co-conspirators have engaged m numerous overt and predicate fraudulent racketeering acts in furtherance of the conspiracy, including material misrepresentations and omissions designed to defraud Plaintiff and the Class of money.

250. The nature of the above-described acts of Defendant's co-conspirator's acts, material misrepresentations, and omissions in furtherance of the conspiracy gives rise to an inference that they not only agreed to the objective of an 18 U.S.C. § 1962(d) violation of RICO by conspiring to violate 18 U.S.C. § 1962(c), but they were aware that their ongoing fraudulent and extortionate acts have been and are part of an overall pattern of racketeering activity.

251. As a direct and proximate result of Defendant's overt acts and predicate acts in furtherance of violating 18 U.S.C. § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c), Plaintiff and the Class have been and are continuing to be injured in their business or property as set forth more fully above.

252. Defendant sought to and has engaged in the commission of and continues to commit overt acts, including the following unlawful racketeering predicate acts:

a. Multiple instances of mail and wire fraud violations of 18 U.S.C. §§ 1341 and 1342;

b. Multiple instances of mail fraud violation of 18 U.S.C. §§ 1341 and 1346;

c. Multiple instances of wire fraud violations of 18 U.S.C. §§ 1341 and 1346; and

d. Multiple instances of unlawful activity in violation of 18 U.S.C. § 1952.

253. Defendant's violations of the above federal laws and the effects thereof detailed above are continuing and will continue. Plaintiff and members of the Class have been injured in their property by reason of these violations in that Plaintiff and members of the Class have paid hundreds of millions of dollars for Avandia that they would not have paid had Defendant's not conspired to violate 18 U.S.C. § 1962(c).

254. Injuries suffered by Plaintiff and members of the Class were directly and proximately caused by Defendant's racketeering activity as described above.

255. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors,

including Plaintiff and the Class, directly relied on the racketeering activities of the Defendant and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the representations as to the efficacy and safety of Avandia as promoted by Defendant. Because Defendant controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendant's representations about Avandia. Further, Defendant perpetuated this reliance by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

256. By virtue of these violations of 18 U.S.C. § 1962(d), Defendant is liable to Plaintiff and the Class for three times the damages Plaintiff and the Class have sustained, plus the cost of this suit, including reasonable attorneys' fees.

257. By reason of the foregoing, and as a direct and proximate result of Defendant's fraudulent misrepresentations, Plaintiff and the Class have suffered damages. Plaintiff and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

258. By reason of the foregoing, Plaintiff and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts.

Appendix G

Third Cause of Action

Violations of the Pennsylvania Unfair Trade Practices and Consumer Protection Law ("UTPCPL"), 73 Pa.C.S.A. § 201-1 *et seq.*.

259. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

260. At all times material hereto, Defendant was a manufacturer, marketer, seller and/or distributor of Avandia within the meaning of the Pennsylvania Unfair Trade Practices and Consumer Protection Law ("UTPCPL"), 73 Pa.C.S.A. § 201-1 *et seq.*

261. At all times material hereto, the conduct described above and throughout this Complaint took place within the Commonwealth of Pennsylvania and constitutes unfair methods of competition or unfair or deceptive acts or practices in violation of § 201-2(4),(v),(vii) and (xxi) of UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

262. The UTPCPL applies to the claims of all the class members because the conduct which constitutes violations of the UTPCPL by Defendant occurred within the Commonwealth of Pennsylvania.

263. At all times relevant and material hereto, Defendant conducted trade and commerce within the meaning of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

264. Defendant's deceptive marketing scheme concerning Avandia violates the UTPCPL because, inter alia, Defendant:

a. knowingly concealed, suppressed, or omitted material information regarding Avandia's safety and effectiveness from Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such concealment, suppression, or omission;

b. knowingly misrepresented the safety and efficacy of Avandia to Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such misrepresentation; and

c. knowingly marketed, promoted, and advertised Avandia as a safe and effective drug when the purported safety and efficacy was deceptive and unfounded.

265. Defendant's unlawful conduct as described herein arose, was directed, and emanated from Defendant's headquarters to the detriment of Plaintiff and Class members.

266. Defendant's concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices has the tendency, capacity, and likelihood to deceive Plaintiff and the Class members.

267. Defendant intended, or consciously disregarded, that Plaintiff and the Class members relied on its concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices, so they would purchase Avandia.

268. Defendant's concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices caused Plaintiff and the Class members to suffer ascertainable losses in the amount of the monies they overpaid for Avandia, and/or pay for more Avandia prescriptions, without knowing the drugs' efficacy or lack thereof in treating the condition for which it was marketed, promoted, or advertised.

269. Defendant deceived and continues to deceive consumers. This conduct constitutes unfair or deceptive acts or practices within the meaning of the UTPCPL. This illegal conduct is continuing, with no indication that Defendant will cease.

270. Defendant's actions in connection with the advertising, marketing, selling and distribution of Avandia as set forth herein evidences a lack of good faith, honesty and observance of fair dealings so as to constitute unconscionable commercial practices, in violation of UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

271. Plaintiff and the Class members would not have overpaid and/or paid for as many Avandia prescriptions as they did had they known of Defendant's deceptive and misleading marketing scheme, or the extent of said scheme.

272. Plaintiff and the Class members are accordingly harmed by Defendant's conduct in violation of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

273. By reason of Defendant's violations of the UTPCPL described above, Plaintiff and the Class members are entitled to recover treble damages, including but not limited to a full refund of all purchase costs Plaintiff and Class members have incurred as a result of purchasing Avandia instead of other less expensive more effective antidiabetic drugs, plus attorney's fees and costs, along with equitable relief prayed for herein in this Complaint.

Fourth Cause of Action

Violations of State Consumer Protection and Unfair and Deceptive Acts or Practices Statutes

274. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

275. Defendant intended that Plaintiff, the Class and the medical and scientific community would rely on its materially deceptive practices and Plaintiff and the Class would purchase or pay for Avandia as a consequence of the deceptive practices, including Defendant's misleading and fraudulent marketing, and misrepresentations and omissions of material fact with respect to Avandia as set forth herein. Defendant's deceptive representations and material omissions to Plaintiff and the Class were and are unfair and deceptive acts and practices. Plaintiff and the

Class were deceived by Defendant's misrepresentations. As a proximate result of Defendant's misrepresentations, Plaintiff and the Class have suffered an ascertainable loss, in an amount to be determined at trial, in that they paid millions upon millions of dollars for Avandia that they would not have paid had Defendant not engaged in unfair and deceptive conduct.

276. By reason of the conduct as alleged herein, by making false and misleading statements about Avandia's safety and effectiveness through false and/or misleading advertising, representations and statements with the intent to induce or cause reliance, Defendant violated the laws prohibiting unfair and deceptive acts and practices of the states wherein Class members reside.

277. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of AS § 45.50.471, *et seq.*

278. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of ARIZ. REV. STAT. § 44-1522, *et seq.*

279. Defendant engaged in unfair competition unfair or deceptive acts or practices in violation of ARK. CODE § 4-88-l0l, *et seq.*

280. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of CAL BUS. & PROF. CODE § 17200, *et seq.*

281. Defendant engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of COLO. REV. STAT. § 6-1-105, *et seq.*

282. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of CONN. GEN. STAT. § 42-110b, *et seq.*

283. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of 6 DEL. CODE § 2511, *et seq.*

284. Defendant engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of D.C. CODE § 28-3901, *et seq.*

285. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of FLA. STAT. § 501.201, *et seq.*

286. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of GA. CODE ANN. § 10-1-392, *et seq.*

287. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of HAW. REV. STAT. § 480, *et seq.*

288. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation Of IDAHO CODE § 48-601, *et seq.*

289. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of 815 ILCS § 50511, *et seq.*

290. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of IND. CODE ANN. § 24-5-0.5.1, *et seq.*

291. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of Iowa Code § 714.1 b, *et seq.*

292. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of KAN. STAT. § 50-623, *et seq.*

293. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of Ky. REV. STAT. § 367.110, *et seq.*

294. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of LA. REV. STAT. § 51:1401, *et seq.*

295. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation MASS. GEN. L. CH. 93A, *et seq.*

296. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of MD. COM. LAW CODE § 13-101, *et seq.*

297. Defendant have engaged in unfair competition or unfair or deceptive acts or practices in violation of ME. REV. STAT. tit. 5, § 205-A, *et seq.*

298. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of MICH. STAT. § 445.901, *et seq.*

299. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of MINN. STAT. § 8.31, *et seq.*

300. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of MO. REV. STAT. § 407.010, *et seq.*

301. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of MONT. CODE § 30-14-101, *et seq.*

302. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of NEB. REV. STAT. § 59-1601, *et seq.*

303. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of NEV. REV. STAT. § 598.0903, *et seq.*

304. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.H. REV. STAT. § 358-A:1 *et seq.*

305. Defendant engaged in unfair competition or unfair, unconscionable or deceptive acts or practices in violation of N.J. REV. STAT. § 56:8-1, *et seq.*

306. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.M. STAT. § 57-12-1, *et seq.*

307. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.Y. GEN. BUS. LAW § 349, *et seq.*

308. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.C. GEN. STAT. § 75-1.1, *et seq.*

309. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.D. CENT. CODE § 51-15-01. *et seq.*

310. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of N.J.S.A. § 56:8-2, *et seq.*

311. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation Of OHlO REV. STAT. § 1345.01, *et seq.*

312. Defendant engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of OKLA. STAT. 15 § 751, *et seq.*

313. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of OR. REV. STAT. § 646.605, *et seq.*

314. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of R.I. GEN. LAWS. § 6-13.1-1, *et seq.*

315. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of S.C. CODE LAWS § 39-5-10, *et seq.*

316. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of S.D. CODE LAWS § 37-24-1, *et seq.*

317. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of TENN. CODE § 47-18-101, *et seq.*

318. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of TEX. BUS. & COM. CODE § 17.41, *et seq.*

319. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of UTAH CODE. § 13-11-1, *et seq.*

320. Defendant engaged in unfair competition or unfair deceptive acts or practices in violation of VT. STAT. ANN. TIT. 9 §2451, *et seq.*

321. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of VA. CODE § 59.1-196, *et seq.*

322. Defendant engaged in unfair competition or unfair, deceptive or fraudulent acts or practices in violation of WASH. REV. CODE. § 19.86.010, *et seq.*

323. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of W. VA. CODE § 46A-6-101, *et seq.*

324. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of WIS. STAT. § 100.18, *et seq.*

325. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of WYO. STAT. ANN. § 40-12-101, *et seq.*

326. As a direct and proximate result of Defendant's statutory violations, Plaintiff and Class paid for plan participants' prescriptions of Avandia, which proximately caused Plaintiff and the Class injury.

327. By reason of Defendant's violations, Plaintiff and the Class are entitled to recover treble damages where available, including but not limited to all monies expended to purchase Avandia, in excess of what they would have spent to purchase other safer, more effective, and cheaper antidiabetic drugs, plus attorney's fees and costs along with the equitable relief prayed for herein.

Appendix G

Fifth Cause of Action

Unjust Enrichment

328. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

329. Defendant has been and continue to be enriched by its fraudulent acts and omissions alleged herein in all states wherein class members reside.

330. In exchange for payments they made for Avandia and at the time these payments were made, Plaintiff and Class members expected that the drug was a safe and medically effective treatment for the condition, illness, disorder or symptoms for which it was prescribed.

331. Defendant voluntarily accepted and retained these payments with full knowledge and awareness that, as a result of its wrongdoing, Plaintiff and Class members paid for Avandia when they otherwise would not have done so and paid for the drug at a higher price than they would have paid but for Defendant's wrongful conduct.

332. These fraudulent acts and omissions allowed Defendant to gain billions of dollars in profits that would not have been gained but for Defendant's fraudulent acts and omissions

333. Plaintiff and Class members paid and continue to pay Defendant an amount that exceeds the value of the products identified herein as a result of Defendant's fraudulent acts and omissions.

334. Plaintiff and the Class members suffered damages due to Defendant's acts and omissions as alleged herein.

335. Defendant has and continue to be unjustly enriched as a result of its fraudulent acts and omissions.

336. Defendant lacks any legal justification for engaging in a course of fraudulent acts and omissions as alleged herein at Plaintiff's and the Class member's expense.

337. No other remedy at law can adequately compensate Plaintiff and Class members for the damages occasioned by Defendant's conscious choice to engage in a course of fraudulent acts and omissions.

338. Plaintiff and Class members are entitled in equity to seek restitution of Defendant's wrongful profits, revenues and benefits to the extent and in an amount, deemed appropriate by the Court and such other relief as the Court deems just and proper to remedy Defendant's unjust enrichment.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff and the Class members pray for relief as follows:

1. For an order certifying this matter as a class action as requested herein and a declaration that this action is a proper class action pursuant to Federal Rule of

Civil Procedure 23, establishing an appropriate class or classes and finding that the Plaintiff and its counsel are proper representatives of the class;

2. For an order appointing the undersigned counsel as Class Counsel;

3. On Plaintiff's and the Class' RICO claims, compensatory damages, and enhancement of damages Plaintiff and the Class have sustained as a result of Defendant's conduct as may be permitted under the relevant statutes, such amount to be determined at trial, plus Plaintiff's costs in this suit, including reasonable attorneys' fees;

4. On Plaintiff's and the Class' claims under the Pennsylvania Unfair Trade Practices and Consumer Protection Law 73 Pa.C.S.A. § 201-1 *et seq.*, three times the damages Plaintiff and the Class have sustained as a result of Defendant's conduct, such amount to be determined at trial, plus Plaintiff's costs in this suit, including attorneys' fees;

5. On Plaintiff's Class' Consumer Fraud Act claims, compensatory damages, and enhancement of damages Plaintiff and the Class have sustained as a result of Defendant's conduct as may be permitted under the relevant statutes, such amount to be determined at trial, plus Plaintiff's costs in this suit, including reasonable attorneys' fees;

6. On Plaintiff's and the Class' claim for unjust enrichment, recovery in the amount of Plaintiff's and the Class' payments for Avandia, such amount to be determined at trial, plus Plaintiff's costs in this suit, including reasonable attorneys' fees;

7. For an order otherwise requiring Defendant to refund and make restitution on all monies acquired from the sale of Avandia to Plaintiff and the Class;

8. For injunctive relief, enjoining Defendant from continuing their misleading, unbalanced, illegal and fraudulent promotion of Avandia;

9. Awarding Plaintiff and the Class prejudgment interest on all damages;

10. Awarding Plaintiff and the Class other appropriate equitable relief;

11. Awarding Plaintiff and the Class their costs and expenses in this litigation, including reasonable attorneys' fees and expert fees; and

12. Awarding Plaintiff and the Class such other and further relief as may be just and proper under the circumstances.

JURY DEMAND

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Plaintiff demands trial by jury on all issues so triable.

Appendix G

Dated: October 13, 2010

/s/_____

FINKELSTEIN THOMPSON LLP
Halley F. Ascher, Esq.
Tracy D. Rezvani, Esq.
Rosalee B. Connell, Esq.
1050 30th Street, N.W.
Washington, DC 20007
Tel: (202) 337-8000
Fax: (202) 337-8090

SIZEMORE TAYLOR LLP
James Paul Sizemore, Esq.
Meghan McCormick, Esq.
2101 Rosencrans Avenue Suite 5290
El Segundo, California 90245
Tel: (310) 322-8800
Fax: (251) 990-4371

On Behalf of the Plaintiff United Benefit Fund

APPENDIX H — FIRST AMENDED CLASS ACTION COMPLAINT, *ALLIED SERVICES DIVISION WELFARE FUND V. GLAXOSMITHKLINE*, UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED OCTOBER 12, 2010

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

MDL No. 1871
07-MD-01871-CMR

IN RE: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT APPLIES TO:

ALLIED SERVICES DIVISION WELFARE FUND,
on behalf of itself and all others similarly situated

Plaintiff,

vs.

SMITHKLINE BEECHAM CORPORATION
d/b/a GALAXOSMITHKLINE and
GLAXOSMITHKLINE, PLC

Defendants.

CIVIL ACTION NO: 09-730

SECOND AMENDED CLASS
ACTION COMPLAINT

Appendix H

DEMAND FOR JURY TRIAL

FIRST AMENDED CLASS ACTION COMPLAINT

Allied Services Division Welfare Fund ("ASD Fund") ("Plaintiff'), on behalf of itself and all others similarly situated, brings this action against Defendants GlaxoSmithKline PLC through its subsidiary, SmithKline Beecham Corporation d/b/a GlaxoSmithKline (collectively "GSK" or "Defendants"), seeking damages and other monetary relief. Plaintiff makes the allegations of this Complaint based upon personal knowledge as to matters relating to itself, and upon investigation of counsel and information and belief as to all other matters.

NATURE OF THE ACTION

1. This complaint stems from Defendants' scheme to market and promote Avandia® (rosiglitazone maleate), Avandamet® (a combination of rosiglitazone maleate and metformin) and Avandaryl® (a combination of rosiglitazone maleate and glimepiride), (collectively, "Avandia"), which are medications indicated to treat Type II diabetes mellitus. Defendants' marketing scheme has included deliberately concealing, suppressing and affirmatively misrepresenting the significant safety risks associated with the use of Avandia, including but not limited to, heart attack, heart failure, or other heart-disease related risks.

2. Defendants marketed and promoted Avandia as a safe and effective means of enabling the body to utilize naturally secreted insulin and to control blood sugar levels

in individuals with Type II diabetes mellitus. However, published findings from 1999—the year Avandia was approved by the FDA for sale in the U.S.—including a study from The New England Journal of Medicine, strongly indicated that studied groups of Avandia users incurred a 43 percent greater risk of heart attacks than those taking other competing diabetes medications, or diabetics taking no medications. Further, the researchers found that patients incurred a 64 percent increased risk of dying from heart attacks or heart-related diseases while taking Avandia.

3. At a congressional hearing held on Wednesday, June 6, 2007, Commissioner Andrew von Eschenbach of the U.S. Food and Drug Administration ("FDA") revealed that the FDA was ordering Defendants to add a "black box" warning to Avandia, strengthening existing warnings regarding the use of Avandia related to an increased risk of developing congestive heart failure ("CHF"), a condition in which the heart does not adequately pump blood. The FDA found that the warnings previously issued by Defendants, advising Avandia users to simply consult their doctors about the continuous use of Avandia, were inadequate to protect such users.

4. On July 30, 2007, two FDA advisory panels, the Endocrine and Metabolic Advisory Committee and the Drug Safety and Risk Management Advisory Committee, met to evaluate Avandia and similar antidiabetic drugs. The panels recognized the increased risk for heart attacks posed by Avandia and voted overwhelming, 20-3, urging the FDA to consider raising its warning level to black-box

status or implementing a patient registration program. On August 14, 2007, the FDA increased the warning for Avandia's increased risk of heart failure, and the following black box warning was added to the label:

> Thiazolidinesdiones, including rosiglitazone, cause or exacerbate congestive heart failure in some patients (see WARNINGS). After initiation of AVANDIA, and after dose increase, observe patient carefully for signs and symptoms of heart failure (including excessive, rapid weight gain, dyspnea, and/or edema). If these signs and symptoms develop, the heart failure should be managed according to current standards of care. Furthermore, discontinuation or dose reduction of AVANDIA must be considered.
>
> AVANDIA is not recommended in patients with symptomatic heart failure. Initiation of AVANDIA in patients with established NYHA Class III or IV heart failure is contraindicated. (See CONTRAINDICATIONS and WARNINGS.)

5. Thereafter, on November 19, 2007, the FDA added a second black box warning for Avandia's increased risk of heart attacks and other myocardial ischemic events, and the following language was added to the black box warning:

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WARNING: CONGESTIVE HEART FAILURE AND MYOCARDIAL ISCHEMIA

> A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared AVANDIA to placebo, showed AVANDIA to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction. Three other studies (mean duration 41 months; 14,067 patients), comparing AVANDIA to some other approved antidiabetic agents or placebo, have not confirmed or excluded this risk. In their entirety, the available data on the risk of myocardial ischemia are inconclusive.

6. In February 2010, the United States Senate Finance Committee released a report concluding, among other things, that:

> The totality of evidence suggests that GSK was aware of the possible cardiac risks associated with Avandia years before such evidence became public. Based on this knowledge, GSK had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner. Instead, GSK executives intimidated independent physicians, [and] focused on strategies to minimize findings that Avandia may increase cardiovascular risk...

Rather than issue proper warnings and provide accurate information about Avandia's risks and benefits, Defendants

chose instead to keep their deceptive propaganda and marketing machine running full steam ahead and never took any affirmative steps to correct the misinformation and deceptive advertising scheme that it had and continued to perpetrate, ensuring that it would continue to maximize the prescription and sale of Avandia so long as consumers, Third-Party Payors, prescribing doctors, and the medical and healthcare community remained unaware of Avandia's true risks.

7. Regarding the Senate Finance Committee report, GSK said that it "fails to present an accurate, balanced, or complete view of the currently available information on Avandia," The company also rejected "any allegations of concealing safety information or acting inappropriately on behalf of patients."

8. Defendants knew or should have known that Avandia was unsafe as compared to other diabetes medications. Moreover, Defendants knew or should have known that Plaintiff and the Class would be injured to the extent they must pay for Avandia and the health care services and facilities resulting from heart-related injuries associated with Avandia's use. As a result of Defendants' failure to adequately warn consumers, Third-Party Payors, prescribing doctors, and the medical and healthcare community that the use of Avandia creates a roughly 50% greater risk of heart attack and heart disease-related death, Plaintiff and the Class were denied the opportunity to make fully informed decisions about whether and how to include Avandia on their formularies and paid for more prescriptions than they otherwise would

have paid for and/or paid for Avandia that would have been sold at a lower price had market forces been allowed to operate unfettered by Defendants' violations.

9. In addition to the resulting personal injuries, unnecessary deaths, and the profound implications for public health, the financial toll that Defendants' false and deceptive marketing of Avandia has had on Plaintiff and the Class has been dramatic. Relying upon Defendants' promises of superior treatment and better cardiovascular outcomes compared with the older diabetes drugs, third-party payors of Avandia have paid a hefty premium. Defendants' omissions of, and deliberate misrepresentations related to, critical information regarding the serious health risks associated with Avandia have caused financial harm to Plaintiff and the Class, who hereby seek compensatory, punitive and statutory damages, injunctive relief to prevent Defendants from continuing their unlawful activities, reasonable attorneys' fees and such other just relief as the Court may award.

PARTIES

10. Plaintiff, Allied Services Division Welfare Fund, is a health and welfare benefit fund with its principal place of business at 53 West Seegers Road, Arlington Heights, Illinois 60005, and is involved in the business of providing health benefits for covered lives. Plaintiff Allied Services is a multi-employer employee welfare benefit plan, within the meaning of the Employee Retirement Income Security Act, 29 U.S.C. § 1001(2), and § 1002(37). Membership comes from different types of unions, many

in transportation services industry such as railroads, and airlines.

11. Allied Services contracts with Sav-Rx, Inc. to provide pharmacy benefit management services for the drug component of its health benefits plans. Allied Services paid or incurred costs for prescriptions of Avandia dispensed to covered lives in several states. These prescriptions would have been restricted or priced differently if the FDA, Plaintiff's PBM and/or [MISSING TEXT]

12. Defendant GlaxoSmithKline PLC ("GSK PLC") is a United Kingdom corporation with its principal place of business at 980 Great West Road, Brentford, London Middlesex TW8 9 GS, United Kingdom. GSK PLC either directly or through its wholly-owned subsidiaries, designs, produces, markets and promotes the drugs Avandia, Avandamet and Avandaryl in Pennsylvania and nationwide. Defendant GlaxoSmithKline USA is a wholly-owned subsidiary of GSK PLC. At all relevant times, GSK PLC acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting in the course and scope of their actual and apparent authority, agency, duties or employment.

13. Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline (GSK USA) is a Pennsylvania corporation with its principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania. GSK USA designs, produces, markets and promotes the drugs Avandia, Avandamet and Avandaryl in Pennsylvania

and nationwide. GSK USA is a whollyowned subsidiary of GSK PLC. At all relevant times, GSK USA acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting in the course and scope of their actual and apparent authority, agency, duties or employment.

14. Defendant, GSK USA along with defendant GSK PLC conducts substantial business in Philadelphia, Pennsylvania, including the sale and distribution of Avandia and has sufficient contacts with Pennsylvania or otherwise intentionally avails itself of the laws and markets of Pennsylvania, so as to sustain this Court's jurisdiction over Defendants.

JURISDICTION AND VENUE

15. This Court has subject matter jurisdiction pursuant to 28 U.S.C. § 1332 (d)(2), which provides federal district courts with original jurisdiction over civil actions in which the matter in controversy exceeds the sum or value of $5,000,000, exclusive of interest and costs, and is a class action in which "any member of a class of Plaintiffs is a citizen of a state different from any defendant."

16. This Court has further jurisdiction over this action pursuant to the Class Action Fairness Act, because at least one member of the Class is a citizen of a different state than the Defendants and the aggregate amount in controversy exceeds $5,000,000.00, exclusive of interest and costs.

17. Venue is proper in this District under 28 U.S.C. §1391 because Defendants engaged in substantial conduct relevant to Plaintiff's claims within this District, and have caused harm to Plaintiff and Class members residing within this District. Defendants received substantial compensation from the sales of Avandia in this District, and Defendants made misrepresentations and material omissions about Avandia in this District.

FACTUAL ALLEGATIONS

I. Avandia's Factual Background

18. Type 2 diabetes, the most common form of diabetes, results from the body's failure to produce enough insulin (insulin deficiency) and/or inability to use insulin properly (insulin resistance). Insulin is necessary to process and remove blood sugar. Without insulin, sugar builds up in the bloodstream and cells are starved for energy. This can cause tissue breakdown, which can lead to numerous health dangers, such as kidney failure, blindness, and amputations. Furthermore, diabetics are at an increased risk, as compared to non-diabetics, for atherosclerosis, heart attacks, strokes, kidney disease, and nervous system damage. Thus, drugs designed to treat diabetes must be sensitive to, among other things, diabetics' preexisting cardiovascular risks.

19. Weight loss has a dramatic effect on diabetes management. As little as 5% loss of body weight results in a disproportionate decrease in insulin resistance and improved glycemic control. Sustained weight loss often

results in a marked improvement or even a cure for Type II diabetes and is, therefore, the most important first line therapy for the disease. Therefore, virtually all physicians treating Type II diabetes concur that weight maintenance is a critical piece of the treatment puzzle. Any benefit derived from other diabetic treatments, such as drugs like insulin, Avandia and metformin, must be weighed against the risks and possible side effects of such treatments, including such treatments' association with weight gain.

20. Exercise also has therapeutic effects on Type II diabetes. Exercise lowers insulin resistance and improves glycemic control. Studies have shown that walking as little as 150 minutes a week lowers insulin resistance.

21. In the 1990s, pharmaceutical companies developed, manufactured and produced a class of drugs known as thiazolidinediones (TZDs). TZDs enable the body to more effectively use insulin by reducing insulin resistance in the body.

22. Prior to TZDs, the "first line" of drug treatment for Type 2 diabetes consisted of established and inexpensive oral medications, primarily sulfonylureas and metformin. Indeed, metformin is recognized as the "gold standard" in Type 2 diabetes treatment. In its "Standards of Medical Care in Diabetes 2009," the American Diabetes Association noted that the consensus for treating Type 2 diabetes begins with "intervention at the time of diagnosis with metformin in combination with lifestyle changes and continuing timely augmentation of therapy with [MISSING TEXT]

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23. The other principal drug treatment available before the introduction of TZDs was injected insulin.

24. Metformin works principally by limiting the production of sugar in the liver; it has no effect on insulin release. Prior to TZDs, metformin was the oral antidiabetic drug of choice in patients with Type II diabetes, except those who were thin and elderly. Metformin was associated in patients with renal complications with an enhanced risk of lactic acidosis, a potentially fatal condition. However, that condition was easily avoided and exceedingly rare; there were zero cases of lactic acidosis observed in the more than 6,000 patients participating in the clinical trials for the metformin drug Glucophage. Further, a published review of the risks of metformin shows that there were no deaths from lactic acidosis in metformin patients for whom the drug was indicated. Patients treated with metformin, unlike those treated with sulfonylureas, do not exhibit weight gain, a significant advantage for Type II diabetes sufferers. Rather, metformin promotes weight loss in persons with Type II diabetes. Its other side effects include nausea and upset stomach.

25. The sulfonylureas work on the insulin-producing cells to increase the release (but not the production) of insulin. Sulfonylureas were used as first line agents, particularly in thin or elderly patients. Sulfonylureas have been associated in rare instances with low blood sugar and often promote weight gain. The benefits of sulfonylurea therapy are shown to decrease over time as approximately 50% of patients will need additional treatments after 2-5 years of taking these drugs. Sulfonylureas combine well

with other diabetes drugs for maximum effect on blood sugar.

26. As a diabetic's disease progresses, medications may be added to the patient's regimen, including the use of insulin.

27. At all times material hereto, the TZD preparations available in the marketplace included Avandia (rosiglitazone), Avadamet (rosiglitazone and metformin), Avandaryl (rosiglitazone and glimepiride), Actos® (pioglitazone) and Actosplus® met (pioglitazone and metformin).

28. Avandia was approved by the FDA on May 25, 1999 as an oral antidiabetic agent which acts primarily by increasing insulin sensitivity. Avandia is recommended and prescribed for the management of Type II diabetes mellitus, also non-insulin-dependent diabetes mellitus ("NIDDM") or adult-onset diabetes. Type II diabetes is a serious and life threatening disease that affects about 18 to 20 million Americans. Avandia has been used by millions of individuals in the United States.

29. On April 23, 1999, just prior to the launch of Avandia in the U.S. market, Defendants issued a press release stating that they had entered into a co-promotion agreement with Bristol-Myers Squibb, the maker of Glucophage brand of metformin, to jointly promote Avandia in the U.S. It also stated that Defendants "recently entered into a co-promotion deal for Avandia with [Bristol-Myers Squibb], and this relationship will

drive the acceptance of the drug in the USA, according to [Defendants], which forecasted Avandia sales to reach $2 billion in 2003." Avandia remains key to [Defendants'] near-term fortunes given that it accounts for 44% of incremental pharma sales growth" between 1998 and 2005.

30. Avandamet was approved by the FDA on October 10, 2002 as a combination of Avandia and metformin in one single pill and is also recommended to treat NIDDM.

31. Avandaryl was approved by the FDA on November 23, 2005 as a combination of Avandia and glimepiride in one single pill and also recommended to treat NIDDM.

32. Since 1999, the FDA has been monitoring several heart-related adverse events (e.g. fluid retention, edema, and congestive heart failure ("CHF")) based on signals seen in controlled clinical trials and from post-marketing reports.

33. Despite the fact that Avandia lowers blood glucose levels in Type II diabetes patients, numerous studies have shown that use of Avandia dramatically increases the risk of cardiovascular events in Type II diabetes patients. Nevertheless, Defendants assured physicians that these studies only illustrate a very slight increase in Low-density lipoprotein, "bad cholesterol" or LDL levels, and continued to falsely and fraudulently promote Avandia as a superior, effective, and safe drug for diabetic patients.

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34. In 2001, the FDA requested that Defendants make a change to Avandia's prescribing label to warn doctors that the drug could cause fluid retention. Around the same time, Defendants were drafting an article, later published in the American Heart Association's journal *Circulation* by Dr. Steven Haffner of the University of Texas Health Science Center at San Antonio, that argued that the class of drugs that includes Avandia could significantly *reduce* cardiovascular risk factors in animals. Shortly after the FDA request, Defendants' sales representatives gave oral presentations at a medical convention denying the existence of serious risks associated with Avandia. The FDA responded with a letter to Defendants warning that the sales representatives and marketers should stop denying or minimizing the risks of heart attacks and heart-related diseases in patients.

35. In 2005, according to a June 1, 2007 *Bloomberg* article, Defendants performed an internal review and found that Avandia raised the risk of heart attacks by 31 percent.

36. In April 2006, the FDA required labeling for Avandia to be updated to include new data in the WARNINGS section about a potential increased incidence of heart attack and heart-related chest pain in some patients. This change was based on the results of a controlled clinical trial in patients with existing CHF. A higher number of heart attacks or angina was observed in patients treated with Avandia compared to those treated with a placebo.

37. On May 9, 2006, Defendants provided the results of its internal analyses to the FDA. The FDA didn't immediately release those studies to the public, because its officials "didn't necessarily agree with some of the methodology used," according to Dr. Janet Woodcock, head of the FDA Center for Drug Evaluation and Research.

38. Although Defendants gave the information to the FDA and included the information on its website amid more than 2,000 studies, Defendants did not highlight the information. Defendants stated that the heart-risk studies, including Defendants' own, were flawed and they are not obligated, or legally required, to highlight every study done on its drugs. Defendant GSK PLC Chief Executive Officer Jean-Pierre Garnier told reporters at the company's annual meeting on May 23, 2007 in London, "Why would you publicize it...We don't publicize every submission we make to the Food and Drug Administration."

39. It was seven years after the drug was approved, and the dangers of Avandia had still not been made sufficiently clear to the public. The FDA was sitting on the new analyses, and GSK, the FDA discovered during an investigation by its inspections unit in the fall of 2007, had failed to report clinical data and other material from 15 tests of Avandia by the end of 2006, according to a March 25, 2008, warning letter to the company. With Defendants and the FDA maintaining exclusive control over the full database of information on Avandia's effectiveness and safety, there was little that independent scientists and physicians could do to assuage their growing concerns about the drug.

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40. In April, 2007, using published literature, the FDA website and a clinical trials registry maintained by Defendants, Cleveland Clinic cardiologist, Steven E. Nissen, M.D., and Kathy Wolski, M.P.H. tabulated and compiled a meta-analysis of Avandia clinical studies with a duration of longer than 24 weeks, using randomized control groups not receiving Avandia, and having available the outcome data for myocardial infarction and death from heart attacks and heart-related diseases. Dr. Nissen and Dr. Wolski used 116 potentially relevant studies, and 42 trials that met the inclusion criteria. The study, published in The New England Journal of Medicine, revealed that Avandia was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from heart attacks and heart-related diseases that had borderline significance. Some have hinted that Dr. Nissen's loyalties were to Defendants' competitors since Dr. Nissen is leading a clinical trial studying Avandia's rival drug, Actos. However, Dr. Nissen has consulted in the past for Defendants on other matters. Moreover, Dr. Nissen gives drug-industry payments to charity. Nevertheless, instead of a responsible and reasoned response to this study, Defendants took steps to encourage aggressive dispensation of Avandia for persons to whom it posed grave health dangers.

41. By chance, the New England Journal of Medicine had chosen as a prepublication reviewer of the Nissen article Dr. Haffner, the University of Texas doctor who was the lead author on the 2001 *Circulation* paper that had suggested that Avandia's class of drug could decrease cardiovascular risk. Dr. Haffner faxed a copy of the draft article to Defendants.

42. Having obtained a leaked copy of the Nissen paper, Defendants prepared for its release in advance, and subsequent to its publication, Defendants engaged in a massive publication and advertising campaign designed to sway physician and consumer confidence. This marketing campaign consisted of advertisements, promotional literature for the offices of doctors and other health care providers, and other promotional materials to be provided to potential users of Avandia. Despite knowledge of the widespread health dangers of Avandia, Defendants failed to effectively warn consumers about the use of this drug as compared to other diabetes medications which posed much lesser health risks.

43. On May 21, 2007, the FDA issued a new safety alert that addressed potential safety issues stemming from the pooled analysis of previously completely controlled clinical trials demonstrating a significant increase in the risk of heart attack and heart-related diseases in patients treated with Avandia.

44. On May 23, 2007, consistent with recommendations made by senior FDA staff at an internal regulatory briefing held in April 2007, the FDA issued letters to Defendants requesting that Avandia's product labeling include a boxed warning to more prominently address the risks of heart failure associated with the use of Avandia.

45. On and around June 5, 2007, Defendants took out full-page ads in newspapers such as the *Washington Post* and *The New York Times* speaking directly to the consumers of Avandia.

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46. On June 6, 2007, the FDA announced a meeting to be held on July 30, 2007 to discuss the risk of heart attacks and heart-related disease associated with thiazolidinediones, with a focus on Avandia, as presented by the FDA and Defendants.

47. On July 30, 2007, two FDA advisory panels, the Endocrine and Metabolic Advisory Committee and the Drug Safety and Risk Management Advisory Committee, met to evaluate Avandia and similar antidiabetic drugs. The panels recognized the increased risk for heart attacks posed by Avandia and voted overwhelming, 20-3, urging the FDA to consider raising its warning level to black-box status or implementing a patient registration program.

48. On August 14, 2007, the FDA increased the warning for Avandia's increased risk of heart failure to a black box warning.

49. Despite such overwhelming evidence, Defendants still insisted and insist to this day that Avandia does not increase the risk of heart attack. "We don't believe that a warning about heart attack should be on the label," states Dr. Andy Zambanini, the company's director of clinical development.

50. Notwithstanding Defendants' refusal to acknowledge the dangers of Avandia, on November 14, 2007, the FDA issued its toughest warning against Avandia linking it to heart attacks and a second black box warning was added to the Avandia label warning of the increased risk of heart attacks and other myocardial ischemic events.

51. On July 13-14, 2010 an FDA advisory panel again reviewed scientific data and information on the safety and efficacy of Avandia and, for a second time, raised safety questions about Avandia. However, unlike in its first review, the panel did not issue a clear recommendation to the FDA about what it should do as a result of the findings. The 33-member panel voted 18-6, with some abstentions, that there are "significant safety concerns" that Avandia raises the risk of heart attack and chest pain. The panel also voted 21-3 that Avandia's risk was higher than that of Actos. 12 panel members recommended that Avandia be taken off the market. Ten others said its black-box warning should be enhanced and additional restrictions added to its use, which could include requiring special physician and patient education on the medication. Seven voted for the warning merely to be enhanced, without restrictions on its prescription. Three said it should be sold with warnings unchanged. One member abstained.

52. According to a Wall Street Journal article, endocrinologist Dr. David Capuzzi of Philadelphia, one of the three panelists who recommended that Defendants be allowed to continue marketing Avandia with no further restrictions or warnings is a paid speaker for the drug company, reportedly having been paid $14,750 to promote Defendants' drug Lovaza.

53. The panel also recommended that GSK continue the Thiazolidinedione Intervention With Vitamin D Evaluation, or TIDE, trial, which compares Avandia and Actos. However, on July 21, the FDA announced that the TIDE trial had been placed on partial clinical hold,

meaning no new patients can be enrolled until the agency gives further notice.

54. In addition, a study posted online June 28, 2010 in JAMA found that compared to Actos, Avandia was associated with an increased risk of stroke, heart failure, and all-cause mortality in patients age 65 and older. GSK rejected these conclusions and still maintains that Avandia is safe.

55. However, in the summer of 2010, Defendants agreed to settle approximately over 10,000 Avandia personal injury lawsuits filed by plaintiffs alleging they suffered personal injury and/or wrongful death due to taking Avandia for over $500 million.

56. On September 23, 2010, in response to the evidence that Avandia increased the risk of adverse cardiovascular events in patients treated with Avandia, announced that it will significantly restrict the use of Avandia to patients with Type 2 diabetes who cannot control their diabetes on other medications.

57. The FDA will require that GSK develop a restricted access program for Avandia under a risk evaluation and mitigation strategy, or REMS. Under the REMS, Avandia will be available to new patients only if they are unable to achieve glucose control on other medications and are unable to take Actos (pioglitazone), the only other drug in this class. Current users of Avandia who are benefiting from the drug will be able to continue using the medication if they choose to do so. Doctors will have to attest to and

document their patients' eligibility; patients will have to review statements describing the cardiovascular safety concerns associated with this drug and acknowledge they understand the risks.

58. GSK is required to develop the REMS program, which must include the following:

a. Provision of complete risk information to all patients and documentation in their medical records that the information was received and understood.

b. Documentation from healthcare providers that all patients receiving rosiglitazone are a) currently taking the drug, or b) not taking the drug and unable to achieve glycemic control with other medications, and decide in consultation with their healthcare providers not to take pioglitazone (Actos, Takeda) for medical reasons.

c. Documentation from healthcare providers that the risk information has been shared with all patients.

d. Physician, patient, and pharmacist enrollment in the REMS program.

59. The agency anticipates that the REMS will significantly limit the use of Avandia.

60. In addition, the agency halted the TIDE clinical trial and rescinded all of the regulatory deadlines for its completion.

61. The FDA also ordered GSK to convene an independent group of scientists to review key aspects of the RECORD clinical trial.

62. The FDA reserved the right to take additional actions after the independent re-analysis of RECORD is completed.

63. Simultaneously, the European Medicines Agency (EMA) suspended marketing authorization for all rosiglitazone-containing medicines (Avandia, Avandamet, and Avaglim). In addition, European physicians are being advised to transition all affected patients to alternative treatment options. According the a GSK press release, the EMA stated that the suspension will remain in place unless convincing data are provided that identify a group of patients in whom the benefits of the medicine outweigh its risks.

64. Since its introduction, Avandia has come to be used on a regular basis by millions of individuals worldwide, including at least one million in the United States. Avandia was Defendants' second best-selling product in 2006, generating revenues of $1.4 billion, with a further $246 million generated from the combination products Avandamet and Avandaryl. A one-month supply of Avandia sells for between $90 and $170. Consumers either paid for the drug completely out of pocket or paid their co-pay. The

typical third-party payor co-payment was approximately $135-$140. This represented a dramatic increase in third-party payors' costs of drug therapy for Type II diabetes patients. Previously, the most prevalent oral drug therapy for Type II diabetes had been metformin, which had a typical retail price for a one-month prescription of approximately $45-$55, of which the typical third-party payor co-payment was approximately $40-$50.

II. Approval, Labeling, and Promotion of Pharmaceuticals Marketed in the United States

65. Pursuant to the Federal Food, Drug and Cosmetic Act ("FDCA"), a pharmaceutical must be approved by the Food and Drug Administration ("FDA") before it is transported or distributed across state lines. *See* 21 C.F.R. § 301; *see also* 21 U.S.C. § 331. The Center for Drug Evaluation and Research is a division of the FDA and conducts limited research in the areas of drug quality, safety, and effectiveness.

66. In order for the FDA to approve a drug, the manufacturer must show that a drug is "safe for use" and effective for all "conditions prescribed, recommended, or suggested" on a drug's label. *See* 21 C.F.R. § 99.103; *see also* 21 C.F.R. §201.5.

67. Because the FDA will only find a drug product to be safe and effective if the proposed use is supported by well-designed, placebo-controlled clinical trials that establish a causal relationship to a statistically significant degree, a statement that a drug is "effective" or "works"

or "has been proven to ..." is understood to mean that well controlled clinical studies support the use. To make such a statement without such clinical trial proof is misleading. Further, failure to inform physicians that no placebo controlled clinical trials support a representation of drug efficacy is a violation of a pharmaceutical company's obligation to disclose. *See* 21 C.F.R. § 99.205.

68. The FDA allows pharmaceutical manufacturers to provide information for dissemination to health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, and Federal and State government agencies after a submission of an application to the FDA, if such information is fair and balanced and under the following circumstances:

- The information concerns a drug that has been approved, licensed and cleared for marketing by the FDA;

- The information is in the form of an unabridged copy of a peer-reviewed scientific or medical journal article or reprint, or an unabridged reference publication that pertains to a clinical investigation involving the drug and that is considered scientifically sound by experts who are qualified to evaluate the product's safety or effectiveness;

- The information does not pose a significant risk to the public health;

- The information is not false or misleading; and

- The information is not derived from clinical research conducted by another manufacturer, unless permission is received from that manufacturer. *See* 21 C.F.R. § 201.6(a). *See also* 21 U.S.C. § 360aaa.

III. Alternatives to Avandia

69. Physicians are free to prescribe FDA-approved drugs as they see fit to treat any condition or symptom for their patients. The medical community generally encourages physicians to prescribe the safest, most effective and cost-efficient treatment for their patients. Research and studies have illustrated that physicians can prescribe safer and/or equally effective alternatives to treat diabetes other than Avandia.

70. Another prescription medication for Type II diabetes mellitus is pioglitazone (Actos®), a drug manufactured and promoted by Takeda Pharmaceuticals North America.

71. On March 15, 2000, Dr. John B. Buse of the University of North Carolina School of Medicine, the incoming president of the American Diabetes Association, wrote Dr. Jane Henney, the Commissioner at the FDA stating that "the frequency of mild and serious adverse events that I have seen with troglitazone [Rezulin®] and pioglitazone [Actos®] is comparable to or less than the number I have observed with other antidiabetic agents." Rezulin was withdrawn from the U.S. market on March

21, 2000. Dr. Buse strongly suggested that Actos is one of the most effective, safe and beneficial drugs in its class and Avandia may be associated with less beneficial cardiac effects or even adverse cardiac outcomes.

72. A prospective, randomized trial of cardiovascular outcomes, called Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROACTIVE) shows lower cardiac risks with Actos. The trial examines whether the observed risks of Avandia represent a "class effect" of thiazolidinediones. Actos was studied, and the primary end point, a broad composite that included coronary and peripheral vascular events, showed a beneficial trend with the use of Actos (hazard ratio, 0.90; P=0.095). A secondary end point consisting of myocardial infarction, stroke, and death from any cause showed a significant effect favoring Actos (hazard ratio, 0.84; P=0.027). Notably, Actos appears to have more favorable effects on lipids, particularly triglycerides, than does Avandia.

73. Additionally, a June 23, 2007 *Bloomberg* article discusses a study that found that Actos may lower the risk of heart attack and death by 44 percent in diabetic patients with kidney disease. The findings, from a subgroup of patients enrolled in a previous study, were reported at the June 23, 2007 meeting of the America Diabetes Association in Chicago. In a separate study, Actos reduced inflammation and blood clots more than a placebo. Thus, Actos may have fewer cardiac risks than Avandia and prove to be a safer alternative to Avandia for the treatment of Type II diabetes mellitus.

74. However, physicians have been misled by Defendants to believe that Avandia is superior in its effectiveness and safety to other equally effective and safer alternatives like Actos. As a result of Defendants widespread misleading marketing and promotion of Avandia's superior safety and effectiveness over safer and equally effective alternative drugs like Actos, many physicians are less inclined to prescribe patients these alternatives antidiabetic drugs.

75. Yet a June 18, 2007 *USA Today* article discusses an increased number of physicians discontinuing Avandia prescriptions and are instead prescribing Actos as an alternative to the diabetes medication. "Before the journal [*The New England Journal of Medicine*] posted the study May 21, U.S. doctors were writing about 240,000 prescriptions [of Avandia] per week, Glaxo spokeswoman Alice Hunt says. That has dropped to about 215,000 to 220,000 per week. Glaxo estimates the number of people taking Avandia have dropped from about 1 million to 900,000 in the USA." Additionally, new prescriptions for Avandia dropped 40% as a result of Dr. Nissen's study. New prescriptions are defined as the first prescription a doctor writes for a patient who might already have been taking Avandia under a different doctor's care. "Prior to Nissen's study, U.S. doctors wrote about 80,000 new Avandia prescriptions weekly; that number has dropped to about 55,000, Hunt says." The *USA Today* article explains that physicians are switching patients to Actos as an alternative.

76. Another study conducted by researchers at Harvard University and published in February 2010 in the journal of the American Diabetes Association, Diabetes Care, found that Avandia increases a diabetic's heart attack risk by 30% compared with the older diabetes drug sulfonylurea. And when compared with metformin, Avandia increases a diabetics' heart attack risk by 120%.

IV. Defendants' Marketing and Promotion of Avandia as Safe and Effective

77. From its product launch to the present, Defendants engaged in widespread fraudulent statements and conduct, and pervasive false and misleading marketing, advertising and promotion of Avandia, spending hundreds of millions of dollars to further these efforts. Defendants deceived physicians, consumers and others in the medical community regarding the comparative efficacy of Avandia to other medications designed to control Type II diabetes mellitus. Defendants failed to warn — and affirmatively misled physicians, consumers, Third-party Payors, and others in the medical community regarding Avandia's association with increased risk of heart attacks and heart-related diseases.

78. Defendants were required to provide fair and balanced information whenever they engaged in promotional activities. Promotional activities encompass not only written material but all presentations. Defendants knew that whenever they were required to provide fair and balanced information, they were required to provide any negative information as well as positive information about their drug.

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79. Since 1999 Defendants have spent millions on Direct-to-Consumer ("DTC") print and television advertising, aimed at convincing patients to request Avandia from their doctors. Defendant's marketing campaign also targeted doctors as well as the individuals and groups responsible for selecting the drugs covered by health coverage plans and included on pharmacy formularies. Defendants sought to influence these targets through, among other tactics, print media, misleading promotional materials, lavish company-sponsored dinners, and "conferences" at posh resorts. Defendants produced and distributed "studies" whose sole purpose was to advance the company's marketing message and which were intended to, and did, deceive diabetics, medical professionals, and the general public. Defendants also employed sales representatives who spread the Avandia message by calling on thousands of physicians throughout the country, paid speakers to likewise deliver the company's messages about the drug, and writers who engaged in the "ghostwriting" of medical and scientific articles in order to advance the Avandia agenda. "Ghostwriting" is a particularly insidious practice where a drug company authors a purportedly independent scientific paper and then pays someone else to place their name on the paper to give the appearance of independence and objectivity by suggesting that the independent person or group, and not the drug company, performed the research and authored the paper.

80. Defendant's Avandia message had two key components. First, Defendants propagated the message that Avandia was better at lowering blood sugar than other established drugs. That is, Avandia had superior efficacy.

Defendants also represented that patients could stay on Avandia longer than the older drugs. Second, Defendants represented that, unlike the older diabetes drugs, Avandia had the additional benefit of actually lowering diabetics' cardiovascular risks. The notion that Avandia would actually lower diabetics' cardiovascular risk was critical to Avandia's marketing. Defendants needed justification for the steep price difference between Avandia and the older established diabetes drugs. Defendants, however, knew or should have known that these representations were false, misleading, and likely to deceive. At best, Defendants had no data to support these claims. At worst, they were wholesale fabrications.

81. In today's health care market, physicians face extreme time constraints in determining which drugs and treatments are best. Physicians, along with formulary committees, purchasers, Pharmacy Benefit Managers ("PBMs") and policy makers rely upon a variety of trusted sources including independent studies for such information. However, often unbeknownst to the public, many of these sources are directly controlled or heavily influenced by pharmaceutical manufacturers such as Defendants. All of these sources contain susceptibilities that have been exploited by pharmaceutical manufacturers such as Defendants.

82. Among the tactics employed by Defendants were plans to create studies designed to illustrate Avandia's superior profile to both (a) placebo and (b) comparable medications designed to control Type II diabetes mellitus while providing funding to engage "key opinion" and "thought" leaders in publication worthy trials.

83. Upon information and belief, this scheme was carried out by: making false statements to consumers, Third-party Payors, physicians and pharmacies concerning the efficacy and safety of Avandia; training Defendants' employees in methods to conceal negative information regarding Avandia to avoid detection of their activities by Plaintiff and the Class, and instructing Defendants' employees to conceal negative information regarding Avandia to avoid detection of their activities by Plaintiff and the Class.

Incentives to Develop Deceptive Medical Literature

84. Upon information and belief, Defendants sought out, and provided incentives and funding to, doctors and researchers to develop deceptive and misleading medical literature for use in marketing.

85. A June 5, 2007 *The Bulletin* article reveals that Dr. Anne E. Peters, a diabetes expert who runs a clinic for Los Angeles County and who is affiliated with the University of Southern California medical school had previously received money from Defendants as a speaker on behalf of Avandia. Dr. Peters resigned from that position when she enumerated her concerns about Avandia's risks. Dr. Peters said that five years ago, she removed Avandia from the formulary (the list of preferred drugs) maintained by the Los Angeles Clinic. That meant that patients would receive Actos instead of Avandia. "The Avandia people, it was just so surprising, they asked me what I wanted to keep Avandia on the formulary." "Dr. Peters said that she asked the company to establish a database at the clinic that

would track the outcomes of patients on both drugs. When she asked for the database, which would have cost several thousand dollars, she said a company representative replied: 'That's all you want? Other doctors ask to go to the Caribbean.'" Dr. Peters said, "They wanted to do everything but approve my request."

86. Despite being on notice of the potential for deadly heart attacks and heart related diseases, Defendants each opted for the bare minima of well-tailored clinical trials, of limited duration, such that little to no side effects were likely to be revealed. Thus, instead of conducting true scientific research in good faith to legitimately test the efficacy and safety of Avandia, Defendants focused on creating narrowly tailored studies specifically designed to enhance commercial value.

Physician Intimidation of Dr. Buse

87. A June 7, 2007 *Washington Post* article discusses Dr. Buse, who told a congressional hearing that in 1999, officials at SmithKline Beecham (a former pharmaceutical company that merged with GlaxoWellcome in 2000 to form GlaxoSmithKline PLC) began pressuring Dr. Buse after he questioned whether Avandia caused heart problems. In or around 1999, Dr. Buse was a presenter at a continuing medical education symposium sponsored by Eli Lilly and Company at which Dr. Buse was asked to discuss new therapies in diabetes. At the symposium, Dr. Buse presented slides stating that Avandia increased the risk of heart-related activities by 50 percent.

88. Thereafter in 1999, Dr. Buse wrote a letter to Tadataka Yamada, MD, the Chairman of Research and Development of Pharmaceuticals at SmithKline Beecham. In the 1999 letter, as the Associate Professor of Medicine and Director of the University of North Carolina Diabetes Care Center, Dr. Buse wrote that he reviewed every paper published and available on diabetic class medications on humans, and identified that Avandia has the potential to increase heart attacks and heart-related diseases, where the increase in heart-related deaths are the "relevant endpoints to be examined in the clinical trial program if one were to look for those kinds of changes in endothelial function." "I strongly believe that the rosiglitazone data set supports this kind of clinical decision making. I believe that caution is required until additional data are available."

89. Shortly after Avandia's FDA approval, Defendants took action against Dr. Buse. In a June 1999 e-mail mail, Dr. Tachi Yamada, Defendant's head of research at the time, wrote to colleagues at the company:

> I plan to speak to Fred Sparling, [Dr. Buse's] former [department] chairman[,] as soon as possible. I think there are two courses of action. One is to sue [Dr. Buse] for knowingly defaming our product ... the other is to launch a well planned offensive on behalf of Avandia ....

Additionally, Defendants prepared and sent a letter to Dr. Buse, to be signed by him, "retracting" his statements about Avandia's increased cardiovascular risk.

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90. In Dr. Buse's June 6, 2007 published statement to the U.S. House of Representatives Committee on Oversight and Government Reform, Dr. Buse recounts that after writing the 1999 letter to Defendants, Defendants called Dr. Buse numerous times emphasizing that there were some in the company who believed that Dr. Buse's actions were scurrilous enough to attempt to hold Dr. Buse liable for a $4 billion loss in market capitalization.

91. As promised, Dr. Yamada called Dr. Sparling at the University of North Carolina. Shortly thereafter and in response to GSK's pressure, Dr. Buse wrote to Dr. Yamada, "clarifying" his position on Avandia. In his letter, Dr. Buse stated that he continued to "believe as a clinical scientist that the null hypothesis should be that [Avandia] has the potential to increase cardiovascular events." Despite this belief, Dr. Buse stated that he had learned of "implied threats of lawsuits from my chairman [Dr. Sparling] and James Huang," who was then a product manager with a GSK, and, succumbing to the threat of legal action, Dr. Buse asked GSK to "call off the dogs." Under pressure, he signed the so-called "retraction letter," which had been authored for his signature by GSK officials.

92. The concealment of Dr. Buse's assessment regarding the dangers of Avandia was encouraged by Defendants, and Defendants continued to overplay favorably misleading articles regarding Avandia's side effects.

93. On March 15, 2000, Dr. Buse followed up his apprehension towards Avandia use by writing Dr. Jane Henney, the Commissioner at the FDA, regarding his concern "about the safety of rosiglitazone in light of its consistent negative impact on lipids documented in the FDA registration data as well as a worrisome trend in cardiovascular deaths and severe adverse events in the subjects exposed to rosiglitazone versus active comparators."

94. In the 2000 letter to the FDA, Dr. Buse suggested that the FDA act forcefully to prevent the rampant abuse of clinical trial data by Defendants. Dr. Buse had knowledge that:

a. Defendants overstated the safety of the drug with respect to heart attacks and heart-related diseases, and that Defendants claimed that Avandia had been uniquely studied on patients with preexisting heart disease, but in fact these patients were excluded in clinical trials as Dr. Buse was the principle investigator in one of their trials;

b. Defendants show misleading materials for professional education touting the lipid lowering effects of Avandia when the data are from a small subset of patients with triglycerides over 400 mg/dl. "The overwhelming preponderance of data suggests that at high doses the drug is most likely to increase triglycerides than lower them;" and

c. Defendants' representatives "detailed" primary care doctors on the safety and efficacy of the antidiabetic medications to suggest that Avandia's "safety and clinical efficacy is greater when there is no comparative data available."

95. In Dr. Buse's letter to the FDA, he states that "there is something pervasive and systematic that I detect in my travels regarding the marketing of rosiglitazone [Avandia]. I have to admit that now when I give CME [continuing medical education] lectures, I spend about half my time discussing these issues. It seems to me that blatant selective manipulation of data has obfuscated relatively straightforward conclusions evident from the FDA data sets."

96. Defendants knew that the dissemination of information about Avandia's true cardiovascular risks would devastate its efforts to promote the drug. When doctors like Dr. Buse raised suspicion about Avandia's safety, Defendants set out to intimidate and silence them. Such was the official finding of the United States Senate's Finance Committee, which concluded in January, 2010 that Defendants had executed "an orchestrated plan to stifle the opinion" of Dr. Buse, and that the intimidation scheme involved "executives at the highest level of Defendants, including then and current CEO Jean-Pierre Gamier."

Dr. Nissen's May 2007 NEJM Article Jolts Defendant's Fraud into High Gear

97. In a December 2007 floor speech, Senator Grassley revealed that Dr. Steve Haffner, a professor of medicine

at the University of Texas Health Sciences Center, San Antonio, and a consultant for Defendants, leaked to Defendants the draft of a study critical of Avandia that was to appear in the New England Journal of Medicine (NEJM). Dr. Haffner was entrusted with a confidential copy of the manuscript draft because he was peer-reviewing the study for the NEJM.

98. The study's lead author, Dr. Steven Nissen, professor of cardiology at the Cleveland Clinic, found that Avandia was associated with a 43-percent increased risk of heart attacks, one of the main health outcomes physicians hoped to avoid by treating diabetic patients with medication. According to documents produced by Defendants, the leaked manuscript was widely disseminated within the Company, and allowed Defendants to launch a public relations plan to protect Avandia, a multi-billion dollar product.

99. The Committee staff reviewed documents showing that over 40 executives at Defendants' received and/or learned of the results in the leaked study, including then CEO Dr. Jean-Pierre Garnier; head of research, Dr. Moncef Slaoui; Vice President of Corporate Media Relations, Nancy Pekarek; and Defendants' Senior Advisor, Sir Colin Dollery.

100. Before Dr. Nissen's study on Avandia was published, Defendant's statistical experts were examining the study for potential flaws. In addition, Defendants officials were drafting "key messages" to undermine the main conclusion of the Nissen study. Defendants

had already published several large trials on Avandia (rosiglitazone) including studies named ADOPT and DREAM. After Nissen's study was published, Defendants began publicly referencing those trials, as well as another trial called RECORD, in what appeared to be an effort to further repudiate any link between Avandia and heart attacks.

101. RECORD is a study Defendants had been conducting for several years. Defendants later published the interim results of the RECORD trial in what appeared to be an attempt to cast doubt on Nissen's results. However, according to the Senate Finance Committee, internal Defendant's emails indicate that Defendant's executives, not the study's independent steering committee, made the final decision to publish the RECORD trial results. Further, according to the Committee, based on a review of emails, it can be argued that the authors of the RECORD trial appeared more concerned about countering claims that Avandia may be associated with heart attacks, than in trying to understand the underlying science. While circulating a draft of a manuscript on the RECORD trial, one of the authors wrote to his colleagues, "[W]hat's to stop [Nissen] adding the events from RECORD to his meta-analysis and re-enforcing his view?"

102. Further, after the authors of the RECORD study submitted their paper to the NEJM, one of the peer reviewers and several of the NEJM editors replied, "an explanation for the continued use of [Avandia] is needed in this manuscript."

103. Committee investigators also learned that Defendants were aware since at least 2004 that the RECORD trial was statistically inadequate, or "underpowered" to answer questions regarding cardiovascular safety. Such "inconclusive" results could be favorable to Defendants and the marketing strategy for Avandia. Further, experts were advising Defendants since 2004 about the possible biological mechanisms related to why Avandia may cause an increased risk for heart attacks.

104. However, Defendants appeared eager to design studies to prove that Avandia was safer than its competitor ACTOS (pioglitazone), which is manufactured by Takeda.

105. At a July 30, 2007, safety panel on Avandia, Food and Drug Administration (FDA) scientists presented an analysis estimating that Avandia use was associated with approximately 83,000 excess heart attacks since the drug came on the market. Had Defendants considered Avandia's potential increased cardiovascular risk more seriously when the issue was first raised in 1999 by Dr. Buse, as well as by some of their own consultants in later years, some of these heart attacks may have been avoided.

Response to the Nissen Study

106. In March 2007, Defendants held a meeting with company officials and academic advisors to discuss several studies on Avandia and its cardiac risks and benefits. Several presentations were made about studies on Avandia's possible cardiac risk. During the discussion

of a Defendants' meta-analysis (integrated study) and a study Defendants commissioned by Ingenix, Defendants noted that the academic advisors stated the following:

> Dr. NAME REDACTED commented that the [cardiovascular] effect seen in the Integrated Clinical Trials Analyses with rosiglitazone was small but real, and that it is counter to the proposed [cardiovascular] benefits associated with Avandia. Dr. NAME REDACTED agreed, noted that all data point to rosiglitazone having a hazard ratio greater than unity.... Dr. NAME REDACTED summarized the discussion on the Integrated Clinical Trials data by stating that rosiglitazone causes weight gain and edema, leading to a greater number of events.

Moreover, during the discussion of the DREAM trial, a cardiologist from Stanford stated:

> [T]he diabetes prevention afforded by rosiglitazone was very impressive, but there was no cardioprotective benefit. He then asked **what the point of diabetes prevention is if there is no cardiovascular benefit.** [Emphasis added]

When discussing ADOPT, the academic advisors concluded that, "The data in ADOPT and DREAM as well as in the CV Clinical Trials are consistent in indicating a signal for heart failure and ischemic events." According to Defendants internal documents, Defendants' experts were discussing problems with DREAM as early as 2006.

107. Around this same time, Dr. Steven Nissen began studying the potential cardiac risks of Avandia, by reviewing data found in previously published studies. He placed several requests to Defendants asking for patient level data on several studies published about Avandia. However, Defendants would provide the requested data only if Dr. Nissen agreed to use one of Defendants statisticians for the analysis. Dr. Nissen refused to use the Company's statistician, citing a need to maintain independence.

108. On May 2, 2007, Dr. Nissen submitted an analysis of 42 published and unpublished clinical trials on Avandia to the NEJM for peer review and publication. NEJM then sent confidential copies of the study to several independent experts, including Dr. Steve Haffner, to peer review the Nissen study. According to NEJM, peer reviewers must acknowledge in writing that the material they are reviewing is confidential, not to be shared with others, and is to be destroyed or returned to the medical journal after a review is completed.

109. However, the very next day, May 3, 2007, Dr. Haffner faxed Dr. Nissen's unpublished study to a GSK executive. Dr. Haffner wrote "confidential" on the fax cover sheet and checked a box marked "urgent."

Leaked Manuscript and a Massive Defensive Campaign

110. One day after receiving the unpublished study from Dr. Haffner, Defendants produced a detailed, 8-page

analysis of Dr. Nissen's paper, weeks before the paper's public release. The Defendant's statistician attempted to find deficiencies in Nissen's meta-analysis but noted, "The selection of trials therefore appears to be thorough, though others more familiar with the trials can comment more knowledgeably."

111. The Defendants' statistician also performed a regression analysis on each study that Dr. Nissen used in his meta-analysis to see if the effects of myocardial infarction and/or cardiovascular death would still appear. The statistician stated, "These results are very similar to the conclusion from the [Nissen] paper using the Peto method. As such there is no statistical reason for disregarding the findings as presented."

112. The Defendant's statistical analysis was circulated to senior executives within the company. These executives then discussed several large trials, such as RECORD, DREAM and ADOPT that Defendants could use to combat Dr. Nissen's analysis. RECORD was an ongoing trial that had not been published. On the other hand, DREAM and ADOPT were published and were included in Dr. Nissen's analysis. Defendants, as well as the FDA, had also performed their own meta-analyses.

113. Both meta-analyses were consistent with Dr. Nissen's results. On May 8, 2007, Dr. Moncef Slaoui, head of research at GSK, wrote an email to several company executives. Commenting on the meta-analyses, he wrote:

—FDA, Nissen and GSK all come to comparable

> conclusions regarding increased risk for ischemic events, ranging from 30 percent to 43 percent!
> —FDA and Nissen (but no final data from GSK [to] date) reach the conclusion of an [hazard ratio] for death (CHF + IHD) of 1.72 or 1.75!

114. Dr. Slaoui also noted in this email that a GSK commissioned study by Ingenix did not find any significant problems with rosiglitazone. Ingenix had performed an epidemiological study of Avandia. While medical experts place greater importance on a clinical trial over an epidemiological study, Dr. Slaoui sought to highlight the Ingenix results. He also expressed concern that a beneficial effect was observed (6 to 16 percent) in the PROactive study of ACTOS [MISSING TEXT]

> [W]hat studies could we offer the FDA to further assess the contradictory data between the integrated study and the two others? can we expand Record? Propose something else (very high risk patients? ok? ethical?), compare to Actos for superiority on some end points?

115. By May 9, 2007, GSK began drafting "key messages" to counteract the findings of the Nissen study. In an email. Defendant's Vice President for Corporate Media Relations noted, "The Nissen analysis is one way of looking at the data, but it doesn't reflect all we know about the safety of this medicine .... [W]e are not seeing a proven link between Avandia and increased cardiovascular deaths ...."

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116. On May 9, 2007, Sir Colin Dollery, a senior consultant to Defendants, laid out many of the problems with Avandia in an email to Dr. Slaoui and others. He wrote:

> To a great extent, the numbers are the numbers, the [Nissen] analysis is very similar to our own .... We cannot undermine the numbers but I think they can be explained so we must concentrate on effective risk management.

Later in the email, Sir Dollery noted that the PROactive study on ACTOS (pioglitazone) is undermining Avandia (rosiglitazone). He wrote:

> The main argument here lies in that pioglitazone [ACTOS] causes a small reduction of LDL [Low-Density Lipoprotein] and rosiglitazone causes a small elevation .... [W]e should search for evidence that the use of statins in diabetics generally and with rosiglitazone in particular has risen steeply over the time the thiazolidenediones have been on the market. We can then argue that any problem that existed with LDL is now controlled or controllable. It would also be worth obtaining the evidence that the use of antihypertensives in diabetics has also been increasing rapidly.

117. On fluid retention and links with cardiovascular disease, Sir Dollery mentioned a possible mechanism to explain how Avandia may cause heart attacks. He wrote:

> If [fluid retention is] substantial in patients with an impaired myocardium it can lead to [cardiac heart failure] and to cardiac ischemia by decreasing myocardial efficiency in the face of existing coronary disease .... If there is criticism of GSK it might be that we were a bit slow off the [mark] in making firm recommendations about the use of diuretics . . . and recognizing that the sodium retention is mediated via distal renal tubular ENaC.

118. On May 21, 2007, NEJM published online Dr. Nissen's meta-analysis that found a link between Avandia and heart attacks. That same day, Defendants responded, "GSK strongly disagrees with the conclusions reached in the NEJM article, which are based on incomplete evidence and a methodology that the author admits has significant limitations." Instead, Defendants highlighted the results of company sponsored trials like RECORD as "the most scientifically rigorous way to examine the safety and benefits of a medicine."

119. In a subsequent letter to The Lancet, GSK maintained that the RECORD trial is "compelling evidence" for the safety of Avandia. On May 23, 2007, a GSK official emailed members of the RECORD steering committee, the group of independent academics overseeing the study, to alert them of a teleconference to be held the following day. GSK officials also emailed internal talking points to help guide their discussion with the steering committee. However, it appears that prior to receiving input from the steering committee, Defendants had

already decided to publish the RECORD results. Later that same day, a GSK official wrote, " ... we've decided to disclose the results ...."

120. The following day, GSK officials discussed potential problems if the academics on the RECORD steering committee raised concerns about publishing the interim results of the RECORD trial. In an email, one GSK official wrote:

> [I]f the Steering Committee [SC] are reluctant to publish—Frank and I will argue the case that there is a balance to be drawn between very negative press coverage and specific reassurance for the patients in the study. However if the SC believe that publishing interim data will fatally damage their ability to bring the study to a completion—Frank and I will bring that opinion with reasons back to GSK, before pursuing the line—that a decision has been made—live with it.

121. A few hours after this email, the acting chair of the RECORD steering committee, contacted the NEJM to inquire about publishing the interim results. The editor of the NEJM responded that the journal would be interested in publishing the study.

122. By May 29, 2007, several authors of the RECORD study began passing around a manuscript, discussing the results, and offering suggestions for improvement. The third author on the RECORD study wrote, "We do

not find more myocardial infarctions with rosiglitazone treatment, but again there is a tendency supporting the Nissen argument. It is important to stress that it does not affect cardiovascular death." That same day, a senior author of the RECORD study, wrote:

> There are several striking issues:
>
> > (1) The HR ratio (and 95 percent CI) for MI in RECORD is not inconsistent with Nissen's—and he had more events; what's to stop him adding the events from RECORD to his meta-analysis and re-enforcing his view?...
> >
> > (2) Same is for CV death, although the number of events in RECORD and in the meta-analysis are similar and at least in RECORD the HR is in the other direction!
> >
> > (3) Manuscript looks to downplay the 239 percent INCREASE in HF. I have taken the liberty of doing some rewording.

123. Once a study is submitted to a journal, the journal editors then send the article to several experts for peer-review. After the review, the editors send the peer-review comments back to the author. On June 1, 2007, the RECORD authors received a reply from NEJM regarding their earlier submitted manuscript. The NEJM editors summarized the issues presented by all 8 peer reviewers, many of whom were highly critical of the study in their reply.

124. Reviewer A, along with other reviewers, asked that the authors "modify the language in multiple locations in the manuscript to tone down your conclusions." The editor also noted, "[I]n the opinion of all the readers, the data that you present are completely compatible with the results of the meta-analysis by Nissen and the meta-analysis for myocardial ischemic events posted on the GSK Web site."

125. Regarding the comments of Reviewer B, the editors wrote that for myocardial infarction the "estimates in the RECORD trial and the Nissen meta-analysis" overlap in their confidence intervals, meaning that they found a similar trend for heart attacks. They continued, "The editors feel strongly that your data do not support the statement that the RECORD results for MI contradict the Nissen meta-analysis; this statement must be removed or modified."

126. Reviewer C noted that the RECORD trial is not blinded, and pointed out "the serious problem of the low event rate, especially for MI events, in this study." He continued to ask, "Do you have an explanation for the very low event rate?" This reviewer also noted the "need to greatly tone down your language to reflect the substantial level of uncertainty in the data."

127. Reviewer D questioned the need for keeping rosiglitazone on the market. "The editors also agree that an explanation for the continued use of rosiglitazone is needed in this manuscript."

128. The NEJM published the interim analysis of the RECORD study on July 5, 2007. The GSK study authors concluded that the data was "insufficient" to find a link between Avandia and heart attacks.

129. However, an editorial by the NEJM questioned the RECORD study, as well as several of Defendants' studies of Avandia such as DREAM and ADOPT. The authors of the editorial wrote, "The DREAM trial and ADOPT focused largely on marketing questions and failed to address questions of myocardial infarction-related risk or benefit directly." In addition, the editorial noted that the RECORD trial had "several weaknesses in design and conduct" including a lack of blinding when treatment was assigned. The authors also pointed out that events of myocardial infarction would have been a preferred clinical endpoint for the study. Studies are normally designed to evaluate certain clinical endpoints or disease symptoms such as heart attack, tumor size, or depression. The authors also added that the RECORD study was not powered (or designed) to detect a myocardial infarction as an endpoint.

130. On June 6, 2007, the House of Representatives Committee on Oversight and Government Reform held a hearing on Avandia. Despite mounting criticism of the RECORD trial, Dr. Slaoui again highlighted the study in his sworn testimony. "I will say that we found the RECORD data which we published yesterday in the New England Journal of Medicine very reassuring, recognizing that it is interim and therefore not fully conclusive."

131. That same day, Defendants dismissed the idea that Dr. Nissen's study spurred the publication of the RECORD interim results. Instead, the Company placed blame on the media. In talking points created for its sales force, GSK stated, "Because of the widespread media coverage of the NEJM [Nissen] meta-analysis and the confusion it has created, the RECORD Steering Committee decided it was important to publish the interim analysis in the interests of patient safety."

132. Regarding its competitor Takeda, which sells ACTOS, Defendants advised its sales force if asked questions about the PROactive study:

> Please do not discuss Actos or the Proactive study with your physicians. For questions regarding Actos or the Proactive study, healthcare providers should contact Takeda. GSK's focus is on Avandia. Communicate the key points from the interim analysis of RECORD to your physicians.

The Record Trial as a Marketing Tool for Competition

133. Despite attempts to highlight the RECORD study, it appears that Defendants knew for years that the study was "underpowered," i.e., the study did not provide sufficient data to test for cardiovascular safety; and executives appeared more concerned about designing a study to limit competition from ACTOS. Such evidence can be found in a GSK slide presentation, emails, and other documents created in 2004 to 2006.

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134. For instance, in an undated slide show, apparently created in 2004, Defendants noted that RECORD does not have sufficient "power." The slide presentation also noted that GSK was trying to create studies to counter the PROactive study on ACTOS that Takeda planned to release.

Slide number 6 titled, "PROactive: Potential Impact," noted that Defendant's challenge was to "maintain share in growing market over next 2-3 years."

Slide number 8 reads:

> Situation Summary:
> • We have a gap
> —In 2005 Actos will have some [cardiovascular] outcome data
> • To keep our share of the growing class
> —Additive benefit to RECORD of non-inferiority result
> • However this gap may be permanent
> —RECORD has a lower event rate than expected
> PROPOSAL
> Fill this gap with an outcome study reporting in 2007

Slide number 10 compared the potential impact of a new GSK study to counter the marketing danger of PROactive and the potential impact on sales in UK pounds in 2010. The slide reads: "Timely CV Outcomes data would more than fill the RECORD 'potential gap' and would have

twice the impact on our sales than PROVerDate active." The final slide pointed out that GSK should do a "kick off study only after review of results from Proactive in Sept 2005 and assessing benefits/risks."

135. A second instance is found in a June 2005 email where GSK executives discussed the need for a study to counter PROactive. In the email, a GSK official wrote, "Clearly no patients will be recruited until [we] have made a decision based on the go-no go criteria from the PROactive data. However, there is a great deal of EU commercial push to initiate this study in 2005."

136. A third case is found in an internal GSK document outlining an upcoming meeting for December 2004. Several points were discussed about RECORD and PROactive. Regarding RECORD, the document noted that RECORD has "low events rates." This means that the study did not have the statistical "power" to give sufficient cardiovascular event data. The document also stated, "PROactive results to be coming soon—need to be able to respond to a variety of different outcomes. Communications plan in place for various possible outcomes of PROactive. "

137. A fourth instance is found in a briefing document for a June 2005 meeting on Avandia's cardiovascular plan. The document notes several "important limitations of RECORD."

> —the study will not be available until 2009
> —the current observed rate for the primary endpoint is very much lower (approximately

> 3.5 percent per annum) than that anticipated in the original protocol (11 percent per annum).

138. A fifth case is found in another of Defendants' emails. On July 26, 2005, Defendants' officials began emailing each other about potential problems with RECORD and how the PROactive study by Takeda on ACTOS will create problems for Avandia. One official wrote:

> Ron Krall [then GSK Chief Medical Officer] has asked Lawson [unknown GSK executive] to provide an urgent update to David Stout [then GSK President of Global Pharmaceutical Operations] regarding RECORD. In particular he has asked for our "intent to manage information flow in Europe to manage the competitive situation." Clearly we can provide a summary of the communications around PROactive but I wonder if you could put a few sentences together regarding the communications piece around RECORD.

139. A sixth incident is documented in July 2005, when Defendants' officials continued expressing concerns about cardiovascular problems with Avandia and potential problems arising from the PROactive study which focused on positive findings with ACTOS. Defendants held a meeting on July 18, 2005 to discuss the need for a study to compete with PROactive. The briefing document from this meeting discussed the "European Commercial Need" for a study:

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> A recently completed evidence gap analysis completed by the Metabolic Centre of Excellence has identified the need for the rapid generation of clinical endpoint data to support the superiority of rosiglitazone [Avandia] for the prevention of future cardiovascular clinical events in patients with [type 2 diabetes mellitus]. Publication of the PROactive data may result in important commercial disadvantage in Europe. We therefore have the opportunity to start a CV outcomes study with the aim of getting superiority data in 2007.

140. The document also noted that Defendant's studies provided insufficient data on cardiovascular outcomes:

> The primary endpoint in RECORD is powered for noninferiority and taking into account the low observed event rate, it is unlikely that this study will demonstrate any potential for [Avandia] combination to be superior in terms of the primary endpoint compared to SU+MET combination therapy. DREAM and ADOPT are collecting CV safety data, but these are low risk populations and it is unlikely that [Avandia] will be superior to controls for the prevention of CV events.

141. In a May 21, 2007 FDA press release, the FDA announced that safety data from controlled clinical trials have shown that there is a potentially significant increase in the risk of heart attack and heart-related disease in

patients taking Avandia. The FDA press release also mentioned an interim analysis of data from the RECORD trial and unpublished re-analyses of data from DREAM, which provide contradictory evidence about the risks in patients treated with Avandia.

142. However, the May 21, 2007 FDA press release also mentions that Defendants provided the FDA with a pooled analysis (meta-analysis) of 42 randomized, controlled clinical trials in which Avandia was compared to either placebo or other antidiabetic therapies in patients with Type II diabetes. The pooled analysis revealed that patients receiving short-term (most studies were 6-months duration) treatment with Avandia may have a 30-40 percent greater risk of heart attack and other heart-related disease than patients treated with placebo or other antidiabetic therapy. "This would be a significant concern since patients with diabetes are already at an increased risk of heart disease." Patients suffering from Type II diabetes have a 20.2 percent risk of experiencing a heart attack within seven years.

143. The May 21, 2007 publication of the New England Journal of Medicine's article *Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes*, which was written by Cleveland Clinic cardiologists Dr. Nissen and Dr. Wolski, called Avandia's safety into question. This published journal article links Avandia to a potential increase in the risk of heart attacks compared to other diabetic drugs or a placebo. The meta-analysis was based on a review of more than 40 existing clinical studies involving nearly

28,000 patients. Defendants' own meta-analysis also found indications of increased risk, but Defendants concluded that the number of adverse events was low, and therefore drew no negative conclusion from that data analysis. Thus, Defendants deliberately concealed critical information regarding the serious health risks associated with Avandia.

144. In a May 31, 2007 *Washington Post* article, Dr. Nissen criticized Defendants' study stating that the company's study referred to such small subsets of data, so that Defendants could not draw a negative conclusion. "Somebody went back and looked for something that would support their contention. This is not a scientifically proper way to analyze data."

145. On May 23, 2007, the FDA disclosed that it asked Defendants to add a more prominent "black box" label warning to address the risks of a different side effect, heart failure, on all Avandia products. Heart failure is a chronic condition in which the heart has trouble pumping blood, as opposed to a heart attack, where blood is prevented from flowing from the heart and immediate death can result. The labels on Avandia already warned patients about heart failure, though not with black box labels.

146. On May 29, 2007, the FDA held a Stakeholder Meeting to discuss the recent safety alert for Avandia. The meeting was composed of invited patients, health care professionals, and government agencies and the FDA's goal was to ensure that "the nuanced message"

about Avandia was both clearly articulated and reached the correct audience.

147. A June 5, 2007 *Houston Chronicle* article states that Defendants released the results of a study that compares Avandia and two other diabetes drugs in nearly 4,500 people around the world. The first few years of a six-year study shows similar rates of heart-related deaths and hospitalizations among those on Avandia versus those on the other drugs. Some doctors said the results showed slightly more heart problems with Avandia — a bad sign even if the difference was so small that it could have occurred by chance alone. "This study, which was designed to show the benefit of rosiglitazone (Avandia), if anything shows the opposite," said Dr. David Nathan, chief of diabetes care at Massachusetts General Hospital. Dr. Nathan had no role in the study or financial ties to any diabetes drug makers.

148. Further, Avandia's pre-marketing clinical trials were specifically designed to produce similar rates of heart-related adverse events and do not support the assertion that the medication is less likely to cause dangerous heart-related conditions. Manufacturers, including Defendants, fund clinical trials, where the manufacturers create and control the research design. In a 2001 study published in the *New England Journal of Medicine*, researchers found that more than two-thirds of the academic institutions accepted research contracts that prohibit researchers from changing the research design of sponsors, including Defendants. Half of the medical centers allowed commercial sponsors to "draft

manuscripts reporting the research results, with the investigators' role limited to review and suggestions for revision."

149. In a 2001 issue of the *New England Journal of Medicine*, thirteen editors of the world's most prestigious medical journals issued an alarming joint statement highlighting the extent and consequences of the commercial takeover of clinical research. In the report they state:

> Until recently, academic, independent clinical investigators were key players in design, patient recruitment, and data interpretation in clinical trials. The intellectual and working home of these investigators, the academic medical center, has been at the hub of this enterprise, and many institutions have developed complex infrastructures devoted to the design and conduct of clinical trials. But, as economic pressures mount, this may be a thing of the past. Investigators may have little or no input into trial design, no access to the raw data, and limited participation in data interpretation. These terms are draconian for self-respecting scientists, but many have accepted them because they know that if they do not, the sponsor will find someone else who will.

150. FDA regulations and industry standards prohibit Defendants from misrepresenting scientific evidence that supports (or fails to support) claims that their respective

drug is safe and effective for a specific condition. Thus, anecdotal evidence of a drug's usefulness for a given condition could not be presented as the equivalent of the findings of a well-designed clinical trial. Failure to comply with these standards violates Defendants' legal duty to provide accurate and non-misleading information.

151. Nevertheless, despite conclusive and reliable studies that conclude Avandia's adverse effect of increased heart attack, heart failure, and heart-related disease, and the FDA's stringent regulations and recommendations to Defendants regarding the black box warning of Avandia's adverse side effects, Defendants continued and continue to mislead and deceive consumers by placing full page advertisements in newspapers nationwide declaring that Defendants have "conducted an unprecedented number of clinical trials in order to continuously evaluate the safety of Avandia, including its impact on the cardiovascular system. The response to this commitment from well-informed experts and researchers has been encouraging."

152. Defendants deceive consumers and members of the medical community by overemphasizing controlled and misleading favorable studies, while failing to disclose studies illustrating Avandia's dangerous side effects. Defendants have and continue to expose vulnerable patients with Type II diabetes, to an increased risk of heart attack and heart-related diseases.

153. Defendants have unfairly and unjustly profited from their failure to adequately inform physicians, consumers, and the medical and healthcare community

that Avandia could cause profound and long-term injury and, in some cases, death.

V. Fraudulent Concealment of Defendants' Conduct

154. The applicable statute of limitations regarding the claims of Plaintiff and the Class has been tolled by Defendants' fraudulent concealment of their unlawful, conspiratorial deceit, as alleged in detail throughout this Complaint.

155. As evidenced by the allegations in this Complaint, Defendants have employed and continue to employ practices and techniques of secrecy in order to avoid detection of, and to fraudulently conceal, their deceptive and conspiratorial behavior regarding the safety and efficacy of Avandia and Avandia's risks associated with heart attacks and heart-related diseases.

156. Despite taking on the responsibility to reveal this information to the general public, Defendants have kept such information hidden.

157. As such, Plaintiff and the Class were not effectively alerted to the existence and scope of this industry-wide fraud and were not on notice of their potential claims until shortly prior to the filing of this Complaint.

158. Plaintiff and the Class could not have acquired such knowledge through the exercise of reasonable diligence.

159. Through their public statements, marketing and advertising, Defendants' self-concealing scheme and affirmative conduct to perpetuate their fraud deprived Plaintiff and the Class members of actual or presumptive knowledge of facts sufficient to put them on notice as to their potential claims.

VI. Injury to Plaintiff and the Class

160. Defendants' deceptive and misleading marketing scheme increased the number of prescriptions of Avandia written and filled during the Class Period. Because Defendants withheld material information about the true safety and efficacy of Avandia, the prescribing physicians did not have the knowledge necessary to make informed decisions regarding Avandia prescriptions. Plaintiff and the Class, unaware of Defendants' scheme, paid for these prescriptions. Although more effective, safer, and less expensive alternatives are available, Defendants' promotion and marketing of Avandia's safety and effectiveness has been highly successful, resulting in Defendants receiving billions of dollars in profits, representing ill-gotten gains to which Defendants were not entitled.

161. Plaintiff and similarly-situated Class members bear the ultimate responsibility of paying for their Avandia prescriptions.

162. PBMs prepare a "formulary," which is a list of the drugs that are approved for coverage by their third-party payor clients, such as Plaintiff and Class members.

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In order for a drug to be listed on the formulary, it must be assessed by the PBM for clinical safety, efficacy, and cost effectiveness. Further, where a PBM finds that a drug has an advantage over competing drugs, that drug is given a preferred status on its formulary.

163. The level of preference on the formulary corresponds with the amount that a plan participant must contribute as a co-payment when purchasing a drug — the higher the preference, the lower the co-payment, the more likely that the drug will be purchased by a prescription plan's beneficiary in lieu of a cheaper or more cost effective alternative, and *vice versa*. As such, the higher a drug's preference on the formulary, the more likely it is for a doctor to prescribe that drug. This system is well known to pharmaceutical manufacturers, including Defendants.

164. Due to the large number of drugs purchased through third-party payors, it is vital to a drug manufacturer's economic interests to have its product listed on as many formularies as possible.

165. By directly and falsely promoting Avandia as safe and effective for Type II diabetes and training their sales forces and representatives to avoid alerting the FDA to their activities and to dismiss any safety concerns raised by physicians, Defendants influenced PBMs to place Avandia on their formularies and at a higher preference on those formularies.

166. Defendants falsely promoted Avandia as safe and effective directly to PBMs in order to get Avandia placed

on, or placed more favorably than its competitor drugs on the PBM formularies.

167. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors relied on the Defendants' misrepresentations of Avandia's safety. Physicians relied on the Defendants' misrepresentations of Avandia's safety in prescribing the drug for their patients. Patients relied on the Defendants' misrepresentations of Avandia's safety in purchasing the drug. PBMs and pharmacy and therapeutic committees relied on the Defendants' misrepresentations of Avandia's safety when approving and/or placing Avandia on formularies. Third-party payors relied on the Defendants' misrepresentations of Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their members.

168. Therefore, Defendants' failure to adequately inform consumers, third-party payors and those in the medical community that the use of Avandia dangerously increases the risk of heart attacks and heart-related diseases, and their false and misleading promotion of Avandia's efficacy over competing less expensive antidiabetic drugs, causes patients and third-party payors to pay for Avandia, which is neither safer nor more effective than other less expensive antidiabetic drugs.

169. But for Defendants actions, third-party payors would not have paid for Avandia but would instead have paid for safer, equally efficacious drugs like metformin and/or sulfonyureas.

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CLASS ACTION ALLEGATIONS

170. Plaintiff brings this suit as a Class action pursuant to Rule 23(b)(2) and (b)(3) of the Federal Rules of Civil Procedure, on behalf of a Class consisting of:

> All health insurance companies, third-party administrators, health maintenance organizations, self-funded health and welfare benefit plans, third-party payors and any other health benefit provider, in the United States of America and its territories, which paid or incurred costs for the drug Avandia, for purposes other than resale, since May 25, 1999. Excluded from the Class are employees of Defendants, including its officers or directors, and the Court to which this case is assigned.

171. The proposed Class is sufficiently numerous, as thousands of members of the Class were induced to pay for Avandia through Defendants' scheme. The Class members are so numerous and dispersed throughout the United States that joinder of all members is impracticable. The Class is composed of thousands of third-party payors, and the disposition of their claims in a Class action will benefit both the parties and the Court. It is estimated that in 2007, at least half a million individuals nationwide received prescriptions for Avandia. Defendants sell millions of doses of Avandia in the United States every year, and thus the Class is sufficiently numerous to make joinder impracticable, if not outright impossible. The Class members can be identified by, *inter alia*, records maintained by Defendants, pharmacies, and PBMs.

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172. Common questions of law and fact exist as to all members of the Class and predominate over any questions affecting solely individual members of the Class. Among the questions of law and fact common to the Class members are:

a. whether Defendants misrepresent the safety and efficacy of Avandia, to the financial detriment of the Class;

b. whether Defendants engaged in a conspiracy to promote the sales of and suppress adverse information about Avandia;

c. whether Defendants' acts and omissions violate, *inter alia*, the Pennsylvania Unfair Trade Practices and State Consumer Protection Laws;

d. whether Defendants make material misrepresentations of fact, or omit to state material facts regarding the severe heart attacks and heart-related diseases and risks associated with Avandia, which material misrepresentations or omissions operate as a fraud and deceit upon the Class;

e. Whether Plaintiff and the class paid more for Avandia than for other efficacious drugs that were available at a cheaper price;

f. whether persons who took Avandia are at increased risk of severe and permanent injuries,

including liver damage and/or failure, cardiac damage and visual impairment and damage;

g. whether, in marketing and selling Avandia, Defendants failed to disclose the dangers and risks to the health of persons ingesting the drug;

h. whether Defendants failed to warn adequately of the adverse effects of Avandia;

i. whether Defendants misrepresented in their advertisements, promotional materials and other materials, among other things, the safety, potential side effects and convenience of Avandia;

j. whether Defendants knew or should have known that the ingestion of Avandia leads to serious adverse health effects;

k. whether Defendants adequately tested Avandia prior to selling it;

l. whether Defendants manufactured, marketed, distributed and sold Avandia notwithstanding their knowledge of the drug's dangerous nature;

m. whether Defendants knowingly omitted, suppressed and/or concealed material facts about the unsafe and defective nature of Avandia from government regulators, the medical community and/or the consuming public;

n. whether the Class has been damaged, and if so, the extent of such damages and/or the nature of the equitable relief, statutory damages, or punitive damages to which the Class is entitled;

o. whether Defendants were and are unjustly enriched by its acts and omissions, at the expense of the Class;

p. the amount of attorneys' fees, prejudgment interest, and costs of the suit to which the Class is entitled.

q. whether Defendants engaged in conduct that violates federal RICO statutes in promoting the sales of and suppressing adverse information about Avandia; and

r. whether Defendants engaged in a conspiracy to promote the sales of and suppress adverse information about Avandia in violation of federal RICO statutes.

173. Plaintiff's claims are typical of the claims of the members of the Class because Plaintiff and the Class sustained damages arising out of the Defendants' wrongful conduct as detailed herein. Specifically, Plaintiff, having expended substantial sums for the purchase of Avandia, assert claims that are typical of the claims of the entire Class, and will fairly and adequately represent and protect the interest of the Class.

174. Plaintiff will fairly and adequately protect the interests of the Class members and has retained counsel competent and experienced in class action lawsuits.

175. Plaintiff has no interests antagonistic to or in conflict with those of the Class members and therefore should be adequate as representatives for the Class members.

176. A Class action is superior to other available methods for the fair and efficient adjudication of this controversy since joinder of all members of the Class is impracticable. Furthermore, because the damages suffered by individual members of the Class may in some instances be relatively small, the expense and burden of individual litigation make it impossible for such Class members individually to redress the wrongs done to them. Also, the adjudication of this controversy through a Class action will avoid the possibility of inconsistent and possibly conflicting adjudications of the claims asserted herein. There will be no difficulty in the management of this action as a Class action.

CAUSES OF ACTION

FIRST CAUSE OF ACTION

VIOLATION OF 18 U.S.C § 1962(C) — Avandia Promotion Enterprise

177. Plaintiff incorporates by reference all preceeding paragraphs as if fully set forth herein.

178. Defendants are "persons" within the meaning of 18 U.S.C. § 1961(3) who conducted the affairs of the enterprise, the Avandia Promotion Enterprise, through a pattern of racketeering activity in violation of 18 U.S.C. § 1962(c).

179. The Avandia Promotion Enterprise is an association-in-fact within the meaning of 18 U.S.C. § 1961(4), consisting of Defendants, including its employees, agents and external consultants like Sir Colin Dollery and Dr. Stephen Haffner, co-promoters Bristol-Myers Squibb, and other as yet unknown consultants, marketing firms and distribution agents employed by Defendants to promote Avandia. All entities are persons within the meaning of 18 U.S.C. § 1961(3) and acted to enable Defendants to fraudulently market Avandia as scientifically proven as safe and effective. The Avandia Promotion Enterprise is an organization that functioned as an ongoing organization and continuing unit. The Avandia Promotion Enterprise was created and/or used as a tool to effectuate a pattern of racketeering activity. Each of these entities, including Defendants, is a "person" distinct from the Avandia Promotion Enterprise.

180. Each of the Defendants, in concert with other participants in the Avandia Promotion Enterprise, created and maintained systematic links for a common purpose-to aid in marketing Avandia as safe for its intended uses, while suppressing evidence to the contrary and improperly inducing physicians to prescribe Avandia. Each of the participants in the Avandia Promotion Enterprise received substantial revenue from the scheme to promote

Avandia as safe for its intended uses. Such revenue was exponentially greater than it would have been if Avandia was marketed appropriately and the true safety risks of Avandia disclosed. All participants of the Avandia Promotion Enterprise were aware of Defendants' control over the activities of the Avandia Promotion Enterprise in promoting Avandia. Furthermore, each portion of the enterprise benefited from the existence of the other parts.

181. The Avandia Promotion Enterprise engaged in and affected interstate commerce, because, *inter alia*, it marketed, promoted, sold, or provided Avandia to thousands of individuals and entities throughout the United States.

182. The named Defendants exerted control over the Avandia Promotion Enterprise and management of the affairs of the Avandia Promotion Enterprise.

183. Defendants conducted and participated in the affairs of the Avandia Promotion Enterprise through patterns of racketeering activity that includes acts indictable under 18 U.S.C. § 1341 (mail fraud), § 1343 (wire fraud), § 1512 (tampering with witnesses), and § 1952 (use of interstate facilities to conduct unlawful activity).

184. Defendants fraudulent scheme consisted of, inter alia: deliberately misrepresenting the safety of Avandia so that Plaintiff and members of the Class paid for this drug to treat symptoms for which it was not scientifically proven to be safe and actively concealing and causing others to conceal, information about the true safety of Avandia.

185. Defendants' use of the mails and wires to perpetuate their fraud involved thousands of communications, including, but not limited to:

a. communications with and among the enterprise participants that misrepresented the safety and risks of Avandia amongst themselves and others;

b. communications with patients and Class Members, including Plaintiff, inducing payments for Avandia by misrepresenting the safety and risks of Avandia;

c. receiving the proceeds in the course of and resulting from Defendants' improper scheme;

d. transmittal and receipt of monies from governmental health organizations and programs, including without limitation Medicare and Medicaid; and

e. transmittal and receipt of payments in exchange for, directly or indirectly, activities in furtherance of the Avandia Promotion Enterprise.

186. At all times during the fraudulent scheme, Defendants' and the Fraud Participants had a legal and ethical obligation of candor to and honest dealing with public and private payors, physicians and the medical community.

187. The conduct of the Avandia Promotion Enterprise described above constitutes "racketeering activity" within the meaning of 18 U.S.C. § 1961(1). Defendants' decisions and activity in connection with the Avandia Promotion Enterprise to routinely conduct its transactions in such a manner constitutes a "pattern of racketeering activity" within the meaning of 18 U.S.C. § 1961(5).

188. The above described racketeering activities amounted to a common course of conduct intended to deceive and harm Plaintiff and the Class. Each such racketeering activity was related, had similar purposes, involved similar or the same participants, and methods of commission, and had similar results affecting the same or similar victims, including Plaintiff and members of the Class. Defendants' racketeering activities were part of their ongoing business and constitute a continuing threat to the property of Plaintiff and the Class.

189. Plaintiff and members of the Class have been injured in their property by reason of these violations in that Plaintiff and members of the Class paid hundreds of millions of dollars for Avandia that they would not have paid had Defendants not engaged in this pattern of racketeering activity.

190. The injuries to Plaintiff and members of the Class were directly and proximately caused by Defendants' racketeering activity.

191. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors,

including Plaintiff and the Class, directly relied on the racketeering activities of the Defendants' and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the respresentations as to the efficacy and safety of Avandia as promoted by Defendants. Because Defendants controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendants' representations about Avandia. Further, Defendants perpetuated this reliance by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

192. By virtue of these violations of 18 U.S.C. § 1962 (c), Defendants are liable to Plaintiff and the Class for three times the damages sustained, plus the costs of this suit, including reasonable attorney's fees.

193. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiff and the Class have suffered damages. Plaintiff and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

194. By reason of the foregoing, Plaintiff and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts

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SECOND CAUSE OF ACTION

VIOLATION OF 18 U.S.C. § 1962 (d) — RICO Conspiracy

195. Plaintiff incorporate by reference all preceding paragraphs as if fully set forth herein.

196. Section 1962(d) of RICO provides that it "shall be unlawful for any person to conspire to violate any of the provision of subsection (a), (b), or (c) of this section."

197. Defendants have violated § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c). The object of this conspiracy has been and is to conduct or participate in, directly or indirectly, the conduct of the affairs of the Avandia Promotion Enterprise described previously through a pattern of racketeering activity. The corporate defendants conspired with, *inter alia*, publicists, sales representatives, medical professionals, academics and other intermediaries to promote Avandia and suppress information about the harms known to result from Avandia use.

198. Defendants' co-conspirators have engaged in numerous overt and predicate fraudulent racketeering acts in furtherance of the conspiracy, including material misrepresentations and omissions designed to defraud Plaintiff and the Class of money.

199. The nature of the above-described Defendants' co-conspirators' acts, material misrepresentations, and omissions in furtherance of the conspiracy gives rise to

an inference that they not only agreed to the objective of an 18 U.S.C. § 1962(d) violation of RICO by conspiring to violate 18 U.S.C. § 1962(c), but they were aware that their ongoing fraudulent and extortionate acts have been and are part of an overall patter of racketeering activity.

200. As a direct and proximate result of Defendants' overt acts and predicate acts in furtherance of violating 18 U.S.C. § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c), Plaintiff and the Class have been and are continuing to be injured in their business or property as set forth more fully above.

201. Defendants sought to and have engaged in the commission of and continue to commit overt acts, including the following unlawful racketeering predicate acts:

a) Multiple instances of mail and wire fraud violations of 18 U.S.C. §§ 1341 and 1342;

b) Multiple instances of mail fraud violation of 18 U.S.C. §§ 1341 and 1346;

c) Multiple instances of wire fraud violations of 18 U.S.C. §§ 1341 and 1346;

d) Multiple instances of unlawful activity in violation of 18 U.S.C. § 1952.

202. Defendants' violations of the above federal laws and the effects thereof detailed above are continuing and will continue. Plaintiff and members of the Class have been

injured in their property by reason of these violations in that Plaintiff and members of the Class have made paid hundreds of millions of dollars for Avandia that they would not have made had Defendants not conspired to violate 18 U.S.C. § 1962(c).

203. Injuries suffered by Plaintiff and members of the Class were directly and proximately caused by Defendants' racketeering activity as described above.

204. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors, including Plaintiff and the Class, directly relied on the racketeering activities of the Defendants' and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the respresentations as to the efficacy and safety of Avandia as promoted by Defendants. Because Defendants controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendants' representations about Avandia. Further, Defendants perpetuated this reliance by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

205. By virtue of these violations of 18 U.S.C. § 1962(d), Defendant is liable to Plaintiff and the Class for three times the damages Plaintiff and the Class have sustained, plus the cost of this suit, including reasonable attorney's fees.

206. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiff and the Class have suffered damages. Plaintiff and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

207. By reason of the foregoing, Plaintiff and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts.

THIRD CAUSE OF ACTION

VIOLATIONS OF THE PENNSYLVANIA UNFAIR TRADE PRACTICES AND CONSUMER PROTECTION LAW ("UTPCPL"), 73 Pa.C.S.A. § 201-1 ET SEQ.

208. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

209. At all times material hereto, Defendants were a manufacturer, marketer, seller and/or distributor of Avandia within the meaning of the Pennsylvania Unfair Trade Practices and Consumer Protection Law ("UTPCPL"), 73 Pa.C.S.A. § 201-1 *et seq.*

210. At all times material hereto, the conduct described above and throughout this Complaint took place within the Commonwealth of Pennsylvania and constitutes unfair methods of competition or unfair or deceptive acts or practices in violation of § 201-2(4),(v),(vii) and (xxi) of

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UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

211. The UTPCPL applies to the claims of all the class members because the conduct which constitutes violations of the UTPCPL by Defendants occurred within the Commonwealth of Pennsylvania.

212. At all times relevant and material hereto, Defendants conducted trade and commerce within the meaning of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

213. Defendants' deceptive marketing scheme concerning Avandia violates the UTPCPL because, *inter alia*, Defendants:

a. knowingly conceal, suppress, or omit material information regarding Avandia's safety and effectiveness from Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such concealment, suppression, or omission;

b. knowingly misrepresent the safety and efficacy of Avandia from Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such misrepresentation; and

c. market, promote, and advertise Avandia as a safe and effective drug when the purported safety and efficacy is deceptive and unfounded.

214. Defendants' unlawful conduct as described herein arose, is directed, and emanates from Defendants' headquarters to the detriment of Plaintiff and Class members.

215. Defendants' concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices has the tendency, capacity, and likelihood to deceive Plaintiff and the Class members.

216. Defendants intend, or consciously disregard, that Plaintiff and the Class members rely on its concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices, so that they are able to purchase Avandia.

217. Defendants' concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices cause Plaintiff and the Class members to suffer ascertainable losses in the amount of the monies they overpay for Avandia, and/or pay for more Avandia prescriptions, without knowing the drugs' efficacy or lack thereof for which they are marketed, promoted, or advertised.

218. Defendants deceived and continue to deceive consumers. This conduct constitutes unfair or deceptive acts or practices within the meaning of the UTPCPL. This illegal conduct is continuing, with no indication that Defendants will cease.

219. Defendants' actions in connection with the advertising, marketing, selling and distribution of Avandia as set forth herein evidences a lack of good faith, honesty and observance of fair dealings so as to constitute unconscionable commercial practices, in violation of UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

220. Plaintiff and the Class members would not have overpaid and/or paid for more Avandia prescriptions had they known of Defendants' deceptive and misleading marketing scheme, or the extent of said scheme.

221. Plaintiff and the Class members are accordingly harmed by Defendants' conduct in violation of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

222. By reason of Defendants' violations of the UTPCPL described above, Plaintiff and the Class members are entitled to recover treble damages, including but not limited to a full refund of all purchase costs Plaintiff and Class members have incurred for Avandia, in excess of what they would have spent to purchase other more effective antidiabetic drugs, plus attorney's fees and costs, along with equitable relief prayed for herein in this Complaint.

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FOURTH CAUSE OF ACTION

VIOLATIONS OF STATE CONSUMER PROTECTION AND UNFAIR AND DECEPTIVE ACTS OR PRACTICES STATUTES

223. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

224. Defendants intended that Plaintiff, the Class and the medical and scientific community would rely on their materially deceptive practices and Plaintiff and the Class would purchase or pay for Avandia as a consequence of the deceptive practices, including Defendants' misleading and fraudulent marketing, and misrepresentations and omissions of material fact with respect to Avandia as set forth herein. Defendants' deceptive representations and material omissions to Plaintiff and the Class were and are unfair and deceptive acts and practices. Plaintiff and the Class were deceived by Defendants' misrepresentations. As a proximate result of Defendants' misrepresentations, Plaintiff and the Class have suffered an ascertainable loss, in an amount to be determined at trial, in that they paid millions upon millions of dollars for Avandia that they would not have paid had Defendants not engaged in unfair and deceptive conduct.

225. By reason of the conduct as alleged herein, by making false and misleading statements about Avandia's safety and effectiveness through false and/or misleading advertising, representations and statements with the intent to induce or cause reliance, Defendants violated the

laws prohibiting unfair and deceptive acts and practices of the states wherein Class members reside.

226. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of ALASKA STAT. § 44-1522, *et seq.*

227. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of ARIZ. REV. STAT. § 44-1522, *et seq.*

228. Defendants engaged in unfair competition unfair or deceptive acts or practices in violation of ARK. CODE § 4-88- 101, *et seq.*

229. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of CAL. BUS. & PROF. CODE § 17200, *et seq.*

230. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of COLO. REV. STAT. § 6-1-105, *et seq.*

231. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of CONN. GEN. STAT. § 42-110b, *et seq.*

232. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of 6 DEL. CODE § 2511, *et seq.*

233. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of D.C. CODE § 28-3901, *et seq.*

234. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of FLA. STAT. § 501.201, *et seq.*

235. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of GA. CODE ANN. §10-1-392, *et seq.*

236. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of HAW. REV. STAT. § 480, *et seq.*

237. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of IDAHO CODE § 48-601, *et seq.*

238. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of 815 ILCS § 50511, *et seq.*

239. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of Ind. Code Ann. § 24-5-0.5.1, *et seq.*

240. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of Iowa Code § 714.1 b, *et seq.*

241. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of KAN. STAT. § 50-623, *et seq.*

242. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of KY. REV. STAT. § 367.110, *et seq.*

243. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of LA. REV. STAT. § 51:1401, *et seq.*

244. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation MASS. GEN. L. CH. 93A, *et seq.*

245. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MD. COM. LAW CODE § 13-101, *et seq.*

246. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of ME. REV. STAT. tit. 5, § 205-A, *et seq.*

247. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MICH. STAT. §445.901, *et seq.*

248. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MINN. STAT. § 8.31, *et seq.*

249. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Mo. Rev. Stat. § 407.010, *et seq.*

250. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Mont. Code §30-14-101, *et seq.*

251. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Neb. Rev. Stat. § 59-1601, *et seq.*

252. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Nev. Rev. Stat. § 598.0903, *et seq.*

253. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.H. Rev. Stat. § 358-A:1, *et seq.*

254. Defendants engaged in unfair competition or unfair, unconscionable or deceptive acts or practices in violation of N.J. Rev. Stat. § 56:8-1, *et seq.*

255. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.M. Stat. § 57-12-1, *et seq.*

256. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.Y. Gen. Bus. Law § 349, *et seq.*

257. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.C. Gen. Stat. § 75-1.1, *et seq.*

258. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.D. Cent. Code § 51-15-01. *et seq.*

259. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.J.S.A. § 56:8-2, *et seq.*

260. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Ohio Rev. Stat. § 1345.01, *et seq.*

261. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of Okla. Stat. 15 § 751, *et seq.*

262. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Or. Rev. Stat. § 646.605, *et seq.*

263. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of R.I. Gen. Laws. § 6-13.1-1, *et seq.*

264. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of S.C. Code Laws § 39-5-10, *et seq.*

265. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of S.D. Code Laws § 37-24-1, *et seq.*

266. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Tenn. Code § 47-18-101, *et seq.*

267. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Tex. Bus, & Com. Code § 17.41, *et seq.*

268. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Utah Code. § 13-11-1, *et seq*

269. Defendants engaged in unfair competition or unfair deceptive acts or practices in violation of Vt. Stat. Ann. Tit. 9 §2451, *et seq.*

270. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Va. Code § 59.1-196, *et seq.*

271. Defendants engaged in unfair competition or unfair, deceptive or fraudulent acts or practices in violation of Wash. Rev. Code. § 19.86.010, *et seq.*

272. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of W. Va. Code § 46A-6-101, *et seq.*

273. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of Wis. Stat. § 100.18, *et seq.*

274. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of Wyo. Stat. Ann. § 40-12-101, *et seq.*

275. As a direct and proximate result of Defendants' statutory violations, Plaintiff and Class members paid for their prescriptions of Avandia, which proximately caused them injury.

276. By reason of Defendants' violations, Plaintiff and the Class members are entitled to recover treble damages where available, including but not limited to all monies expended to purchase Avandia, in excess of what they would have spent to purchase other safer, more effective, and cheaper antidiabetic drugs, plus attorney's fees and costs along with equitable relief prayed for herein in this complaint.

FIFTH CAUSE OF ACTION

UNJUST ENRICHMENT

277. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

278. Defendants have been and continue to be enriched by their fraudulent acts and omissions alleged herein for all states wherein class members reside.

279. In exchange for payments they made for Avandia and at the time these payments were made, Plaintiff and Class members expected that the drugs were a safe and medically effective treatment for the condition, illness, disorder or symptoms for which it was prescribed.

280. Defendants voluntarily accepted and retained these payments with full knowledge and awareness that, as a result of their wrongdoing, Plaintiff and Class members paid for Avandia when they otherwise would not have done so and paid for the drug at a higher price than would have been paid for but for Defendants' wrongful conduct.

281. These fraudulent acts and omissions allow Defendants to gain billions of dollars in profits that would not have been gained but for Defendants' fraudulent acts and omissions

282. Plaintiff and Class members and those similarly situated paid and continue to pay Defendants an amount that exceeds the value of the products identified herein as a result of Defendants' fraudulent acts and omissions.

283. Plaintiff and the Class members suffered damages due to Defendants' acts and omissions as alleged herein.

284. Defendants have and continue to be unjustly enriched as a result of their fraudulent acts and omissions.

285. Defendants lack any legal justification for engaging in a course of fraudulent acts and omissions as alleged herein at Plaintiff's and the Class' expense.

286. No other remedy at law can adequately compensate Plaintiff and Class members for the damages occasioned by Defendants' conscious choice to engage in a course of fraudulent acts and omissions.

287. Plaintiff and Class members are entitled in equity to seek restitution of Defendants' wrongful profits, revenues and benefits to the extent and in the amount, deemed appropriate by the Court and such other relief as the Court deems just and proper to remedy Defendants' unjust enrichment.

SIXTH CAUSE OF ACTION

EQUITABLE RELIEF

288. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

289. Defendant is under a legal duty imposed by the FDA to advise physicians of the latest changes in its labeling of Avandia. Such communication, however, is limited to physicians. No notice is going to be provided to the proposed Class herein.

290. Pursuant to the equitable relief provisions of RICO and applicable laws of the 50 states, Plaintiff seeks temporary and/or permanent injunctive relief directing

Defendants to notify in writing, and through other appropriate forms of notice, all members of the class as to the restrictions imposed on Defendants as to the limited indicated use of Avandia as defined by the FDA.

291. Avandia has been heavily marketed to the medical community and the public. Not all prescribing physicians, nor all consumers of Avandia, will necessarily be aware of the action required of Defendants by the FDA. In order to ascertain that Avandia is only being paid for or reimbursed by Third Party Payors, it is imperative that Third Party Payors also be advised as to the highly limited and restricted uses of Avandia as mandated by the FDA.

292. Such notice is necessary to enable Third Party Payors prospectively to limit the payments or reimbursements of their covered lives only to those on label uses of Avandia as permitted by the FDA and to be aware of any off-label prescriptions. While physicians may be placed on notice as to the new label restrictions imposed on Defendants by the FDA, physicians are not the ones who bear the risk of loss for prescriptions beyond the bases approved by the FDA. Third Party Payors pay the overwhelming majority of the cost for Avandia presecriptions. Without such notice, Third Party Payors will be unable to perform their obligation to only pay or reimburse for prescription drugs within the various Third Party Payor plan provisions and protect themselves from incurring improper costs or charges in future.

293. Without such notice, Third Party Payors risk irreparable harm in paying or reimbursing for

prescriptions of Avandia beyond the limits set by the FDA. Third Party Payors may not be able to fully recover monetary losses resulting from the payment or reimbursement for prescriptions of Avandia beyond the on label indications currently in force and effect.

294. As Defendants are now limited in their marketing and promotion of Avandia pursuant to FDA regulations and statutory authority, there should be no basis for opposition to advising Third Party Payors in the same or similar fashion that they are notifying physicians of recent label changes mandated by the FDA.

295. The equitable relief sought pursuant to RICO and the applicable laws of the 50 states is within the jurisdiction of this Honorable Court. The proposed notice class meets the requirements of FRCP 23(b)(2). Under this claim, Plaintiff seeks no monetary damages on behalf of the proposed (b)(2) class. As noted herein, the proposed class meets the requirements of Rule 23. As such, equitable relief under Rule 23(b)(2) is appropriate and a (b)(2) class should be certified for the purposes of notice to Third Party Payors as set forth herein.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff and the Class members, pray for relief as follows:

1. For an order certifying this matter as a class action as requested herein and a declaration that this action is a proper class action pursuant to

Federal Rule of Civil Procedure 23, establishing an appropriate class or classes and finding that the Plaintiff and its counsel are proper representatives of the class;

2. For an Order appointing the undersigned counsel as Class counsel;

3. On Plaintiff's and the Class's RICO claims, compensatory damages, and enhancement of damages Plaintiff and the Class have sustained as a result of Defendants' conduct as may be permitted under the relevant statutes, such amount to be determined at trial, plus Plaintiff's costs in this suit, including reasonable attorneys' fees.

4. On Plaintiff's and the Class's claims under the Pennsylvania Unfair Trade Practices and Consumer Protection Law 73 Pa.C.S.A. § 201-1 *et seq.*, three times the damages Plaintiff and the Class have sustained as a result of Defendants' conduct, such amount to be determined at trial, plus Plaintiff's costs in this suit, including attorneys' fees;

5. On Plaintiff's and the Class's Consumer Fraud Act claims, compensatory damages, and enhancement of damages Plaintiff and the Class have sustained as a result of Defendants' conduct as may be permitted under the relevant statutes, such an amount to be determined at trial, plus Plaintiff's

costs in this suit, including reasonable attorneys' fees;

6. On Plaintiff's and the Class's claim for unjust enrichment, recovery in the amount of Plaintiff's and the Class's payment for Avandia, such amount to be determined at trial, plus Plaintiff's costs in this suit, including all reasonable expert fees and attorneys' fees;

7. For an order otherwise requiring Defendants to refund and make restitution of all monies acquired from the sale of Avandia to Plaintiff and the Class;

8. On Plaintiff's and the Class's claim for equitable relief, for an order certifying this matter as a class action pursuant to Fed. R. Civ. Pro. 23(b)(2) and temporary and/or permanent injunctive relief directing Defendants to notify in writing, and through other appropriate forms of notice, all members of the class as to the restrictions imposed on Defendants as to the limited indicated use of Avandia as defined by the FDA.

9. For injunctive relief, enjoining Defendants from continuing their misleading, unbalanced, illegal and fraudulent promotion of Avandia;

10. Awarding Plaintiff and the Class prejudgment interest on all damages;

11. Awarding Plaintiff and the Class other appropriate equitable relief;

12. Awarding Plaintiff and the Class their costs and expenses in this litigation, including reasonable attorneys' fees and expert fees; and

13. Awarding Plaintiff and the Class such other and further relief as may be just and proper under the circumstances.

JURY DEMAND

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiff demands trial by jury on all issues so triable.

Dated: October 8, 2010

Respectfully submitted,

MURRAY LAW FIRM

/s/ Douglas R. Plymale
Douglas R. Plymale
James R. Dugan, II
Stephen B. Murray, Jr.
Stephen B. Murray, Sr.
650 Poydras Street, Suite 2150
New Orleans, LA 70130
Phone: (504) 648-0180
Fax: (504) 648-0181

Appendix H

Art Sadin
Sadin Law Firm, P.C.
121 Magnolia St.
Suite 102
Friendswood, Texas 77546
Phone: (281) 648-7711
Fax: (281) 648-7799

Arnold Levin 02280
Frederick S. Longer 46653
Charles Schaffer 76259
Levin, Fishbein, Sedran & Berman
510 Walnut Street, Suite 500
Philadelphia, PA 19106
Phone: (215) 592-1500
Fax: (215) 592-1500

Christopher A. Seeger
TerriAnne Benedetto
Seeger Weiss LLP
1515 Market Street, Suite 1380
Philadelphia, PA 19102
Phone: (215) 564-2300
Fax: (215) 851-8029

Eric L. Young
Gerard P. Egan
Egan Young
526 E. Township Line Road
Suite 100
Blue Bell, Pennsylvania 19422
Phone: (215) 367-5151
Fax: (215) 367-5143

Appendix H

Samuel Issacharoff
40 Washington Square South
New York, New York 10012
Telephone: (212) 998-6580

Counsel for Plaintiff

APPENDIX I — FIRST AMENDED CLASS ACTION COMPLAINT, *UFCW LOCAL 1776 AND PARTICIPATING EMPLOYERS HEALTH AND WELFARE FUND V. GLAXOSMITHKLINE*, UNITED STATES DISTRICT COURT FOR THE EASTERN DISTRICT OF PENNSYLVANIA, FILED AUGUST 20, 2010

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

MDL No. 1871
07-MD-01871-CMR
IN RE: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT APPLIES TO:

UFCW LOCAL 1776 AND PARTICIPATING EMPLOYERS HEALTH AND WELFARE FUND, on behalf of itself and all others similarly situated,

Plaintiff,

vs.

SMITHKLINE BEECHAM CORPORATION d/b/a GLAXOSMITHKLINE and GLAXOSMITHKLINE, PLC,

Defendants.

CIVIL ACTION NO: 10-2475

FIRST AMENDED CLASS ACTION COMPLAINT

Appendix I

DEMAND FOR JURY TRIAL

FIRST AMENDED CLASS ACTION COMPLAINT

UFCW Local 1776 and Participating Employers Health and Welfare Fund ("UFCW Fund") ("Plaintiff"), on behalf of itself and all others similarly situated, brings this action against Defendants GlaxoSmithKline PLC through its subsidiary, SmithKline Beecham Corporation d/b/a GlaxoSmithKline, seeking damages and other monetary relief. Plaintiff makes the allegations of this Complaint based upon personal knowledge as to matters relating to itself, and upon investigation of counsel and information and belief as to all other matters.

NATURE OF THE ACTION

1. This complaint stems from Defendants' scheme to market and promote Avandia® (rosiglitazone maleate), Avandamet® (a combination of rosiglitazone maleate and metformin) and Avandaryl® (a combination of rosiglitazone maleate and glimepiride), (collectively, "Avandia"), which are medications indicated to treat Type II diabetes mellitus. Defendants' marketing scheme has included deliberately concealing, suppressing and affirmatively misrepresenting the significant safety risks associated with the use of Avandia, including but not limited to, heart attack, heart failure, or other heart-disease related risks.

2. Defendants marketed and promoted Avandia as a safe and effective means of enabling the body to utilize naturally secreted insulin and to control blood sugar levels

in individuals with Type II diabetes mellitus. However, published findings from 1999—the year Avandia was approved by the FDA for sale in the U.S.—including a study from The New England Journal of Medicine, strongly indicated that studied groups of Avandia users incurred a 43 percent greater risk of heart attacks than those taking other competing diabetes medications, or diabetics taking no medications. Further, the researchers found that patients incurred a 64 percent increased risk of dying from heart attacks or heart-related diseases while taking Avandia.

3. At a congressional hearing held on Wednesday, June 6, 2007, Commissioner Andrew von Eschenbach of the U.S. Food and Drug Administration ("FDA") revealed that the FDA was ordering Defendants to add a "black box" warning to Avandia, strengthening existing warnings regarding the use of Avandia related to an increased risk of developing congestive heart failure ("CHF"), a condition in which the heart does not adequately pump blood. The FDA found that the warnings previously issued by Defendants, advising Avandia users to simply consult their doctors about the continuous use of Avandia, were inadequate to protect such users.

4. On July 30, 2007, two FDA advisory panels, the Endocrine and Metabolic Advisory Committee and the Drug Safety and Risk Management Advisory Committee, met to evaluate Avandia and similar antidiabetic drugs. The panels recognized the increased risk for heart attacks posed by Avandia and voted overwhelming, 20-3, urging the FDA to consider raising its warning level to black-box

status or implementing a patient registration program. On August 14, 2007, the FDA increased the warning for Avandia's increased risk of heart failure, and the following black box warning was added to the label:

> Thiazolidinesdiones, including rosiglitazone, cause or exacerbate congestive heart failure in some patients (see WARNINGS). After initiation of AVANDIA, and after dose increase, observe patient carefully for signs and symptoms of heart failure (including excessive, rapid weight gain, dyspnea, and/or edema). If these signs and symptoms develop, the heart failure should be managed according to current standards of care. Furthermore, discontinuation or dose reduction of AVANDIA must be considered.
>
> AVANDIA is not recommended in patients with symptomatic heart failure. Initiation of AVANDIA in patients with established NYHA Class III or IV heart failure is contraindicated. (See CONTRAINDICATIONS and WARNINGS.)

5. Thereafter, on November 19, 2007, the FDA added a second black box warning for Avandia's increased risk of heart attacks and other myocardial ischemic events, and the following language was added to the black box warning:

> WARNING: CONGESTIVE HEART FAILURE AND MYOCARDIAL ISCHEMIA

> A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared AVANDIA to placebo, showed AVANDIA to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction. Three other studies (mean duration 41 months; 14,067 patients), comparing AVANDIA to some other approved antidiabetic agents or placebo, have not confirmed or excluded this risk. In their entirety, the available data on the risk of myocardial ischemia are inconclusive.

6. In February 2010, the United States Senate Finance Committee released a report concluding, among other things, that:

> The totality of evidence suggests that GSK was aware of the possible cardiac risks associated with Avandia years before such evidence became public. Based on this knowledge, GSK had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner. Instead, GSK executives intimidated independent physicians, [and] focused on strategies to minimize findings that Avandia may increase cardiovascular risk ...

Rather than issue proper warnings and provide accurate information about Avandia's risks and benefits, Defendants chose instead to keep their deceptive propaganda and marketing machine running full steam ahead and never

took any affirmative steps to correct the misinformation and deceptive advertising scheme that it had and continued to perpetrate, ensuring that it would continue to maximize the prescription and sale of Avandia so long as consumers, Third-Party Payors, prescribing doctors, and the medical and healthcare community remained unaware of Avandia's true risks.

7. Regarding the Senate Finance Committee report, GSK said that it "fails to present an accurate, balanced, or complete view of the currently available information on Avandia." The company also rejected "any allegations of concealing safety information or acting inappropriately on behalf of patients."

8. Defendants knew or should have known that Avandia was unsafe as compared to other diabetes medications. Moreover, Defendants knew or should have known that Plaintiff and the Class would be injured to the extent they must pay for Avandia and the health care services and facilities resulting from heart-related injuries associated with Avandia's use. As a result of Defendants' failure to adequately warn consumers, Third-Party Payors, prescribing doctors, and the medical and healthcare community that the use of Avandia creates a roughly 50% greater risk of heart attack and heart disease-related death, Plaintiff and the Class were denied the opportunity to make fully informed decisions about whether and how to include Avandia on their formularies and paid for more prescriptions than they otherwise would have paid for and/or paid for Avandia that would have been sold at a lower price had market forces been allowed to operate unfettered by Defendants' violations.

9. In addition to the resulting personal injuries, unnecessary deaths, and the profound implications for public health, the financial toll that Defendants' false and deceptive marketing of Avandia has had on Plaintiff and the Class has been dramatic. Relying upon Defendants' promises of superior treatment and better cardiovascular outcomes compared with the older diabetes drugs, third-party payors of Avandia have paid a hefty premium. Defendants' omissions of, and deliberate misrepresentations related to, critical information regarding the serious health risks associated with Avandia have caused financial harm to Plaintiff and the Class, who hereby seek compensatory, punitive and statutory damages, injunctive relief to prevent Defendants from continuing their unlawful activities, reasonable attorneys' fees and such other just relief as the Court may award.

PARTIES

10. Plaintiff UFCW Local 1776 and Participating Employers Health and Welfare Fund ("UFCW Fund") is a citizen of the Commonwealth of Pennsylvania, and has its principal place of business at 3031B Walton Road, Plymouth Meeting, Montgomery County, Pennsylvania. UFCW Fund is an "employee welfare benefit plan" and an "employee benefit plan" as defined in Employee Retirement Income Security Act (ERISA), 29 USC §§ 1002(1), 1002(3), 1003(a). As such, UFCW Fund is a legal entity entitled to bring suit in its own name pursuant to 29 USC § 1132(d). UFCW Fund is a not-for-profit-trust, sponsored by and administered by a Board of Trustees, established and maintained to provide comprehensive

health care benefits to participant-workers, who are employed under various collective bargaining agreements, and to their dependents.

11. UFCW Fund's participant-workers are members of the United Food and Commercial Workers Union, Local 1776, which represents 24,000 members who work in southeast, northeast and central Pennsylvania, northeast Maryland and southern New York in supermarkets, drug stores, food processing plants, government services, manufacturing facilities, nursing homes, professional offices and Pennsylvania's Wine and Spirits Shops.

12. UFCW Fund has paid all or part of the cost of its participants' purchases of Avandia during the Class Period, as defined herein. Pursuant to its plan, Plaintiff, through a pharmacy benefit manager ("PBM") and a third-party administrator, purchased prescription drugs for its participants and provided coverage for medical testing and visits to physicians. Each plan participant has a prescription drug plan identification card which he/she presents at a participating pharmacy. The pharmacy collects a co-payment from the participant and bills the UFCW Fund (through a prescription benefit manager) for the remaining cost of Avandia purchases. Avandia prescriptions would have been restricted or priced differently if the FDA, Plaintiff's PBM and/or prescribers had truthful and complete information about the drug. Plaintiff has been injured as a result of the unlawful conduct of Defendant as alleged herein.

13. Defendant GlaxoSmithKline PLC ("GSK PLC") is a United Kingdom corporation with its principal place of business at 980 Great West Road, Brentford, London Middlesex TW8 9 GS, United Kingdom. GSK PLC either directly or through its wholly-owned subsidiaries, designs, produces, markets and promotes the drugs Avandia, Avandamet and Avandaryl in Pennsylvania and nationwide. Defendant GlaxoSmithKline USA is a wholly-owned subsidiary of GSK PLC. At all relevant times, GSK PLC acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting in the course and scope of their actual and apparent authority, agency, duties or employment.

14. Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline (GSK USA) is a Pennsylvania corporation with its principal place of business at One Franklin Plaza, P.O. Box 7929, Philadelphia, Pennsylvania. GSK USA designs, produces, markets and promotes the drugs Avandia, Avandamet and Avandaryl in Pennsylvania and nationwide. GSK USA is a whollyowned subsidiary of GSK PLC. At all relevant times, GSK USA acted by and through its agents, servants, workers, employees, officers and directors, all of whom were acting in the course and scope of their actual and apparent authority, agency, duties or employment.

15. Defendant, GSK USA along with defendant GSK PLC conducts substantial business in Philadelphia, Pennsylvania, including the sale and distribution of Avandia and has sufficient contacts with Pennsylvania or otherwise intentionally avails itself of the laws and

markets of Pennsylvania, so as to sustain this Court's jurisdiction over Defendants.

JURISDICTION AND VENUE

16. This Court has subject matter jurisdiction pursuant to 28 U.S.C. § 1332 (d)(2), which provides federal district courts with original jurisdiction over civil actions in which the matter in controversy exceeds the sum or value of $5,000,000, exclusive of interest and costs, and is a class action in which "any member of a class of Plaintiffs is a citizen of a state different from any defendant."

17. This Court has further jurisdiction over this action pursuant to the Class Action Fairness Act, because at least one member of the Class is a citizen of a different state than the Defendants and the aggregate amount in controversy exceeds $5,000,000.00, exclusive of interest and costs.

18. Venue is proper in this District under 28 U.S.C. § 1391 because Defendants engaged in substantial conduct relevant to Plaintiff's claims within this District, and have caused harm to Plaintiff and Class members residing within this District. Defendants received [MISSING TEXT]

FACTUAL ALLEGATIONS

I. Avandia's Factual Background

19. Type 2 diabetes, the most common form of diabetes,

results from the body's failure to produce enough insulin (insulin deficiency) and/or inability to use insulin properly (insulin resistance). Insulin is necessary to process and remove blood sugar. Without insulin, sugar builds up in the bloodstream and cells are starved for energy. This can cause tissue breakdown, which can lead to numerous health dangers, such as kidney failure, blindness, and amputations. Furthermore, diabetics are at an increased risk, as compared to non-diabetics, for atherosclerosis, heart attacks, strokes, kidney disease, and nervous system damage. Thus, drugs designed to treat diabetes must be sensitive to, among other things, diabetics' preexisting cardiovascular risks.

20. Weight loss has a dramatic effect on diabetes management. As little as 5% loss of body weight results in a disproportionate decrease in insulin resistance and improved glycemic control. Sustained weight loss often results in a marked improvement or even a cure for Type II diabetes and is, therefore, the most important first line therapy for the disease. Therefore, virtually all physicians treating Type II diabetes concur that weight maintenance is a critical piece of the treatment puzzle. Any benefit derived from other diabetic treatments, such as drugs like insulin, Avandia and metformin, must be weighed against the risks and possible side effects of such treatments, including such treatments' association with weight gain.

21. Exercise also has therapeutic effects on Type II diabetes. Exercise lowers insulin resistance and improves glycemic control. Studies have shown that walking as little as 150 minutes a week lowers insulin resistance.

22. In the 1990s, pharmaceutical companies developed, manufactured and produced a class of drugs known as thiazolidinediones (TZDs). TZDs enable the body to more effectively use insulin by reducing insulin resistance in the body.

23. Prior to TZDs, the "first line" of drug treatment for Type 2 diabetes consisted of established and inexpensive oral medications, primarily sulfonylureas and metformin. Indeed, metformin is recognized as the "gold standard" in Type 2 diabetes treatment. In its "Standards of Medical Care in Diabetes 2009," the American Diabetes Association noted that the consensus for treating Type 2 diabetes begins with "intervention at the time of diagnosis with metformin in combination with lifestyle changes and continuing timely augmentation of therapy with additional agents (including early initiation of insulin therapy) as a means of achieving and maintaining recommended levels of glycemic control."

24. The other principal drug treatment available before the introduction of TZDs was injected insulin.

25. Metformin works principally by limiting the production of sugar in the liver; it has no effect on insulin release. Prior to TZDs, metformin was the oral antidiabetic drug of choice in patients with Type II diabetes, except those who were thin and elderly. Metformin was associated in patients with renal complications with an enhanced risk of lactic acidosis, a potentially fatal condition. However, that condition was easily avoided and exceedingly rare; there were zero cases of lactic acidosis observed in the

more than 6,000 patients participating in the clinical trials for the metformin drug Glucophage. Further, a published review of the risks of metformin shows that there were no deaths from lactic acidosis in metformin patients for whom the drug was indicated. Patients treated with metformin, unlike those treated with sulfonylureas, do not exhibit weight gain, a significant advantage for Type II diabetes sufferers. Rather, metformin promotes weight loss in persons with Type II diabetes. Its other side effects include nausea and upset stomach.

26. The sulfonylureas work on the insulin-producing cells to increase the release (but not the production) of insulin. Sulfonylureas were used as first line agents, particularly in thin or elderly patients. Sulfonylureas have been associated in rare instances with low blood sugar and often promote weight gain. The benefits of sulfonylurea therapy are shown to decrease over time as approximately 50% of patients will need additional treatments after 2-5 years of taking these drugs. Sulfonylureas combine well with other diabetes drugs for maximum effect on blood sugar.

27. As a diabetic's disease progresses, medications may be added to the patient's regimen, including the use of insulin.

28. At all times material hereto, the TZD preparations available in the marketplace included Avandia (rosiglitazone), Avadamet (rosiglitazone and metformin), Avandaryl (rosiglitazone and glimepiride), Actos® (pioglitazone) and Actosplus® met (pioglitazone and metformin).

29. Avandia was approved by the FDA on May 25, 1999 as an oral antidiabetic agent which acts primarily by increasing insulin sensitivity. Avandia is recommended and prescribed for the management of Type II diabetes mellitus, also non-insulin-dependent diabetes mellitus ("NIDDM") or adult-onset diabetes. Type II diabetes is a serious and life threatening disease that affects about 18 to 20 million Americans. Avandia has been used by millions of individuals in the United States.

30. On April 23, 1999, just prior to the launch of Avandia in the U.S. market, Defendants issued a press release stating that they had entered into a co-promotion agreement with Bristol-Myers Squibb, the maker of Glucophage brand of metformin, to jointly promote Avandia in the U.S. It also stated that Defendants "recently entered into a co-promotion deal for Avandia with [Bristol-Myers Squibb], and this relationship will drive the acceptance of the drug in the USA, according to [Defendants], which forecasted Avandia sales to reach $2 billion in 2003." Avandia remains key to [Defendants'] near-term fortunes given that it accounts for 44% of incremental pharma sales growth" between 1998 and 2005.

31. Avandamet was approved by the FDA on October 10, 2002 as a combination of Avandia and metformin in one single pill and is also recommended to treat NIDDM.

32. Avandaryl was approved by the FDA on November 23, 2005 as a combination of Avandia and glimepiride in one single pill and also recommended to treat NIDDM.

33. Since 1999, the FDA has been monitoring several heart-related adverse events (*e.g.* fluid retention, edema, and congestive heart failure ("CHF")) based on signals seen in controlled clinical trials and from post-marketing reports.

34. Despite the fact that Avandia lowers blood glucose levels in Type II diabetes patients, numerous studies have shown that use of Avandia dramatically increases the risk of cardiovascular events in Type II diabetes patients. Nevertheless, Defendants assured physicians that these studies only illustrate a very slight increase in low-density lipoprotein, "bad cholesterol" or LDL levels, and continued to falsely and fraudulently promote Avandia as a superior, effective, and safe drug for diabetic patients.

35. In 2001, the FDA requested that Defendants make a change to Avandia's prescribing label to warn doctors that the drug could cause fluid retention. Around the same time, Defendants were drafting an article, later published in the American Heart Association's journal *Circulation* by Dr. Steven Haffner of the University of Texas Health Science Center at San Antonio, that argued that the class of drugs that includes Avandia could significantly *reduce* cardiovascular risk factors in animals. Shortly after the FDA request, Defendants' sales representatives gave oral presentations at a medical convention denying the existence of serious risks associated with Avandia The FDA responded with a letter to Defendants warning that the sales representatives and marketers should stop denying or minimizing the risks of heart attacks and heart-related diseases in patients.

36. In 2005, according to a June 1, 2007 *Bloomberg* article, Defendants performed an internal review and found that Avandia raised the risk of heart attacks by 31 percent.

37. In April 2006, the FDA required labeling for Avandia to be updated to include new data in the WARNINGS section about a potential increased incidence of heart attack and heart-related chest pain in some patients. This change was based on the results of a controlled clinical trial in patients with existing CHF. A higher number of heart attacks or angina was observed in patients treated with Avandia compared to those treated with a placebo.

38. On May 9, 2006, Defendants provided the results of its internal analyses to the FDA. The FDA didn't immediately release those studies to the public, because its officials "didn't necessarily agree with some of the methodology used," according to Dr. Janet Woodcock, head of the FDA Center for Drug Evaluation and Research.

39. Although Defendants gave the information to the FDA and included the information on its website amid more than 2,000 studies, Defendants did not highlight the information. Defendants stated that the heart-risk studies, including Defendants' own, were flawed and they are not obligated, or legally required, to highlight every study done on its drugs. Defendant GSK PLC Chief Executive Officer Jean-Pierre Garnier told reporters at the company's annual meeting on May 23, 2007 in London, "Why would you publicize it...We don't

publicize every submission we make to the Food and Drug Administration."

40. It was seven years after the drug was approved, and the dangers of Avandia had still not been made sufficiently clear to the public. The FDA was sitting on the new analyses, and GSK, the FDA discovered during an investigation by its inspections unit in the fall of 2007, had failed to report clinical data and other material from 15 tests of Avandia by the end of 2006, according to a March 25, 2008, warning letter to the company. With Defendants and the FDA maintaining exclusive control over the full database of information on Avandia's effectiveness and safety, there was little that independent scientists and physicians could do to assuage their growing concerns about the drug.

41. In April, 2007, using published literature, the FDA website and a clinical trials registry maintained by Defendants, Cleveland Clinic cardiologist, Steven E. Nissen, M.D., and Kathy Wolski, M.P.H. tabulated and compiled a meta-analysis of Avandia clinical studies with a duration of longer than 24 weeks, using randomized control groups not receiving Avandia, and having available the outcome data for myocardial infarction and death from heart attacks and heart-related diseases. Dr. Nissen and Dr. Wolski used 116 potentially relevant studies, and 42 trials that met the inclusion criteria. The study, published in The New England Journal of Medicine, revealed that Avandia was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from heart attacks and heart-related

diseases that had borderline significance. Some have hinted that Dr. Nissen's loyalties were to Defendants' competitors since Dr. Nissen is leading a clinical trial studying Avandia's rival drug, Actos. However, Dr. Nissen has consulted in the past for Defendants on other matters. Moreover, Dr. Nissen gives drug-industry payments to charity. Nevertheless, instead of a responsible and reasoned response to this study, Defendants took steps to encourage aggressive dispensation of Avandia for persons to whom it posed grave health dangers.

42. By chance, the New England Journal of Medicine had chosen as a prepublication reviewer of the Nissen article Dr. Haffner, the University of Texas doctor who was the lead author on the 2001 *Circulation* paper that had suggested that Avandia's class of drug could decrease cardiovascular risk. Dr. Haffner faxed a copy of the draft article to Defendants.

43. Having obtained a leaked copy of the Nissen paper, Defendants prepared for its release in advance, and subsequent to its publication, Defendants engaged in a massive publication and advertising campaign designed to sway physician and consumer confidence. This marketing campaign consisted of advertisements, promotional literature for the offices of doctors and other health care providers, and other promotional materials to be provided to potential users of Avandia. Despite knowledge of the widespread health dangers of Avandia, Defendants failed to effectively warn consumers about the use of this drug as compared to other diabetes medications which posed much lesser health risks.

44. On May 21, 2007, the FDA issued a new safety alert that addressed potential safety issues stemming from the pooled analysis of previously completely controlled clinical trials demonstrating a significant increase in the risk of heart attack and heart-related diseases in patients treated with Avandia.

45. On May 23, 2007, consistent with recommendations made by senior FDA staff at an internal regulatory briefing held in April 2007, the FDA issued letters to Defendants [MISSING TEXT]

46. On and around June 5, 2007, Defendants took out full-page ads in newspapers such as the *Washington Post* and *The New York Times* speaking directly to the consumers of Avandia.

47. On June 6, 2007, the FDA announced a meeting to be held on July 30, 2007 to discuss the risk of heart attacks and heart-related disease associated with thiazolidinediones, with a focus on Avandia, as presented by the FDA and Defendants.

48. On July 30, 2007, two FDA advisory panels, the Endocrine and Metabolic Advisory Committee and the Drug Safety and Risk Management Advisory Committee, met to evaluate Avandia and similar antidiabetic drugs. The panels recognized the increased risk for heart attacks posed by Avandia and voted overwhelming, 20-3, urging the FDA to consider raising its warning level to black-box status or implementing a patient registration program.

49. On August 14, 2007, the FDA increased the warning for Avandia's increased risk of heart failure to a black-box warning.

50. Despite such overwhelming evidence, Defendants still insisted and insist to this day that Avandia does not increase the risk of heart attack. "We don't believe that a warning about heart attack should be on the label," states Dr. Andy Zambanini, the company's director of clinical development.

51. Notwithstanding Defendants' refusal to acknowledge the dangers of Avandia, on November 14, 2007, the FDA issued its toughest warning against Avandia linking it to heart attacks and a second black-box warning was added to the Avandia label warning of the increased risk of heart attacks and other myocardial ischemic events.

52. On July 13-14, 2010 an FDA advisory panel again reviewed scientific data and information on the safety and efficacy of Avandia and, for a second time, raised safety questions about Avandia. However, unlike in its first review, the panel did not issue a clear recommendation to the FDA about what it should do as a result of the findings. The 33-member panel voted 18-6, with some abstentions, that there are "significant safety concerns" that Avandia raises the risk of heart attack and chest pain. The panel also voted 21-3 that Avandia's risk was higher than that of Actos. 12 panel members recommended that Avandia be taken off the market. Ten others said its black-box warning should be enhanced and additional restrictions

added to its use, which could include requiring special physician and patient education on the medication. Seven voted for the warning merely to be enhanced, without restrictions on its prescription. Three said it should be sold with warnings unchanged. One member abstained.

53. According to a *Wall Street Journal* article, endocrinologist Dr. David Capuzzi of Philadelphia, one of the three panelists who recommended that Defendants be allowed to continue marketing Avandia with no further restrictions or warnings is a paid speaker for the drug company, reportedly having been paid $14,750 to promote Defendants' drug Lovaza.

54. The panel also recommended that GSK continue the Thiazolidinedione Intervention With Vitamin D Evaluation, or TIDE, trial, which compares Avandia and Actos. However, on July 21, the FDA announced that the TIDE trial had been placed on partial clinical hold, meaning no new patients can be enrolled until the agency gives further notice.

55. While the FDA often follows advisory panel recommendations, it is not required to do so, and the FDA's decision on whether to take Avandia off the market could take weeks or months.

56. In addition, a study posted online June 28, 2010 in JAMA found that compared to Actos, Avandia was associated with an increased risk of stroke, heart failure, and all-cause mortality in patients age 65 and older. GSK rejected these conclusions and still maintains that Avandia is safe.

57. In the summer of 2010, Defendants agreed to settle approximately over 10,000 Avandia personal injury lawsuits filed by plaintiffs alleging they suffered personal injury and/or wrongful death due to taking Avandia for over $500 million.

58. Since its introduction, Avandia has come to be used on a regular basis by millions of individuals worldwide, including at least one million in the United States. Avandia was Defendants' second best-selling product in 2006, generating revenues of $1.4 billion, with a further $246 million generated from the combination products Avandamet and Avandaryl. A one-month supply of Avandia sells for between $90 and $170. Consumers either paid for the drug completely out of pocket or paid their co-pay. The typical third-party payor co-payment was approximately $135-$140. This represented a dramatic increase in third-party payors' costs of drug therapy for Type II diabetes patients. Previously, the most prevalent oral drug therapy for Type II diabetes had been metformin, which had a typical retail price for a one-month prescription of approximately $45-$55, of which the typical third-party payor co-payment was approximately $40-$50.

II. Approval, Labeling, and Promotion of Pharmaceuticals Marketed in the United States

59. Pursuant to the Federal Food, Drug and Cosmetic Act ("FDCA"), a pharmaceutical must be approved by the Food and Drug Administration ("FDA") before it is transported or distributed across state lines. *See* 21 C.F.R. § 301; *see also* 21 U.S.C. § 331. The Center for

Drug Evaluation and Research is a division of the FDA and conducts limited research in the areas of drug quality, safety, and effectiveness.

60. In order for the FDA to approve a drug, the manufacturer must show that a drug is "safe for use" and effective for all "conditions prescribed, recommended, or suggested" on a drug's label. *See* 21 C.F.R. § 99.103; *see also* 21 C.F.R. § 201.5.

61. Because the FDA will only find a drug product to be safe and effective if the proposed use is supported by well-designed, placebo-controlled clinical trials that establish a causal relationship to a statistically significant degree, a statement that a drug is "effective" or "works" or "has been proven to ..." is understood to mean that well controlled clinical studies support the use. To make such a statement without such clinical trial proof is misleading. Further, failure to inform physicians that no placebo controlled clinical trials support a representation of drug efficacy is a violation of a pharmaceutical company's obligation to disclose. *See* 21 C.F.R. § 99.205.

62. The FDA allows pharmaceutical manufacturers to provide information for dissemination to health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, and Federal and State government agencies after a submission of an application to the FDA, if such information is fair and balanced and under the following circumstances:

- The information concerns a drug that has been approved, licensed and cleared for marketing by the FDA;

- The information is in the form of an unabridged copy of a peer-reviewed scientific or medical journal article or reprint, or an unabridged reference publication that pertains to a clinical investigation involving the drug and that is considered scientifically sound by experts who are qualified to evaluate the product's safety or effectiveness;

- The information does not pose a significant risk to the public health;

- The information is not false or misleading; and

- The information is not derived from clinical research conducted by another manufacturer, unless permission is received from that manufacturer. *See* 21 C.F.R. § 201.6(a). *See also* 21 U.S.C. § 360aaa.

III. Alternatives to Avandia

63. Physicians are free to prescribe FDA-approved drugs as they see fit to treat any condition or symptom for their patients. The medical community generally encourages physicians to prescribe the safest, most effective and cost-efficient treatment for their patients. Research and studies have illustrated that physicians can prescribe safer and/or equally effective alternatives to treat diabetes other than Avandia.

64. Another prescription medication for Type II diabetes mellitus is pioglitazone (Actos®), a drug manufactured and promoted by Takeda Pharmaceuticals North America.

65. On March 15, 2000, Dr. John B. Buse of the University of North Carolina School of Medicine, the incoming president of the American Diabetes Association, wrote Dr. Jane Henney, the Commissioner at the FDA stating that "the frequency of mild and serious adverse events that I have seen with troglitazone [Rezulin®] and pioglitazone [Actos®] is comparable to or less than the number I have observed with other antidiabetic agents." Rezulin was withdrawn from the U.S. market on March 21, 2000. Dr. Buse strongly suggested that Actos is one of the most effective, safe and beneficial drugs in its class and Avandia may be associated with less beneficial cardiac effects or even adverse cardiac outcomes.

66. A prospective, randomized trial of cardiovascular outcomes, called Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROACTIVE) shows lower cardiac risks with Actos. The trial examines whether the observed risks of Avandia represent a "class effect" of thiazolidinediones. Actos was studied, and the primary end point, a broad composite that included coronary and peripheral vascular events, showed a beneficial trend with the use of Actos (hazard ratio, 0.90; P=0.095). A secondary end point consisting of myocardial infarction, stroke, and death from any cause showed a significant effect favoring Actos (hazard ratio, 0.84; P=0.027). Notably, Actos appears to have more favorable effects on lipids, particularly triglycerides, than does Avandia.

67. Additionally, a June 23, 2007 *Bloomberg* article discusses a study that found that Actos may lower the risk of heart attack and death by 44 percent in diabetic patients with kidney disease. The findings, from a subgroup of patients enrolled in a previous study, were reported at the June 23, 2007 meeting of the America Diabetes Association in Chicago. In a separate study, Actos reduced inflammation and blood clots more than a placebo. Thus, Actos may have fewer cardiac risks than Avandia and prove to be a safer alternative to Avandia for the treatment of Type II diabetes mellitus.

68. However, physicians have been misled by Defendants to believe that Avandia is superior in its effectiveness and safety to other equally effective and, safer alternatives like Actos. As a result of Defendants widespread misleading marketing and promotion of Avandia's superior safety and effectiveness over safer and equally effective alternative drugs like Actos, many physicians are less inclined to prescribe patients these alternative antidiabetic drugs.

69. Yet a June 18, 2007 *USA Today* article discusses an increased number of physicians discontinuing Avandia prescriptions and are instead prescribing Actos as an alternative to the diabetes medication. "Before the journal [*The New England Journal of Medicine*] posted the study May 21, U.S. doctors were writing about 240,000 prescriptions [of Avandia] per week, Glaxo spokeswoman Alice Hunt says. That has dropped to about 215,000 to 220,000 per week. Glaxo estimates the number of people taking Avandia have dropped from about 1 million to

900,000 in the USA." Additionally, new prescriptions for Avandia dropped 40% as a result of Dr. Nissen's study. New prescriptions are defined as the first prescription a doctor writes for a patient who might already have been taking Avandia under a different doctor's care. "Prior to Nissen's study, U.S. doctors wrote about 80,000 new Avandia prescriptions weekly; that number has dropped to about 55,000, Hunt says." The *USA Today* article explains that physicians are switching patients to Actos as an alternative.

70. Another study conducted by researchers at Harvard University and published in February 2010 in the journal of the American Diabetes Association, Diabetes Care, found that Avandia increases a diabetic's heart attack risk by 30% compared with the older diabetes drug sulfonylurea. And when compared with metformin, Avandia increases a diabetics' heart attack risk by 120%.

IV. Defendants' Marketing and Promotion of Avandia as Safe and Effective

71. From its product launch to the present, Defendants engaged in widespread fraudulent statements and conduct, and pervasive false and misleading marketing, advertising and promotion of Avandia, spending hundreds of millions of dollars to further these efforts. Defendants deceived physicians, consumers and others in the medical community regarding the comparative efficacy of Avandia to other medications designed to control Type II diabetes mellitus. Defendants failed to warn — and affirmatively misled physicians, consumers, Third-party Payors, and

others in the medical community regarding Avandia's association with increased risk of heart attacks and heart-related diseases.

72. Defendants were required to provide fair and balanced information whenever they engaged in promotional activities. Promotional activities encompass not only written material but all presentations. Defendants knew that whenever they were required to provide fair and balanced information, they were required to provide any negative information as well as positive information about their drug."

73. Since 1999 Defendants have spent millions on Direct-to-Consumer ("DTC") print and television advertising, aimed at convincing patients to request Avandia from their doctors. Defendant's marketing campaign also targeted doctors as well as the individuals and groups responsible for selecting the drugs covered by health coverage plans and included on pharmacy formularies. Defendants sought to influence these targets through, among other tactics, print media, misleading promotional materials, lavish company-sponsored dinners, and "conferences" at posh resorts. Defendants produced and distributed "studies" whose sole purpose was to advance the company's marketing message and which were intended to, and did, deceive diabetics, medical professionals, and the general public. Defendants also employed sales representatives who spread the Avandia message by calling on thousands of physicians throughout the country, paid speakers to likewise deliver the company's messages about the drug, and writers who engaged in the "ghostwriting"

of medical and scientific articles in order to advance the Avandia agenda. "Ghostwriting" is a particularly insidious practice where a drug company authors a purportedly independent scientific paper and then pays someone else to place their name on the paper to give the appearance of independence and objectivity by suggesting that the independent person or group, and not the drug company, performed the research and authored the paper.

74. Defendant's Avandia message had two key components. First, Defendants propagated the message that Avandia was better at lowering blood sugar than other established drugs. That is, Avandia had superior efficacy. Defendants also represented that patients could stay on Avandia longer than the older drugs. Second, Defendants represented that, unlike the older diabetes drugs, Avandia had the additional benefit of actually lowering diabetics' cardiovascular risks. The notion that Avandia would actually lower diabetics' cardiovascular risk was critical to Avandia's marketing. Defendants needed justification for the steep price difference between Avandia and the older established diabetes drugs. Defendants, however, knew or should have known that these representations were false, misleading, and likely to deceive. At best, Defendants had no data to support these claims. At worst, they were wholesale fabrications.

75. In today's health care market, physicians face extreme time constraints in determining which drugs and treatments are best. Physicians, along with formulary committees, purchasers, Pharmacy Benefit Managers ("PBMs") and policy makers rely upon a variety of

trusted sources including independent studies for such information. However, often unbeknownst to the public, many of these sources are directly controlled or heavily influenced by pharmaceutical manufacturers such as Defendants. All of these sources contain susceptibilities that have been exploited by pharmaceutical manufacturers such as Defendants.

76. Among the tactics employed by Defendants were plans to create studies designed to illustrate Avandia's superior profile to both (a) placebo and (b) comparable medications designed to control Type II diabetes mellitus while providing funding to engage "key opinion" and "thought" leaders in publication worthy trials.

77. Upon information and belief, this scheme was carried out by: making false statements to consumers, Third-party Payors, physicians and pharmacies concerning the efficacy and safety of Avandia; training Defendants' employees in methods to conceal negative information regarding Avandia to avoid detection of their activities by Plaintiff and the Class, and instructing Defendants' employees to conceal negative information regarding Avandia to avoid detection of their activities by Plaintiff and the Class.

Incentives to Develop Deceptive Medical Literature

78. Upon information and belief, Defendants sought out, and provided incentives and funding to, doctors and researchers to develop deceptive and misleading medical literature for use in marketing.

79. A June 5, 2007 *The Bulletin* article reveals that Dr. Anne E. Peters, a diabetes expert who runs a clinic for Los Angeles County and who is affiliated with the University of Southern California medical school had previously received money from Defendants as a speaker on behalf of Avandia. Dr. Peters resigned from that position when she enumerated her concerns about Avandia's risks. Dr. Peters said that five years ago, she removed Avandia from the formulary (the list of preferred drugs) maintained by the Los Angeles Clinic. That meant that patients would receive Actos instead of Avandia. "The Avandia people, it was just so surprising, they asked me what I wanted to keep Avandia on the formulary." "Dr. Peters said that she asked the company to establish a database at the clinic that would track the outcomes of patients on both drugs. When she asked for the database, which would have cost several thousand dollars, she said a company representative replied: 'That's all you want? Other doctors ask to go to the Caribbean.'" Dr. Peters said, "They wanted to do everything but approve my request."

80. Despite being on notice of the potential for deadly heart attacks and heart-related diseases, Defendants each opted for the bare minima of well-tailored clinical trials, of limited duration, such that little to no side effects were likely to be revealed. Thus, instead of conducting true scientific research in good faith to legitimately test the efficacy and safety of Avandia, Defendants focused on creating narrowly tailored studies specifically designed to enhance commercial value.

Appendix I

Physician Intimidation of Dr. Buse

81. A June 7, 2007 *Washington Post* article discusses Dr. Buse, who told a congressional hearing that in 1999, officials at SmithKline Beecham (a former pharmaceutical company that merged with GlaxoWellcome in 2000 to form GlaxoSmithKline PLC) began pressuring Dr. Buse after he questioned whether Avandia caused heart problems. In or around 1999, Dr. Buse was a presenter at a continuing medical education symposium sponsored by Eli Lilly and Company at which Dr. Buse was asked to discuss new therapies in diabetes. At the symposium, Dr. Buse presented slides stating that Avandia increased the risk of heart-related activities by 50 percent.

82. Thereafter in 1999, Dr. Buse wrote a letter to Tadataka Yamada, MD, the Chairman of Research and Development of Pharmaceuticals at SmithKline Beecham. In the 1999 letter, as the Associate Professor of Medicine and Director of the University of North Carolina Diabetes Care Center, Dr. Buse wrote that he reviewed every paper published and available on diabetic class medications on humans, and identified that Avandia has the potential to increase heart attacks and heart-related diseases, where the increase in heart-related deaths are the "relevant endpoints to be examined in the clinical trial program if one were to look for those kinds of changes in endothelial function." "I strongly believe that the rosiglitazone data set supports this kind of clinical decision making. I believe that caution is required until additional data are available."

83. Shortly after Avandia's FDA approval, Defendants took action against Dr. Buse. In a June 1999 e-mail mail, Dr. Tachi Yamada, Defendant's head of research at the time, wrote to colleagues at the company:

> I plan to speak to Fred Sparling, [Dr. Buse's] former [department] chairman[,] as soon as possible. I think there are two courses of action. One is to sue [Dr. Buse] for knowingly defaming our product…the other is to launch a well planned offensive on behalf of Avandia....

Additionally, Defendants prepared and sent a letter to Dr. Buse, to be signed by him, "retracting" his statements about Avandia's increased cardiovascular risk.

84. In Dr. Buse's June 6, 2007 published statement to the U.S. House of Representatives Committee on Oversight and Government Reform, Dr. Buse recounts that after writing the 1999 letter to Defendants, Defendants called Dr. Buse numerous times emphasizing that there were some in the company who believed that Dr. Buse's actions were scurrilous enough to attempt to hold Dr. Buse liable for a $4 billion loss in market capitalization.

85. As promised, Dr. Yamada called Dr. Sparling at the University of North Carolina. Shortly thereafter and in response to GSK's pressure, Dr. Buse wrote to Dr. Yamada, "clarifying" his position on Avandia. In his letter, Dr. Buse stated that he continued to "believe as a clinical scientist that the null hypothesis should be that [Avandia] has the potential to increase cardiovascular

events." Despite this belief, Dr. Buse stated that he had learned of "implied threats of lawsuits from my chairman [Dr. Sparling] and James Huang," who was then a product manager with a GSK, and, succumbing to the threat of legal action, Dr. Buse asked GSK to "call off the dogs." Under pressure, he signed the so-called "retraction letter," which had been authored for his signature by GSK officials.

86. The concealment of Dr. Buse's assessment regarding the dangers of Avandia was encouraged by Defendants, and Defendants continued to overplay favorably misleading articles regarding Avandia's side effects.

87. On March 15, 2000, Dr. Buse followed up his apprehension towards Avandia use by writing Dr. Jane Henney, the Commissioner at the FDA, regarding his concern "about the safety of rosiglitazone in light of its consistent negative impact on lipids documented in the FDA registration data as well as a worrisome trend in cardiovascular deaths and severe adverse events in the subjects exposed to rosiglitazone versus active comparators."

88. In the 2000 letter to the FDA, Dr. Buse suggested that the FDA act forcefully to prevent the rampant abuse of clinical trial data by Defendants. Dr. Buse had knowledge that:

a. Defendants overstated the safety of the drug with respect to heart attacks and heart-related

diseases, and that Defendants claimed that Avandia had been uniquely studied on patients with preexisting heart disease, but in fact these patients were excluded in clinical trials as Dr. Buse was the principle investigator in one of their trials;

b. Defendants show misleading materials for professional education touting the lipid lowering effects of Avandia when the data are from a small subset of patients with triglycerides over 400 mg/dl. "The overwhelming preponderance of data suggests that at high doses the drug is most likely to increase triglycerides than lower them;" and

c. Defendants' representatives "detailed" primary care doctors on the safety and efficacy of the antidiabetic medications to suggest that Avandia's "safety and clinical efficacy is greater when there is no comparative data available."

89. In Dr. Buse's letter to the FDA, he states that "there is something pervasive and systematic that I detect in my travels regarding the marketing of rosiglitazone [Avandia]. I have to admit that now when I give CME [continuing medical education] lectures, I spend about half my time discussing these issues. It seems to me that blatant selective manipulation of data has obfuscated relatively straightforward conclusions evident from the FDA data sets."

90. Defendants knew that the dissemination of information about Avandia's true cardiovascular risks would devastate its efforts to promote the drug. When doctors like Dr. Buse raised suspicion about Avandia's safety, Defendants set out to intimidate and silence them. Such was the official finding of the United States Senate's Finance Committee, which concluded in January, 2010 that Defendants had executed "an orchestrated plan to stifle the opinion" of Dr. Buse, and that the intimidation scheme involved "executives at the highest level of Defendants, including then and current CEO Jean-Pierre Gamier."

Dr. Nissen's May 2007 NEJM Article Jolts Defendant's Fraud into High Gear

91. In a December 2007 floor speech, Senator Grassley revealed that Dr. Steve Haffner, a professor of medicine at the University of Texas Health Sciences Center, San Antonio, and a consultant for Defendants, leaked to Defendants the draft of a study critical of Avandia that was to appear in the New England Journal of Medicine (NEJM). Dr. Haffner was entrusted with a confidential copy of the manuscript draft because he was peer-reviewing the study for the NEJM.

92. The study's lead author, Dr. Steven Nissen, professor of cardiology at the Cleveland Clinic, found that Avandia was associated with a 43-percent increased risk of heart attacks, one of the main health outcomes physicians hoped to avoid by treating diabetic patients with medication. According to documents produced by Defendants, the leaked manuscript was widely disseminated within the

Company, and allowed Defendants to launch a public relations plan to protect Avandia, a multi-billion dollar product.

93. The Committee staff reviewed documents showing that over 40 executives at Defendants' received and/or learned of the results in the leaked study, including then CEO Dr. Jean-Pierre Garnier; head of research, Dr. Moncef Slaoui; Vice President of Corporate Media Relations, Nancy Pekarek; and Defendants' Senior Advisor, Sir Colin Dollery.

94. Before Dr. Nissen's study on Avandia was published, Defendant's statistical experts were examining the study for potential flaws. In addition, Defendant's officials were drafting "key messages" to undermine the main conclusion of the Nissen study. Defendants had already published several large trials on Avandia (rosiglitazone) including studies named ADOPT and DREAM. After Nissen's study was published, Defendants began publicly referencing those trials, as well as another trial called RECORD, in what appeared to be an effort to further repudiate any link between Avandia and heart attacks.

95. RECORD is a study Defendants had been conducting for several years. Defendants later published the interim results of the RECORD trial in what appeared to be an attempt to cast doubt on Nissen's results. However, according to the Senate Finance Committee, internal Defendant's emails indicate that Defendant's executives, not the study's independent steering committee, made the final decision to publish the RECORD trial results.

Further, according to the Committee, based on a review of emails, it can be argued that the authors of the RECORD trial appeared more concerned about countering claims that Avandia may be associated with heart attacks, than in trying to understand the underlying science. While circulating a draft of a manuscript on the RECORD trial, one of the authors wrote to his colleagues, "[W]hat's to stop [Nissen] adding the events from RECORD to his meta-analysis and re-enforcing his view?"

96. Further, after the authors of the RECORD study submitted their paper to the NEJM, one of the peer reviewers and several of the NEJM editors replied, "an explanation for the continued use of [Avandia] is needed in this manuscript."

97. Committee investigators also learned that Defendants were aware since at least 2004 that the RECORD trial was statistically inadequate, or "underpowered" to answer questions regarding cardiovascular safety. Such "inconclusive" results could be favorable to Defendants and the marketing strategy for Avandia. Further, experts were advising Defendants since 2004 about the possible biological mechanisms related to why Avandia may cause an increased risk for heart attacks.

98. However, Defendants appeared eager to design studies to prove that Avandia was safer than its competitor ACTOS (pioglitazone), which is manufactured by Takeda.

99. At a July 30, 2007, safety panel on Avandia, Food and Drug Administration (FDA) scientists presented an analysis estimating that Avandia use was associated with approximately 83,000 excess heart attacks since the drug came on the market. Had Defendants considered Avandia's potential increased cardiovascular risk more seriously when the issue was first raised in 1999 by Dr. Buse, as well as by some of their own consultants in later years, some of these heart attacks may have been avoided.

Response to the Nissen Study

100. In March 2007, Defendants held a meeting with company officials and academic advisors to discuss several studies on Avandia and its cardiac risks and benefits. Several presentations were made about studies on Avandia's possible cardiac risk. During the discussion of a Defendants' meta-analysis (integrated study) and a study Defendants commissioned by Ingenix, Defendants noted that the academic advisors stated the following:

> Dr. NAME REDACTED commented that the [cardiovascular] effect seen in the Integrated Clinical Trials Analyses with rosiglitazone was small but real, and that it is counter to the proposed [cardiovascular] benefits associated with Avandia. Dr. NAME REDACTED agreed, noted that all data point to rosiglitazone having a hazard ratio greater than unity.…Dr. NAME REDACTED summarized the discussion on the Integrated Clinical Trials data by stating that rosiglitazone causes weight gain and edema, leading to a greater number of events.

Moreover, during the discussion of the DREAM trial, a cardiologist from Stanford stated:

> [T]he diabetes prevention afforded by rosiglitazone was very impressive, but there was no cardioprotective benefit. He then asked **what the point of diabetes prevention is if there is no cardiovascular benefit.** [Emphasis added]

When discussing ADOPT, the academic advisors concluded that, "The data in ADOPT and DREAM as well as in the CV Clinical Trials are consistent in indicating a signal for heart failure and ischemic events." According to Defendants internal documents, Defendants' experts were discussing problems with DREAM as early as 2006.

101. Around this same time, Dr. Steven Nissen began studying the potential cardiac risks of Avandia, by reviewing data found in previously published studies. He placed several requests to Defendants asking for patient level data on several studies published about Avandia. However, Defendants would provide the requested data only if Dr. Nissen agreed to use one of Defendants statisticians for the analysis. Dr. Nissen refused to use the Company's statistician, citing a need to maintain independence.

102. On May 2, 2007, Dr. Nissen submitted an analysis of 42 published and unpublished clinical trials on Avandia to the NEJM for peer review and publication. NEJM then sent confidential copies of the study to several independent

experts, including Dr. Steve Haffner, to peer review the Nissen study. According to NEJM, peer reviewers must acknowledge in writing that the material they are reviewing is confidential, not to be shared with others, and is to be destroyed or returned to the medical journal after a review is completed.

103. However, the very next day, May 3, 2007, Dr. Haffner faxed Dr. Nissen's unpublished study to a GSK executive. Dr. Haffner wrote "confidential" on the fax cover sheet and checked a box marked "urgent."

Leaked Manuscript and a Massive Defensive Campaign

104. One day after receiving the unpublished study from Dr. Haffner, Defendants produced a detailed, 8-page analysis of Dr. Nissen's paper, weeks before the paper's public release. The Defendant's statistician attempted to find deficiencies in Nissen's meta-analysis but noted, "The selection of trials therefore appears to be thorough, though others more familiar with the trials can comment more knowledgeably."

105. The Defendants' statistician also performed a regression analysis on each study that Dr. Nissen used in his meta-analysis to see if the effects of myocardial infarction and/or cardiovascular death would still appear. The statistician stated, "These results are very similar to the conclusion from the [Nissen] paper using the Peto method. As such there is no statistical reason for disregarding the findings as presented."

106. The Defendant's statistical analysis was circulated to senior executives within the company. These executives then discussed several large trials, such as RECORD, DREAM and ADOPT that Defendants could use to combat Dr. Nissen's analysis. RECORD was an ongoing trial that had not been published. On the other hand, DREAM and ADOPT were published and were included in Dr. Nissen's analysis. Defendants, as well as the FDA, had also performed their own meta-analyses.

107. Both meta-analyses were consistent with Dr. Nissen's results. On May 8, 2007, Dr. Moncef Slaoui, head of research at GSK, wrote an email to several company executives. Commenting on the meta-analyses, he wrote:

> —FDA, Nissen and GSK all come to comparable conclusions regarding increased risk for ischemic events, ranging from 30 percent to 43 percent! —FDA and Nissen (but no final data from GSK [to] date) reach the conclusion of an [hazard ratio] for death (CHF + IHD) of 1.72 or 1.75!

108. Dr. Slaoui also noted in this email that a GSK commissioned study by Ingenix did not find any significant problems with rosiglitazone. Ingenix had performed an epidemiological study of Avandia. While medical experts place greater importance on a clinical trial over an epidemiological study, Dr. Slaoui sought to highlight the Ingenix results. He also expressed concern that a beneficial effect was observed (6 to 16 percent) in the PROactive study of ACTOS in high-risk cardiovascular

disease patients. Dr. Slaoui asked, "How can we reinforce the value of the [Ingenix] study? The FDA criticizes the fact that we excluded cases of sudden cardiac death." He then asked his team to strategize further on the issue:

> [W]hat studies could we offer the FDA to further assess the contradictory data between the integrated study and the two others? can we expand Record? Propose something else (very high risk patients? ok? ethical?), compare to Actos for superiority on some end points?

109. By May 9, 2007, GSK began drafting "key messages" to counteract the findings of the Nissen study. In an email, Defendant's Vice President for Corporate Media Relations noted, "The Nissen analysis is one way of looking at the data, but it doesn't reflect all we know about the safety of this medicine.... [W]e are not seeing a proven link between Avandia and increased cardiovascular deaths...."

110. On May 9, 2007, Sir Colin Dollery, a senior consultant to Defendants, laid out many of the problems with Avandia in an email to Dr. Slaoui and others. He wrote:

> To a great extent, the numbers are the numbers, the [Nissen] analysis is very similar to our own.... We cannot undermine the numbers but I think they can be explained so we must concentrate on effective risk management.

Later in the email, Sir Dollery noted that the PROactive study on ACTOS (pioglitazone) is undermining Avandia (rosiglitazone). He wrote:

> The main argument here lies in that pioglitazone [ACTOS] causes a small reduction of LDL [Low-Density Lipoprotein] and rosiglitazone causes a small elevation....[W]e should search for evidence that the use of statins in diabetics generally and with rosiglitazone in particular has risen steeply over the time the thiazolidenediones have been on the market. We can then argue that any problem that existed with LDL is now controlled or controllable. It would also be worth obtaining the evidence that the use of antihypertensives in diabetics has also been increasing rapidly.

111. On fluid retention and links with cardiovascular disease, Sir Dollery mentioned a possible mechanism to explain how Avandia may cause heart attacks. He wrote:

> If [fluid retention is] substantial in patients with an impaired myocardium it can lead to [cardiac heart failure] and to cardiac ischemia by decreasing myocardial efficiency in the face of existing coronary disease.... If there is criticism of GSK it might be that we were a bit slow off the [mark] in making firm recommendations about the use of diuretics…and recognizing that the sodium retention is mediated via distal renal tubular ENaC.

112. On May 21, 2007, NEJM published online Dr. Nissen's meta-analysis that found a link between Avandia and heart attacks. That same day, Defendants responded, "GSK strongly disagrees with the conclusions reached in the NEJM article, which are based on incomplete evidence and a methodology that the author admits has significant limitations." Instead, Defendants highlighted the results of company sponsored trials like RECORD as "the most scientifically rigorous way to examine the safety and benefits of a medicine."

113. In a subsequent letter to The Lancet, GSK maintained that the RECORD trial is "compelling evidence" for the safety of Avandia. On May 23, 2007, a GSK official emailed members of the RECORD steering committee, the group of independent academics overseeing the study, to alert them of a teleconference to be held the following day. GSK officials also emailed internal talking points to help guide their discussion with the steering committee. However, it appears that prior to receiving input from the steering committee, Defendants had already decided to publish the RECORD results. Later that same day, a GSK official wrote, "...we've decided to disclose the results...."

114. The following day, GSK officials discussed potential problems if the academics on the RECORD steering committee raised concerns about publishing the interim results of the RECORD trial. In an email, one GSK official wrote:

> [I]f the Steering Committee [SC] are reluctant to publish— Frank and I will argue the case that there is a balance to be drawn between very negative press coverage and specific reassurance for the patients in the study. However if the SC believe that publishing interim data will fatally damage their ability to bring the study to a completion— Frank and I will bring that opinion with reasons back to GSK, before pursuing the line— that a decision has been made—live with it.

115. A few hours after this email, the acting chair of the RECORD steering committee, contacted the NEJM to inquire about publishing the interim results. The editor of the NEJM responded that the journal would be interested in publishing the study.

116. By May 29, 2007, several authors of the RECORD study began passing around a manuscript, discussing the results, and offering suggestions for improvement. The third author on the RECORD study wrote, "We do not find more myocardial infarctions with rosiglitazone treatment, but again there is a tendency supporting the Nissen argument. It is important to stress that it does not affect cardiovascular death." That same day, a senior author of the RECORD study, wrote:

> There are several striking issues:
>
> (1) The HR ratio (and 95 percent CI) for MI in RECORD is not inconsistent with Nissen's—

> and he had more events; what's to stop him adding the events from RECORD to his meta-analysis and re-enforcing his view?...
>
> (2) Same is for CV death, although the number of events in RECORD and in the meta-analysis are similar and at least in RECORD the HR is in the other direction!
>
> (3) Manuscript looks to downplay the 239 percent INCREASE in HF. I have taken the liberty of doing some rewording.

117. Once a study is submitted to a journal, the journal editors then send the article to several experts for peer-review. After the review, the editors send the peer-review comments back to the author. On June 1, 2007, the RECORD authors received a reply from NEJM regarding their earlier submitted manuscript. The NEJM editors summarized the issues presented by all 8 peer reviewers, many of whom were highly critical of the study in their reply.

118. Reviewer A, along with other reviewers, asked that the authors "modify the language in multiple locations in the manuscript to tone down your conclusions." The editor also noted, "[I]n the opinion of all the readers, the data that you present are completely compatible with the results of the meta-analysis by Nissen and the meta-analysis for myocardial ischemic events posted on the GSK Web site."

119. Regarding the comments of Reviewer B, the editors wrote that for myocardial infarction the "estimates in the RECORD trial and the Nissen meta-analysis" overlap in their confidence intervals, meaning that they found a similar trend for heart attacks. They continued, "The editors feel strongly that your data do not support the statement that the RECORD results for MI contradict the Nissen meta-analysis; this statement must be removed or modified."

120. Reviewer C noted that the RECORD trial is not blinded, and pointed out "the serious problem of the low event rate, especially for MI events, in this study." He continued to ask, "Do you have an explanation for the very low event rate" This reviewer also noted the "need to greatly tone down your language to reflect the substantial level of uncertainty in the data."

121. Reviewer D questioned the need for keeping rosiglitazone on the market. "The editors also agree that an explanation for the continued use of rosiglitazone is needed in this manuscript."

122. The NEJM published the interim analysis of the RECORD study on July 5, 2007. The GSK study authors concluded that the data was "insufficient" to find a link between Avandia and heart attacks.

123. However, an editorial by the NEJM questioned the RECORD study, as well as several of Defendants' studies of Avandia such as DREAM and ADOPT. The authors of the editorial wrote, "The DREAM trial and

ADOPT focused largely on marketing questions and failed to address questions of myocardial infarction-related risk or benefit directly." In addition, the editorial noted that the RECORD trial had "several weaknesses in design and conduct" including a lack of blinding when treatment was assigned. The authors also pointed out that events of myocardial infarction would have been a preferred clinical endpoint for the study. Studies are normally designed to evaluate certain clinical endpoints or disease symptoms such as heart attack, tumor size, or depression. The authors also added that the RECORD study was not powered (or designed) to detect a myocardial infarction as an endpoint.

124. On June 6, 2007, the House of Representatives Committee on Oversight and Government Reform held a hearing on Avandia. Despite mounting criticism of the RECORD trial, Dr. Slaoui again highlighted the study in his sworn testimony. "I will say that we found the RECORD data which we published yesterday in the New England Journal of Medicine very reassuring, recognizing that it is interim and therefore not fully conclusive."

125. That same day, Defendants dismissed the idea that Dr. Nissen's study spurred the publication of the RECORD interim results. Instead, the Company placed blame on the media. In talking points created for its sales force, GSK stated, "Because of the widespread media coverage of the NEJM [Nissen] meta-analysis and the confusion it has created, the RECORD Steering Committee decided it was important to publish the interim analysis in the interests of patient safety."

126. Regarding its competitor Takeda, which sells ACTOS, Defendants advised its sales force if asked questions about the PROactive study:

> Please do not discuss Actos or the Proactive study with your physicians. For questions regarding Actos or the Proactive study, healthcare providers should contact Takeda. GSK's focus is on Avandia. Communicate the key points from the interim analysis of RECORD to your physicians.

The Record Trial as a Marketing Tool for Competition

127. Despite attempts to highlight the RECORD study, it appears that Defendants knew for years that the study was "underpowered," *i.e.*, the study did not provide sufficient data to test for cardiovascular safety; and executives appeared more concerned about designing a study to limit competition from ACTOS. Such evidence can be found in a GSK slide presentation, emails, and other documents created in 2004 to 2006.

128. For instance, in an undated slide show, apparently created in 2004, Defendants noted that RECORD does not have sufficient "power." The slide presentation also noted that GSK was trying to create studies to counter the PROactive study on ACTOS that Takeda planned to release.

Appendix I

Slide number 6 titled, "PROactive: Potential Impact," noted that Defendant's challenge was to "maintain share in growing market over next 2-3 years."

Slide number 8 reads:

Situation Summary:

- We have a gap

—In 2005 Actos will have some [cardiovascular] outcome data

- To keep our share of the growing class

—Additive benefit to RECORD of non-inferiority result

- However this gap may be permanent

—RECORD has a lower event rate than expected PROPOSAL

Fill this gap with an outcome study reporting in 2007

Slide number 10 compared the potential impact of a new GSK study to counter the marketing danger of PROactive and the potential impact on sales in UK pounds in 2010. The slide reads: "Timely CV Outcomes data would more than fill the RECORD 'potential gap' and would have twice the impact on our sales than PROVerDate active."

The final slide pointed out that GSK should do a "kick off study only after review of results from Proactive in Sept 2005 and assessing benefits/risks."

129. A second instance is found in a June 2005 email where GSK executives discussed the need for a study to counter PROactive. In the email, a GSK official wrote, "Clearly no patients will be recruited until [we] have made a decision based on the go-no go criteria from the PROactive data. However, there is a great deal of EU commercial push to initiate this study in 2005."

130. A third case is found in an internal GSK document outlining an upcoming meeting for December 2004. Several points were discussed about RECORD and PROactive. Regarding RECORD, the document noted that RECORD has "low events rates." This means that the study did not have the statistical "power" to give sufficient cardiovascular event data. The document also stated, "PROactive results to be coming soon—need to be able to respond to a variety of different outcomes. Communications plan in place for various possible outcomes of PROactive."

131. A fourth instance is found in a briefing document for a June 2005 meeting on Avandia's cardiovascular plan. The document notes several "important limitations of RECORD."

—the study will not be available until 2009

> —the current observed rate for the primary endpoint is very much lower (approximately 3.5 percent per annum) than that anticipated in the original protocol (11 percent per annum).

132. A fifth case is found in another of Defendants' emails. On July 26, 2005, Defendants' officials began emailing each other about potential problems with RECORD and how the PROactive study by Takeda on ACTOS will create problems for Avandia. One official wrote:

> Ron Krall [then GSK Chief Medical Officer] has asked Lawson [unknown GSK executive] to provide an urgent update to David Stout [then GSK President of Global Pharmaceutical Operations] regarding RECORD. In particular he has asked for our "intent to manage information flow in Europe to manage the competitive situation." Clearly we can provide a summary of the communications around PROactive but I wonder if you could put a few sentences together regarding the communications piece around RECORD.

133. A sixth incident is documented in July 2005, when Defendants' officials continued expressing concerns about cardiovascular problems with Avandia and potential problems arising from the PROactive study which focused on positive findings with ACTOS. Defendants held a meeting on July 18, 2005 to discuss the need for a study to compete with PROactive. The briefing document from

this meeting discussed the "European Commercial Need" for a study:

> A recently completed evidence gap analysis completed by the Metabolic Centre of Excellence has identified the need for the rapid generation of clinical endpoint data to support the superiority of rosiglitazone [Avandia] for the prevention of future cardiovascular clinical events in patients with [type 2 diabetes mellitus]. Publication of the PROactive data may result in important commercial disadvantage in Europe. We therefore have the opportunity to start a CV outcomes study with the aim of getting superiority data in 2007.

134. The document also noted that Defendant's studies provided insufficient data on cardiovascular outcomes:

> The primary endpoint in RECORD is powered for noninferiority and taking into account the low observed event rate, it is unlikely that this study will demonstrate any potential for [Avandia] combination to be superior in terms of the primary endpoint compared to SU+MET combination therapy. DREAM and ADOPT are collecting CV safety data, but these are low risk populations and it is unlikely that [Avandia] will be superior to controls for the prevention of CV events.

135. In a May 21, 2007 FDA press release, the FDA announced that safety data from controlled clinical trials have shown that there is a potentially significant increase in the risk of heart attack and heart-related disease in patients taking Avandia. The FDA press release also mentioned an interim analysis of data from the RECORD trial and unpublished re-analyses of data from DREAM, which provide contradictory evidence about the risks in patients treated with Avandia.

136. However, the May 21, 2007 FDA press release also mentions that Defendants provided the FDA with a pooled analysis (meta-analysis) of 42 randomized, controlled clinical trials in which Avandia was compared to either placebo or other antidiabetic therapies in patients with Type II diabetes. The pooled analysis revealed that patients receiving short-term (most studies were 6-months duration) treatment with Avandia may have a 30-40 percent greater risk of heart attack and other heart-related disease than patients treated with placebo or other antidiabetic therapy. "This would be a significant concern since patients with diabetes are already at an increased risk of heart disease." Patients suffering from Type II diabetes have a 20.2 percent risk of experiencing a heart attack within seven years.

137. The May 21, 2007 publication of the New England Journal of Medicine's article *Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes,* which was written by Cleveland Clinic cardiologists Dr. Nissen and Dr. Wolski, called Avandia's safety into question. This published journal

article links Avandia to a potential increase in the risk of heart attacks compared to other diabetic drugs or a placebo. The meta-analysis was based on a review of more than 40 existing clinical studies involving nearly 28,000 patients. Defendants' own meta-analysis also found indications of increased risk, but Defendants concluded that the number of adverse events was low, and therefore drew no negative conclusion from that data analysis. Thus, Defendants deliberately concealed critical information regarding the serious health risks associated with Avandia.

138. In a May 31, 2007 *Washington Post* article, Dr. Nissen criticized Defendants' study stating that the company's study referred to such small subsets of data, so that Defendants could not draw a negative conclusion. "Somebody went back and looked for something that would support their contention. This is not a scientifically proper way to analyze data."

139. On May 23, 2007, the FDA disclosed that it asked Defendants to add a more prominent "black box" label warning to address the risks of a different side effect, heart failure, on all Avandia products. Heart failure is a chronic condition in which the heart has trouble pumping blood, as opposed to a heart attack, where blood is prevented from flowing from the heart and immediate death can result. The labels on Avandia already warned patients about heart failure, though not with black box labels.

140. On May 29, 2007, the FDA held a Stakeholder Meeting to discuss the recent safety alert for Avandia. The meeting was composed of invited patients, health care professionals, and government agencies and the FDA's goal was to ensure that "the nuanced message" about Avandia was both clearly articulated and reached the correct audience.

141. A June 5, 2007 *Houston Chronicle* article states that Defendants released the results of a study that compares Avandia and two other diabetes drugs in nearly 4,500 people around the world. The first few years of a six-year study shows similar rates of heart-related deaths and hospitalizations among those on Avandia versus those on the other drugs. Some doctors said the results showed slightly more heart problems with Avandia — a bad sign even if the difference was so small that it could have occurred by chance alone. "This study, which was designed to show the benefit of rosiglitazone (Avandia), if anything shows the opposite," said Dr. David Nathan, chief of diabetes care at Massachusetts General Hospital. Dr. Nathan had no role in the study or financial ties to any diabetes drug makers.

142. Further, Avandia's pre-marketing clinical trials were specifically designed to produce similar rates of heart-related adverse events and do not support the assertion that the medication is less likely to cause dangerous heart-related conditions. Manufacturers, including Defendants, fund clinical trials, where the manufacturers create and control the research design. In a 2001 study published in the *New England Journal*

of Medicine, researchers found that more than two-thirds of the academic institutions accepted research contracts that prohibit researchers from changing the research design of sponsors, including Defendants. Half of the medical centers allowed commercial sponsors to "draft manuscripts reporting the research results, with the investigators' role limited to review and suggestions for revision."

143. In a 2001 issue of the *New England Journal of Medicine,* thirteen editors of the world's most prestigious medical journals issued an alarming joint statement highlighting the extent and consequences of the commercial takeover of clinical research. In the report they state:

> Until recently, academic, independent clinical investigators were key players in design, patient recruitment, and data interpretation in clinical trials. The intellectual and working home of these investigators, the academic medical center, has been at the hub of this enterprise, and many institutions have developed complex infrastructures devoted to the design and conduct of clinical trials. But, as economic pressures mount, this may be a thing of the past. Investigators may have little or no input into trial design, no access to the raw data, and limited participation in data interpretation. These terms are draconian for self-respecting scientists, but many have accepted them because they know that if they do not, the sponsor will find someone else who will.

144. FDA regulations and industry standards prohibit Defendants from misrepresenting scientific evidence that supports (or fails to support) claims that their respective drug is safe and effective for a specific condition. Thus, anecdotal evidence of a drug's usefulness for a given condition could not be presented as the equivalent of the findings of a well-designed clinical trial. Failure to comply with these standards violates Defendants' legal duty to provide accurate and non-misleading information.

145. Nevertheless, despite conclusive and reliable studies that conclude Avandia's adverse effect of increased heart attack, heart failure, and heart-related disease, and the FDA's stringent regulations and recommendations to Defendants regarding the black box warning of Avandia's adverse side effects, Defendants continued and continue to mislead and deceive consumers by placing full page advertisements in newspapers nationwide declaring that Defendants have "conducted an unprecedented number of clinical trials in order to continuously evaluate the safety of *Avandia*, including its impact on the cardiovascular system. The response to this commitment from well-informed experts and researchers has been encouraging."

146. Defendants deceive consumers and members of the medical community by overemphasizing controlled and misleading favorable studies, while failing to disclose studies illustrating Avandia's dangerous side effects. Defendants have and continue to expose vulnerable patients with Type II diabetes, to an increased risk of heart attack and heart-related diseases.

147. Defendants have unfairly and unjustly profited from their failure to adequately inform physicians, consumers, and the medical and health care community that Avandia could cause profound and long-term injury and, in some cases, death.

V. Fraudulent Concealment of Defendants' Conduct

148. The applicable statute of limitations regarding the claims of Plaintiff and the Class has been tolled by Defendants' fraudulent concealment of their unlawful, conspiratorial deceit, as alleged in detail throughout this Complaint.

149. As evidenced by the allegations in this Complaint, Defendants have employed and continue to employ practices and techniques of secrecy in order to avoid detection of, and to fraudulently conceal, their deceptive and conspiratorial behavior regarding the safety and efficacy of Avandia and Avandia's risks associated with heart attacks and heart-related diseases.

150. Despite taking on the responsibility to reveal this information to the general public, Defendants have kept such information hidden.

151. As such, Plaintiff and the Class were not effectively alerted to the existence and scope of this industry-wide fraud and were not on notice of their potential claims until shortly prior to the filing of this Complaint.

152. Plaintiff and the Class could not have acquired such knowledge through the exercise of reasonable diligence.

153. Through their public statements, marketing and advertising, Defendants' self-concealing scheme and affirmative conduct to perpetuate their fraud deprived Plaintiff and the Class members of actual or presumptive knowledge of facts sufficient to put them on notice as to their potential claims.

VI. Injury to Plaintiff and the Class

154. Defendants' deceptive and misleading marketing scheme increased the number of prescriptions of Avandia written and filled during the Class Period. Because Defendants withheld material information about the true safety and efficacy of Avandia, the prescribing physicians did not have the knowledge necessary to make informed decisions regarding Avandia prescriptions. Plaintiff and the Class, unaware of Defendants' scheme, paid for these prescriptions. Although more effective, safer, and less expensive alternatives are available, Defendants' promotion and marketing of Avandia's safety and effectiveness has been highly successful, resulting in Defendants receiving billions of dollars in profits, representing ill-gotten gains to which Defendants were not entitled.

155. Plaintiff and similarly-situated Class members bear the ultimate responsibility of paying for their Avandia prescriptions.

156. PBMs prepare a "formulary," which is a list of the drugs that are approved for coverage by their third-party payor clients, such as Plaintiff and Class members. In order for a drug to be listed on the formulary, it must be assessed by the PBM for clinical safety, efficacy, and cost effectiveness. Further, where a PBM finds that a drug has an advantage over competing drugs, that drug is given a preferred status on its formulary.

157. The level of preference on the formulary corresponds with the amount that a plan participant must contribute as a co-payment when purchasing a drug — the higher the preference, the lower the co-payment, the more likely that the drug will be purchased by a prescription plan's beneficiary in lieu of a cheaper or more cost effective alternative, and *vice versa.* As such, the higher a drug's preference on the formulary, the more likely it is for a doctor to prescribe that drug. This system is well known to pharmaceutical manufacturers, including Defendants.

158. Due to the large number of drugs purchased through third-party payors, it is vital to a drug manufacturer's economic interests to have its product listed on as many formularies as possible.

159. By directly and falsely promoting Avandia as safe and effective for Type II diabetes and training their sales forces and representatives to avoid alerting the FDA to their activities and to dismiss any safety concerns raised by physicians, Defendants influenced PBMs to place Avandia on their formularies and at a higher preference on those formularies.

160. Defendants falsely promoted Avandia as safe and effective directly to PBMs in order to get Avandia placed on, or placed more favorably than its competitor drugs on the PBM formularies.

161. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors relied on the Defendants' misrepresentations of Avandia's safety. Physicians relied on the Defendants' misrepresentations of Avandia's safety in prescribing the drug for their patients. Patients relied on the Defendants' misrepresentations of Avandia's safety in purchasing the drug. PBMs and pharmacy and therapeutic committees relied on the Defendants' misrepresentations of Avandia's safety when approving and/or placing Avandia on formularies. Third-party payors relied on the Defendants' misrepresentations of Avandia's safety in reimbursing and/or paying for prescriptions of Avandia for their members.

162. Therefore, Defendants' failure to adequately inform consumers, third-party payors and those in the medical community that the use of Avandia dangerously increases the risk of heart attacks and heart-related diseases, and their false and misleading promotion of Avandia's efficacy over competing less expensive antidiabetic drugs, causes patients and third-party payors to pay for Avandia, which is neither safer nor more effective than other less expensive antidiabetic drugs.

163. But for Defendants' actions, third-party payors would not have paid for Avandia but would instead have paid for safer, equally efficacious drugs like metformin and/or sulfonyureas.

Appendix I

CLASS ACTION ALLEGATIONS

164. Plaintiff brings this suit as a Class action pursuant to Rule 23(b)(2) and (b)(3) of the Federal Rules of Civil Procedure, on behalf of a Class consisting of:

> All health insurance companies, third-party administrators, health maintenance organizations, self-funded health and welfare benefit plans, third-party payors and any other health benefit provider, in the United States of America and its territories, which paid or incurred costs for the drug Avandia, for purposes other than resale, since May 25, 1999. Excluded from the Class are employees of Defendants, including its officers or directors, and the Court to which this case is assigned.

165. The proposed Class is sufficiently numerous, as thousands of members of the Class were induced to pay for Avandia through Defendants' scheme. The Class members are so numerous and dispersed throughout the United States that joinder of all members is impracticable. The Class is composed of thousands of third-party payors, and the disposition of their claims in a Class action will benefit both the parties and the Court. It is estimated that in 2007, at least half a million individuals nationwide received prescriptions for Avandia. Defendants sell millions of doses of Avandia in the United States every year, and thus the Class is sufficiently numerous to make joinder impracticable, if not outright impossible. The Class members can be identified by, *inter alia,* records maintained by Defendants, pharmacies, and PBMs.

166. Common questions of law and fact exist as to all members of the Class and predominate over any questions affecting solely individual members of the Class. Among the questions of law and fact common to the Class members are:

a. whether Defendants misrepresent the safety and efficacy of Avandia, to the financial detriment of the Class;

b. whether Defendants engaged in a conspiracy to promote the sales of and suppress adverse information about Avandia;

c. whether Defendants' acts and omissions violate, *inter alia,* the Pennsylvania Unfair Trade Practices and State Consumer Protection Laws;

d. whether Defendants make material misrepresentations of fact, or omit to state material facts regarding the severe heart attacks and heart-related diseases and risks associated with Avandia, which material misrepresentations or omissions operate as a fraud and deceit upon the Class;

e. Whether Plaintiff and the class paid more for Avandia than for other efficacious drugs that were available at a cheaper price;

f. whether persons who took Avandia are at increased risk of severe and permanent injuries,

including liver damage and/or failure, cardiac damage and visual impairment and damage;

g. whether, in marketing and selling Avandia, Defendants failed to disclose the dangers and risks to the health of persons ingesting the drug;

h. whether Defendants failed to warn adequately of the adverse effects of Avandia;

i. whether Defendants misrepresented in their advertisements, promotional materials and other materials, among other things, the safety, potential side effects and convenience of Avandia;

j. whether Defendants knew or should have known that the ingestion of Avandia leads to serious adverse health effects;

k. whether Defendants adequately tested Avandia prior to selling it;

l. whether Defendants manufactured, marketed, distributed and sold Avandia notwithstanding their knowledge of the drug's dangerous nature;

m. whether Defendants knowingly omitted, suppressed and/or concealed material facts about the unsafe and defective nature of Avandia from government regulators, the medical community and/or the consuming public;

n. whether the Class has been damaged, and if so, the extent of such damages and/or the nature of the equitable relief, statutory damages, or punitive damages to which the Class is entitled;

o. whether Defendants were and are unjustly enriched by its acts and omissions, at the expense of the Class;

p. the amount of attorneys' fees, prejudgment interest, and costs of the suit to which the Class is entitled;

q. whether Defendants engaged in conduct that violates federal RICO statutes in promoting the sales of and suppressing adverse information about Avandia; and

r. whether Defendants engaged in a conspiracy to promote the sales of and suppress adverse information about Avandia in violation of federal RICO statutes.

167. Plaintiff's claims are typical of the claims of the members of the Class because Plaintiff and the Class sustained damages arising out of the Defendants' wrongful conduct as detailed herein. Specifically, Plaintiff, having expended substantial sums for the purchase of Avandia, assert claims that are typical of the claims of the entire Class, and will fairly and adequately represent and protect the interest of the Class.

168. Plaintiff will fairly and adequately protect the interests of the Class members and has retained counsel competent and experienced in class action lawsuits.

169. Plaintiff has no interests antagonistic to or in conflict with those of the Class members and therefore should be adequate as representatives for the Class members.

170. A Class action is superior to other available methods for the fair and efficient adjudication of this controversy since joinder of all members of the Class is impracticable. Furthermore, because the damages suffered by individual members of the Class may in some instances be relatively small, the expense and burden of individual litigation make it impossible for such Class members individually to redress the wrongs done to them. Also, the adjudication of this controversy through a Class action will avoid the possibility of inconsistent and possibly conflicting adjudications of the claims asserted herein. There will be no difficulty in the management of this action as a Class action.

CAUSES OF ACTION

FIRST CAUSE OF ACTION

VIOLATION OF 18 U.S.C. § 1962(C) — Avandia Promotion Enterprise

171. Plaintiffs incorporate by reference all preceeding paragraphs as if fully set forth herein.

172. Defendants are "persons" within the meaning of 18 U.S.C. § 1961(3) who conducted the affairs of the enterprise, the Avandia Promotion Enterprise, through a pattern of racketeering activity in violation of 18 U.S.C. § 1962(c).

173. The Avandia Promotion Enterprise is an association-in-fact within the meaning of 18 U.S.C. § 1961(4), consisting of Defendants, including its employees, agents and external consultants like Sir Colin Dollery and Dr. Stephen Haffner, co-promoters Bristol-Myers Squibb, and other as yet unknown consultants, marketing firms and distribution agents employed by Defendants to promote Avandia. All entities are persons within the meaning of 18 U.S.C. § 1961(3) and acted to enable Defendants to fraudulently market Avandia as scientifically proven as safe and effective. The Avandia Promotion Enterprise is an organization that functioned as an ongoing organization and continuing unit. The Avandia Promotion Enterprise was created and/or used as a tool to effectuate a pattern of racketeering activity. Each of these entities, including Defendants, is a "person" distinct from the Avandia Promotion Enterprise.

174. Each of the Defendants, in concert with other participants in the Avandia Promotion Enterprise, created and maintained systematic links for a common purpose-to aid in marketing Avandia as safe for its intended uses, while suppressing evidence to the contrary and improperly inducing physicians to prescribe Avandia. Each of the participants in the Avandia Promotion Enterprise received substantial revenue from the scheme to promote

Avandia as safe for its intended uses. Such revenue was exponentially greater than it would have been if Avandia was marketed appropriately and the true safety risks of Avandia disclosed. All participants of the Avandia Promotion Enterprise were aware of Defendants' control over the activities of the Avandia Promotion Enterprise in promoting Avandia. Furthermore, each portion of the enterprise benefited from the existence of the other parts.

175. The Avandia Promotion Enterprise engaged in and affected interstate commerce, because, *inter alia,* it marketed, promoted, sold, or provided Avandia to thousands of individuals and entities throughout the United States.

176. The named Defendants exerted control over the Avandia Promotion Enterprise and management of the affairs of the Avandia Promotion Enterprise.

177. Defendants conducted and participated in the affairs of the Avandia Promotion Enterprise through patterns of racketeering activity that includes acts indictable under 18 U.S.C. § 1341 (mail fraud), § 1343 (wire fraud), § 1512 (tampering with witnesses), and § 1952 (use of interstate facilities to conduct unlawful activity).

178. Defendants' fraudulent scheme consisted of, *inter alia*: deliberately misrepresenting the safety of Avandia so that Plaintiff and members of the Class paid for this drug to treat symptoms for which it was not scientifically proven to be safe and actively concealing and causing others to conceal, information about the true safety of Avandia.

179. Defendants' use of the mails and wires to perpetuate their fraud involved thousands of communications, including, but not limited to:

a. communications with and among the enterprise participants that misrepresented the safety and risks of Avandia amongst themselves and others;

b. communications with patients and Class Members, including Plaintiffs, inducing payments for Avandia by misrepresenting the safety and risks of Avandia;

c. receiving the proceeds in the course of and resulting from Defendants' improper scheme;

d. transmittal and receipt of monies from governmental health organizations and programs, including without limitation Medicare and Medicaid; and

e. transmittal and receipt of payments in exchange for, directly or indirectly, activities in furtherance of the Avandia Promotion Enterprise.

180. At all times during the fraudulent scheme, Defendants' and the Fraud Participants had a legal and ethical obligation of candor to and honest dealing with public and private payors, physicians and the medical community.

181. The conduct of the Avandia Promotion Enterprise described above constitutes "racketeering activity" within the meaning of 18 U.S.C. § 1961(1). Defendants' decisions and activity in connection with the Avandia Promotion Enterprise to routinely conduct its transactions in such a manner constitutes a "pattern of racketeering activity" within the meaning of 18 U.S.C. § 1961(5).

182. The above described racketeering activities amounted to a common course of conduct intended to deceive and harm Plaintiffs and the Class. Each such racketeering activity was related, had similar purposes, involved similar or the same participants, and methods of commission, and had similar results affecting the same or similar victims, including Plaintiffs and members of the Class. Defendants' racketeering activities were part of their ongoing business and constitute a continuing threat to the property of Plaintiffs and the Class.

183. Plaintiffs and members of the Class have been injured in their property by reason of these violations in that Plaintiffs and members of the Class paid hundreds of millions of dollars for Avandia that they would not have paid had Defendants not engaged in this pattern of racketeering activity.

184. The injuries to Plaintiffs and members of the Class were directly and proximately caused by Defendants' racketeering activity.

185. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors, including Plaintiffs and the Class, directly relied on the

racketeering activities of the Defendants and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the respresentations as to the efficacy and safety of Avandia as promoted by Defendants. Because Defendants controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendants' representations about Avandia. Further, Defendants perpetuated this reliance by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

186. By virtue of these violations of 18 U.S.C. § 1962 (c), Defendants are liable to Plaintiffs and the Class for three times the damages sustained, plus the costs of this suit, including reasonable attorney's fees.

187. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiffs and the Class have suffered damages. Plaintiffs and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

188. By reason of the foregoing, Plaintiffs and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts.

Appendix I

SECOND CAUSE OF ACTION

VIOLATION OF 18 U.S.C. § 1962 (d) — RICO Conspiracy

189. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

190. Section 1962(d) of RICO provides that it "shall be unlawful for any person to conspire to violate any of the provision of subsection (a), (b), or (c) of this section."

191. Defendants have violated § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c). The object of this conspiracy has been and is to conduct or participate in, directly or indirectly, the conduct of the affairs of the Avandia Promotion Enterprise described previously through a pattern of racketeering activity. The corporate defendants conspired with, *inter alia,* publicists, sales representatives, medical professionals, academics and other intermediaries to promote Avandia and suppress information about the harms known to result from Avandia use.

192. Defendants' co-conspirators have engaged in numerous overt and predicate fraudulent racketeering acts in furtherance of the conspiracy, including material misrepresentations and omissions designed to defraud Plaintiffs and the Class of money.

193. The nature of the above-described Defendants' co-conspirators' acts, material misrepresentations, and omissions in furtherance of the conspiracy gives rise to

an inference that they not only agreed to the objective of an 18 U.S.C. § 1962(d) violation of RICO by conspiring to violate 18 U.S.C. § 1962(c), but they were aware that their ongoing fraudulent and extortionate acts have been and are part of an overall patter of racketeering activity.

194. As a direct and proximate result of Defendants' overt acts and predicate acts in furtherance of violating 18 U.S.C. § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c), Plaintiffs and the Class have been and are continuing to be injured in their business or property as set forth more fully above.

195. Defendants sought to and have engaged in the commission of and continue to commit overt acts, including the following unlawful racketeering predicate acts:

a) Multiple instances of mail and wire fraud violations of 18 U.S.C. §§ 1341 and 1342;

b) Multiple instances of mail fraud violation of 18 U.S.C. §§ 1341 and 1346;

c) Multiple instances of wire fraud violations of 18 U.S.C. §§ 1341 and 1346;

d) Multiple instances of unlawful activity in violation of 18 U.S.C. § 1952.

196. Defendants' violations of the above federal laws and the effects thereof detailed above are continuing and will continue. Plaintiffs and members of the Class have

been injured in their property by reason of these violations in that Plaintiffs and members of the Class have made hundreds of millions of dollars for Avandia that they would not have made had Defendants not conspired to violate 18 U.S.C. § 1962(c).

197. Injuries suffered by Plaintiffs and members of the Class were directly and proximately caused by Defendants' racketeering activity as described above.

198. Patients, physicians, PBMs, pharmacy and therapeutic committee members, and third-party payors, including Plaintiffs and the Class, directly relied on the racketeering activities of the Defendants and the Avandia Promotion Enterprise. Plaintiff and Class members, both directly and indirectly, relied on the respresentations as to the efficacy and safety of Avandia as promoted by Defendants. Because Defendants controlled all knowledge of the tests upon which the claims of Avandia's efficacy and safety were based, all Class members, as well as other members of the medical and consuming public were obligated to rely on Defendants' representations about Avandia. Further, Defendants perpetuated this reliance by taking the steps itemized above to suppress the dissemination of any critical information about Avandia.

199. By virtue of these violations of 18 U.S.C. § 1962(d), Defendant is liable to Plaintiffs and the Class for three times the damages Plaintiffs and the Class have sustained, plus the cost of this suit, including reasonable attorney's fees.

200. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiffs and the Class have suffered damages. Plaintiffs and the Class members are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

201. By reason of the foregoing, Plaintiffs and the Class have been damaged as against the Defendant in a sum that exceeds the jurisdiction of all lower courts.

THIRD CAUSE OF ACTION

VIOLATIONS OF THE PENNSYLVANIA UNFAIR TRADE PRACTICES AND CONSUMER PROTECTION LAW ("UTPCPL"), 73 PA.C.S.A. § 201-1 *ET SEQ.*

202. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

203. At all times material hereto, Defendants were a manufacturer, marketer, seller and/or distributor of Avandia within the meaning of the Pennsylvania Unfair Trade Practices and Consumer Protection Law ("UTPCPL"), 73 Pa.C.S.A. § 201-1 *et seq.*

204. At all times material hereto, the conduct described above and throughout this Complaint took place within the Commonwealth of Pennsylvania and constitutes unfair methods of competition or unfair or deceptive acts or practices in violation of § 201-2(4), (v), (vii) and (xxi) of UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

205. The UTPCPL applies to the claims of all the class members because the conduct which constitutes violations of the UTPCPL by Defendants occurred within the Commonwealth of Pennsylvania.

206. At all times relevant and material hereto, Defendants conducted trade and commerce within the meaning of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

207. Defendants' deceptive marketing scheme concerning Avandia violates the UTPCPL because, *inter alia,* Defendants:

a. knowingly conceal, suppress, or omit material information regarding Avandia's safety and effectiveness from Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such concealment, suppression, or omission;

b. knowingly misrepresent the safety and efficacy of Avandia from Plaintiff and Class members and to their financial detriment, with the intent to induce reliance upon such misrepresentation; and

c. market, promote, and advertise Avandia as a safe and effective drug when the purported safety and efficacy is deceptive and unfounded.

208. Defendants' unlawful conduct as described herein arose, is directed, and emanates from Defendants'

headquarters to the detriment of Plaintiff and Class members.

209. Defendants' concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices has the tendency, capacity, and likelihood to deceive Plaintiff and the Class members.

210. Defendants intend, or consciously disregard, that Plaintiff and the Class members rely on its concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices, so that they are able to purchase Avandia.

211. Defendants' concealment, suppression, omissions, misrepresentations, deceptions, and unconscionable and fraudulent practices cause Plaintiff and the Class members to suffer ascertainable losses in the amount of the monies they overpay for Avandia, and/or pay for more Avandia prescriptions, without knowing the drugs' efficacy or lack thereof for which they are marketed, promoted, or advertised.

212. Defendants deceived and continue to deceive consumers. This conduct constitutes unfair or deceptive acts or practices within the meaning of the UTPCPL. This illegal conduct is continuing, with no indication that Defendants will cease.

213. Defendants' actions in connection with the advertising, marketing, selling and distribution of Avandia as set forth herein evidences a lack of good faith,

honesty and observance of fair dealings so as to constitute unconscionable commercial practices, in violation of UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

214. Plaintiff and the Class members would not have overpaid and/or paid for more Avandia prescriptions had they known of Defendants' deceptive and misleading marketing scheme, or the extent of said scheme.

215. Plaintiff and the Class members are accordingly harmed by Defendants' conduct in violation of the UTPCPL, 73 Pa.C.S.A. § 201-1 *et seq.*

216. By reason of Defendants' violations of the UTPCPL described above, Plaintiff and the Class members are entitled to recover treble damages, including but not limited to a full refund of all purchase costs Plaintiff and Class members have incurred for Avandia, in excess of what they would have spent to purchase other more effective antidiabetic drugs, plus attorney's fees and costs, along with equitable relief prayed for herein in this Complaint.

FOURTH CAUSE OF ACTION

VIOLATIONS OF STATE CONSUMER PROTECTION AND UNFAIR AND DECEPTIVE ACTS OR PRACTICES STATUTES

217. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

218. Defendants intended that Plaintiff, the Class and the medical and scientific community would rely on their materially deceptive practices and Plaintiff and the Class would purchase or pay for Avandia as a consequence of the deceptive practices, including Defendants' misleading and fraudulent marketing, and misrepresentations and omissions of material fact with respect to Avandia as set forth herein. Defendants' deceptive representations and material omissions to Plaintiff and the Class were and are unfair and deceptive acts and practices. Plaintiff and the Class were deceived by Defendants' misrepresentations. As a proximate result of Defendants' misrepresentations, Plaintiff and the Class have suffered an ascertainable loss, in an amount to be determined at trial, in that they paid millions upon millions of dollars for Avandia that they would not have paid had Defendants not engaged in unfair and deceptive conduct.

219. By reason of the conduct as alleged herein, by making false and misleading statements about Avandia's safety and effectiveness through false and/or misleading advertising, representations and statements with the intent to induce or cause reliance, Defendants violated the laws prohibiting unfair and deceptive acts and practices of the states wherein Class members reside.

220. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Alaska Stat. § 44-1522, *et seq.*

221. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Ariz. Rev. Stat. § 44-1522, *et seq.*

222. Defendants engaged in unfair competition unfair or deceptive acts or practices in violation of Ark. Code § 4-88-101, *et seq.*

223. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Cal Bus. & Prof. Code § 17200, *et seq.*

224. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of Colo. Rev. Stat. § 6-1-105, *et seq.*

225. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Conn. Gen. Stat. § 42-110b, *et seq.*

226. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of 6 Del. Code § 2511, *et seq.*

227. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of D.C. Code § 28-3901, *et seq.*

228. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Fla. Stat. § 501.201, *et seq.*

229. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Ga. Code Ann. § 10-1-392, *et seq.*

230. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Haw. Rev. Stat. § 480, *et seq.*

231. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Idaho Code § 48-601, *et seq.*

232. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of 815 ILCS § 50511, *et seq.*

233. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of Ind. Code Ann. § 24-5-0.5.1, *et seq.*

234. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of Iowa Code § 714.1b, *et seq.*

235. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Kan. Stat. § 50-623, *et seq.*

236. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Ky. Rev. Stat. § 367.110, *et seq.*

237. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of La. Rev. Stat. § 51:1401, *et seq.*

238. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation MASS. GEN. L. CH. 93A, *et seq.*

239. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MD. COM. LAW CODE § 13-101, *et seq.*

240. Defendants have engaged in unfair competition or unfair or deceptive acts or practices in violation of ME. REV. STAT. tit. 5, § 205-A, *et seq.*

241. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MICH. STAT. § 445.901, *et seq.*

242. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MINN. STAT. § 8.31, *et seq.*

243. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MO. REV. STAT. § 407.010, *et seq.*

244. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of MONT. CODE § 30-14-101, *et seq.*

245. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of NEB. REV. STAT. § 59-1601, *et seq.*

246. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Nev. Rev. Stat. § 598.0903, *et seq.*

247. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.H. Rev. Stat. § 358-A:1, *et seq.*

248. Defendants engaged in unfair competition or unfair, unconscionable or deceptive acts or practices in violation of N.J. Rev. Stat. § 56:8-1, *et seq.*

249. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.M. Stat. § 57-12-1, *et seq.*

250.Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.Y. Gen. Bus. Law § 349, *et seq.*

251. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.C. Gen. Stat. § 75-1.1, *et seq.*

252. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.D. Cent. Code § 51-15-01, *et seq.*

253. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of N.J.S.A. § 56:8-2, *et seq.*

254. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Ohio Rev. Stat. § 1345.01, *et seq.*

255. Defendants engaged in unfair competition or unfair or deceptive acts or practices or make false representations in violation of Okla. Stat. 15 § 751, *et seq.*

256. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Or. Rev. Stat. § 646.605, *et seq.*

257. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of R.I. Gen. Laws § 6-13.1-1, *et seq.*

258. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of S.C. Code Laws § 39-5-10, *et seq.*

259. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of S.D. Code Laws § 37-24-1, *et seq.*

260. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Tenn. Code § 47-18-101, *et seq.*

261. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of Tex. Bus. & Com. Code § 17.41, *et seq.*

262. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of UTAH CODE. § 13-11-1, *et seq.*

263. Defendants engaged in unfair competition or unfair deceptive acts or practices in violation of VT. STAT. ANN. TIT. 9 §2451, *et seq.*

264. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of VA. CODE § 59.1-196, *et seq.*

265. Defendants engaged in unfair competition or unfair, deceptive or fraudulent acts or practices in violation of WASH. REV. CODE. § 19.86.010, *et seq.*

266. Defendants engaged in unfair competition or unfair or deceptive acts or practices in violation of W. VA. CODE § 46A-6-101, *et seq.*

267. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of WIS. STAT. § 100.18, *et seq.*

268. Defendant engaged in unfair competition or unfair or deceptive acts or practices in violation of WYO. STAT. ANN. § 40-12-101, *et seq.*

269. As a direct and proximate result of Defendants' statutory violations, Plaintiff and Class members paid for their prescriptions of Avandia, which proximately caused them injury.

270. By reason of Defendants' violations, Plaintiff and the Class members are entitled to recover treble damages where available, including but not limited to all monies expended to purchase Avandia, in excess of what they would have spent to purchase other safer, more effective, and cheaper antidiabetic drugs, plus attorney's fees and costs along with equitable relief prayed for herein in this complaint.

FIFTH CAUSE OF ACTION

UNJUST ENRICHMENT

271. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

272. Defendants have been and continue to be enriched by their fraudulent acts and omissions alleged herein for all states wherein class members reside.

273. In exchange for payments they made for Avandia and at the time these payments were made, Plaintiff and Class members expected that the drugs were a safe and medically effective treatment for the condition, illness, disorder or symptoms for which it was prescribed.

274. Defendants voluntarily accepted and retained these payments with full knowledge and awareness that, as a result of their wrongdoing, Plaintiff and Class members paid for Avandia when they otherwise would not have done so and paid for the drug at a higher price than would have been paid for but for Defendants' wrongful conduct.

275. These fraudulent acts and omissions allow Defendants to gain billions of dollars in profits that would not have been gained but for Defendants' fraudulent acts and omissions.

276. Plaintiff and Class members and those similarly situated paid and continue to pay Defendants an amount that exceeds the value of the products identified herein as a result of Defendants' fraudulent acts and omissions.

277. Plaintiff and the Class members suffered damages due to Defendants' acts and omissions as alleged herein.

278. Defendants have and continue to be unjustly enriched as a result of their fraudulent acts and omissions.

279. Defendants lack any legal justification for engaging in a course of fraudulent acts and omissions as alleged herein at Plaintiff's and the Class' expense.

280. No other remedy at law can adequately compensate Plaintiff and Class members for the damages occasioned by Defendants' conscious choice to engage in a course of fraudulent acts and omissions.

281. Plaintiff and Class members are entitled in equity to seek restitution of Defendants' wrongful profits, revenues and benefits to the extent and in the amount, deemed appropriate by the Court and such other relief as the Court deems just and proper to remedy Defendants' unjust enrichment.

Appendix I

PRAYER FOR RELIEF

WHEREFORE, Plaintiff and the Class members, pray for relief as follows:

1. For an order certifying this matter as a class action as requested herein and a declaration that this action is a proper class action pursuant to Federal Rule of Civil Procedure 23, establishing an appropriate class or classes and finding that the Plaintiff and its counsel are proper representatives of the class;

2. For an Order appointing the undersigned counsel as Class counsel;

3. On Plaintiffs' and the Class's RICO claims, compensatory damages, and enhancement of damages Plaintiffs and the Class have sustained as a result of Defendants' conduct as may be permitted under the relevant statutes, such amount to be determined at trial, plus Plaintiffs' costs in this suit, including reasonable attorneys' fees;

4. On Plaintiff's and the Class's claims under the Pennsylvania Unfair Trade Practices and Consumer Protection Law 73 Pa.C.S.A. § 201-1 *et seq.,* three times the damages Plaintiff and the Class have sustained as a result of Defendants' conduct, such amount to be determined at trial, plus Plaintiff's costs in this suit, including attorneys' fees;

5. On Plaintiff's and the Class's Consumer Fraud Act claims, compensatory damages, and enhancement of damages Plaintiff and the Class have sustained as a result of Defendants' conduct as may be permitted under the relevant statutes, such an amount to be determined at trial, plus Plaintiff's costs in this suit, including reasonable attorneys' fees;

6. On Plaintiff's and the Class's claim for unjust enrichment, recovery in the amount of Plaintiff's and the Class's payment for Avandia, such amount to be determined at trial, plus Plaintiff's costs in this suit, including all reasonable expert fees and attorneys' fees;

7. For an order otherwise requiring Defendants to refund and make restitution of all monies acquired from the sale of Avandia to Plaintiff and the Class;

8. For injunctive relief, enjoining Defendants from continuing their misleading, unbalanced, illegal and fraudulent promotion of Avandia;

9. Awarding Plaintiff and the Class prejudgment interest on all damages;

10. Awarding Plaintiff and the Class other appropriate equitable relief;

11. Awarding Plaintiff and the Class their costs and expenses in this litigation, including reasonable attorneys' fees and expert fees; and

12. Awarding Plaintiff and the Class such other and further relief as may be just and proper under the circumstances.

JURY DEMAND

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiff demands trial by jury on all issues so triable.

Dated: August 20, 2010

Respectfully submitted,

MURRAY LAW FIRM

/s/ Douglas R. Plymale
Douglas R. Plymale
James R. Dugan, II
Stephen B. Murray, Jr.
Stephen B. Murray, Sr.
650 Poydras Street, Suite 2150
New Orleans, LA 70130
Phone: (504) 648-0180
Fax: (504) 648-0181

Appendix I

Eric L. Young
Gerard P. Egan
Egan Young
526 E. Township Line Road, Suite 100
Blue Bell, Pennsylvania 19422
Phone: (215) 367-5151
Fax: (215) 367-5143

Samuel Issacharoff
40 Washington Square South
New York, New York 10012
Telephone: (212) 998-6580

Counsel for Plaintiff