UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: VIOXX PRODUCTS LIABILITY LITIGATION	:	MDL NO. 1657
	:	SECTION: L (3)
	:	JUDGE FALLON
	:	MAG. JUDGE KNOWLES

THIS DOCUMENT RELATES TO:
STATE OF LOUISIANA, ex rel. JAMES D. CALDWELL, ATTORNEY GENERAL v. MERCK AND CO., INC., Case No. 05-3700

FINDINGS OF FACT & CONCLUSIONS OF LAW

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I. BACKGROUND AND PROCEDURAL HISTORY

Vioxx, known generically as rofecoxib, is a prescription drug used to treat chronic pain. It was designed and manufactured by Defendant, Merck. On September 30, 2004, Defendant Merck, removed Vioxx from the market after determining that the use of Vioxx increased the risk of cardiovascular thrombotic events. Thousands of lawsuits followed in both state and federal courts. On February 16, 2005, as a result of the sheer mass of these lawsuits and the potential for many more, the Judicial Panel on Multidistrict Litigation ("JPML") ordered that the Vioxx litigation be centralized, designated as an MDL, and assigned to this Court.

One of this Court's first priorities was to assist the parties in conducting effective and efficient discovery and selecting and preparing certain test cases to proceed as bellwether trials in the personal injury cases. In total, the Court conducted six Vioxx bellwether trials.[1] One of the trials resulted in a verdict for the Plaintiff, four resulted in verdicts for the Defendant and one resulted in a hung jury. During the same period that this Court conducted six bellwether trials, approximately thirteen additional Vioxx-related cases were tried before juries in the state courts of Texas, New Jersey, California, Alabama, Illinois, and Florida. With the benefit of experience from these bellwether trials, as well as the encouragement of the several coordinated courts, the parties soon began settlement discussions in earnest.

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[1] *See Plunkett v. Merck & Co.*, No. 05-4046 (E.D. La. Filed Aug. 23, 2005) (comprising both the first and second bellwether trials, as the first trial resulted in a hung jury); *Barnett v. Merck & Co.*, No. 06-485 (E.D. La. Filed Jan. 31, 2006) (third bellwether trial); *Smith v. Merck & Co.*, No. 05-4379 (E.D. La. Filed Sept. 29, 2005) (fourth bellwether trial); *Mason v. Merck & Co.*, No. 06-0810 (E.D. La. Filed Feb. 16, 2006 (fifth bellwether trial); *Dedrick v. Merck & Co.*, No. 05-2524 (E.D. La. Filed June 21, 2005) (sixth bellwether trial).

On November 9, 2007, Merck and the Plaintiff's Negotiating Committee ("PNC") formally announced that they had reached a Settlement Agreement. *See* Settlement Agreement, *In re Vioxx Prods. Liab. Litig.*, MDL 1657 (E.D.La. Nov. 9, 2007) ("Settlement Agreement"), *available at* http://www.browngreer.com/vioxxsettlement.[2] The private Settlement Agreement establishes a pre-funded voluntary opt-in program for resolving pending or tolled state and federal Vioxx claims against Merck as of the date of the settlement, involving claims of heart attack ("MI"), ischemic stroke ("IS"), and sudden cardiac death ("SCD"), for an overall amount of $4.85 billion. *Id.*

Having settled a large majority of the personal injury cases within this MDL, the Court turned its attention to government actions suits filed against Merck. Several government entities have pending litigation in this MDL, including suits brought on behalf of various states, including but not limited to Alaska, Colorado, Florida, Louisiana, Mississippi, Montana, Pennsylvania, Utah, Oklahoma, and South Carolina. These suits seek damages for monies paid by the state for Vioxx, through the state's Medicaid program. These suits are based around similar claims - that each respective state would not have approved payment for Vioxx, through their Medicaid programs, had they known of its cardiovascular risks.

On July 6 2005, the Louisiana Attorney General filed suit against Merck in state court seeking injunctive relief and damages. On August 5, 2005, Merck removed the case, after which it was transferred into the Vioxx MDL proceeding before this Court. On May 11, 2009, James D.

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[2]When the parties formally announced the Settlement Agreement, Vioxx-related discovery had been moving forward in the coordinate jurisdictions for more than six years. Over 50 million pages of documents had been produced and reviewed, more than 2,000 depositions had been taken, and counsel for both sides had filed thousands of motions and consulted with hundreds of experts in the fields of cardiology, pharmacology, and neurology.

Caldwell, the Attorney General for the State of Louisiana filed Plaintiff's Second Supplemental and Amending Complaint for Injunctive Relief and Damages ("Second Amended Complaint"). In the Second Amended Complaint, as *parens patriae* on behalf of the State of Louisiana, its citizens, and the Louisiana Department of Health and Hospitals ("LDHH"), the Plaintiff asserted claims for : 1) redhibition; 2) violations of the Louisiana Unfair Trade Practices Act ("LUTPA"); 3) violations of the New Jersey Consumer Fraud Act ("NJCFA"); and 4) unjust enrichment.

On February 19, 2010, Merck filed a motion for summary judgment seeking dismissal of all claims asserted by the Louisiana Attorney General. On March 31, 2010, the Court granted in part and denied in part Merck's motion for summary judgment against Plaintiff's claims (See Rec. Doc. No. 38797). The Court dismissed Plaintiff's claims under LUTPA, NJCFA, and for unjust enrichment and preserved Plaintiff's redhibition claim.

A bench trial was held in this matter from April 12, 2010, to April 21, 2010. The Court has carefully considered the testimony of all witnesses, including those witnesses who testified by deposition, the exhibits entered into evidence, and the record as a whole and pursuant to Rule 52(a) of the Federal Rules of Civil Procedure issues the following Findings of Fact and Conclusions of Law. To the extent that any finding of fact may be construed as a conclusion of law, the Court hereby adopts it as such and to the extent that any conclusion of law constitutes a finding of fact, the Court adopts it as such.

II. FINDINGS OF FACT

A. MEDICAL/SCIENTIFIC HISTORY AND BACKGROUND OF VIOXX

Vioxx belongs to a general class of pain relievers known as non-steroidal anti-inflammatory drugs ("NSAIDs"). This class of drugs contains well-known medications sold

either over the counter–such as Advil (ibuprofen) and Aleve (naproxen)–or by prescription–such as Daypro (oxaprozin) and Voltaren (diclofenac). NSAIDs work by inhibiting cyclooxygenase ("COX"), an enzyme that stimulates synthesis of prostaglandins, which are chemicals produced in the body that promote certain effects. (Nies Dep. 384:17-385:16, Apr. 1, 2005.)

Traditional NSAIDs work by inhibiting cyclooxygenase (COX), an enzyme that promotes pain and inflammation, and have been a longstanding treatment option for patients needing relief from chronic or acute inflammation and pain associated with osteoarthritis, rheumatoid arthritis, and other musculoskeletal conditions. However, it is well recognized that chronic use of traditional NSAIDs significantly increases the risk of gastrointestinal problems, including perforations, ulcers and bleeds ("PUBs"), causing thousands of deaths and many thousands of hospitalizations every year. (*See, e.g.*, Trial Tr. 1114:2-9, Apr. 20, 2010; Nies Dep. 386:7-18, Apr. 1, 2005.)

In the early 1990s, scientists discovered that the COX enzyme contained two forms–COX-1 and COX-2–each of which appeared to have several distinct functions. Scientists believed that COX-1 affected the synthesis or production of prostaglandins responsible for protection of the stomach lining, whereas COX-2 mediated the synthesis or production of prostaglandins responsible for pain and inflammation. This belief led scientists to hypothesize that "selective" NSAIDs designed to inhibit COX-2, but not COX-1, could offer the same pain relief as traditional NSAIDs with the reduced risk of fatal or debilitating PUBs. In addition, scientists believed that such drugs might be able to prove beneficial for the prevention or treatment of other conditions, such as Alzheimer's disease and certain cancers, where evidence suggested that inflammation may play a causative role. (Nies Dep. 384:17-385:16, Apr. 1, 2005.)

In light of these scientific developments, Merck & Co., Inc. ("Merck") and several other

pharmaceutical companies began the development of such drugs, which became known as "COX-2 inhibitors" or "coxibs." Merck developed a COX-2 inhibitor and named it Vioxx.

On November 23, 1998, Merck submitted a new drug application for Vioxx to the Food and Drug Administrations ("FDA") and requested an expedited review of its application. Six months later, on May 20, 1999, the FDA approved Vioxx for sale in the United States. (DX 73.) From its initial approval, Vioxx gained widespread acceptance among physicians treating patients with arthritis and other conditions causing chronic or acute pain.

B. VIOXX'S GASTROINTESTINAL SAFETY IS SUPERIOR TO OTHER NSAIDS

1. CLINICAL DATA INDICATES VIOXX'S GASTROINTESTINAL SAFETY RELATIVE TO OTHER NSAIDS

The totality of the data, including clinical trials of Vioxx and meta-analyses of trials of Vioxx and other COX-2 inhibitors, shows that COX-2 inhibitors, including Vioxx, pose a lower risk of gastrointestinal complications than do traditional NSAIDs. (Trial Tr. 1136:3-25, Apr. 20, 2010.)

Endoscopy studies have been a standard and well-established means of evaluating the gastrointestinal toxicity and safety of drugs in clinical trials. (Trial Tr. 313:3-14, Apr. 13, 2010.) Two endoscopy studies with a total of 1516 patients compared Vioxx to placebo and ibuprofen and found treatment with Vioxx was associated with a significantly lower percentage of patients with endoscopic gastroduodenal ulcers than treatment with ibuprofen. (DX 73, MRK-99420021418:207-209.)

Merck's pre-marketing investigation of Vioxx's gastrointestinal safety also included an analysis of pooled osteoarthritis efficacy studies. Using a predefined set of diagnostic criteria, these studies found a significantly lower incidence of perforations, ulcers and bleeds in patients

taking Vioxx, as compared to patients taking a traditional NSAID. In the pooled studies, the comparator NSAIDs were ibuprofen 2400 mg daily, diclofenac 150 mg daily, and nabumetone 1500 mg daily. (Trial Tr. 1143:1-7, April 20, 2010.) Each of these dosages was listed in the product label as an appropriate and approved dose for chronic use in the treatment of osteoarthritis. (Trial Tr. 1246:17-1247:6, 1254:4-10, Apr. 20, 2010.) The study protocols, including the dosages of comparator drugs, were approved by the FDA, which gave no indication it believed the dosing of comparator drugs was in any way improper. (*Id.* at 1247:7-13, 1250:15-1251:6; *see also id.* at 1251:11- 1254:3.)

Merck continued to study Vioxx's gastrointestinal safety after FDA approval. The VIGOR trial compared gastrointestinal outcomes in approximately 8,000 rheumatoid arthritis patients taking either 500 mg of naproxen twice daily (totaling 1000 mg of naproxen per day) or 50 mg of Vioxx daily. (Trial Tr. 1115:5-14, Apr. 20, 2010; Reicin Test. 2195:25-2196:19, Sept. 20, 2006.) Designed to perform a "rigorous testing of the GI safety of rofecoxib," VIGOR's objective was "to demonstrate that rofecoxib at twice the maximum chronic dosage would be associated with a significant reduction in confirmed clinical upper GI events." (DX 187 32:15-18, 30:1-4; Reicin Test. 2196:20-2197:2, Sept. 20, 2006.) Its primary endpoint was all clinical gastrointestinal events: perforations, ulcers, bleeding and obstruction. (Trial Tr. 1116:2-5, Apr. 20, 2010; *see also* Morrison Dep. 62:18-63:5, Dec. 18, 2003.) The comparator dose of naproxen 1000 mg daily is within the range of commonly used doses of naproxen. (*See* Trial Tr. 327:10-328:25, Apr. 13, 2010.)

Data from the VIGOR study confirmed that patients taking Vioxx 50 mg daily -- double the recommended dose for chronic use -- had approximately half the number of clinically serious perforations, ulcers and bleeds as did patients taking naproxen 500 mg twice daily -- a

recommended dose for chronic use. (Trial Tr. 1118:11-1119:10, Apr. 20, 2010.) A statistically significant reduction in confirmed gastrointestinal events was also seen in predefined subgroups of patients over 65 years old, under 65 years old, with a history of previous gastrointestinal events, without a history of gastrointestinal events, positive for the bacteria *H. pylori,* negative for *H. pylori*, and with concomitant steroid use. (*Id.* at 1124:4-1125:11.) Although there was a risk reduction in the VIGOR subgroup of patients without concomitant steroid use, the reduction was not statistically significant. (*Id.* at 1121:15-1122:7.) However, the rate of adverse gastrointestinal events in the Vioxx arm of the study was similar in both the steroid users and steroid non-users subgroups. (*Id.* at 1125:12-1126:2.)

The fact that there was not a statistically significant risk reduction for all PUBs in the steroid non-users group did not mean that Vioxx's gastrointestinal benefits relative to naproxen extended only to steroid users. (Trial Tr. 1123:12-16, Apr. 20, 2010.) There was a reduction of gastrointestinal complications in the steroid non-users group, although it did not reach statistical significance, and the most important endpoint was the entire study population, which included steroid non-users. (*Id.* at 1123:17-1124:3.) Vioxx demonstrated superior gastrointestinal safety on the basis of that endpoint. (*Id.*) As a general matter, the fact that some subgroups do not reach statistical significance does not alter the validity of a study or its outcomes. (*Id.*)

The VIGOR gastrointestinal results have been confirmed by more recent studies. A meta-analysis of Vioxx clinical studies involving approximately 17,000 patients showed that, relative to traditional NSAIDs, Vioxx use resulted in better gastrointestinal outcomes and that this benefit extended to steroid non-users. (Trial Tr. 1126:3-15, 1129:4-14, Apr. 20, 2010.)

A second meta-analysis by Rostom examined 69 clinical studies of COX-2 inhibitors and traditional NSAIDs. (Trial Tr. 1131:18-1132:20, Apr. 20, 2010.) The studies consistently

showed that COX-2 inhibitors are safer than other NSAIDs in terms of gastrointestinal side effects. (Trial Tr. 1132:21-1134:17, Apr. 20, 2010.) The authors specifically found that Vioxx reduced the risk of perforations, ulcers, obstructions and bleeds ("POBs") by 58% and PUBs by 56%. (*Id.* at 1134:18-24.)

Plaintiff contends that Vioxx is toxic to the gastrointestinal system, and that Vioxx does not differ substantially from other NSAIDs in terms of its gastric toxicity. Plaintiff argued at trial that Merck exaggerated GI benefits by using comparator NSAID dosages in their clinical trials that did not reflect real world conditions, and that Merck GI studies used clinically insignificant endpoints of endoscopic ulcers in its studies comparing GI toxicity of Vioxx to placebo and other NSAIDs. However, the weight of the evidence indicates that Vioxx has gastrointestinal benefits as compared to traditional NSAIDS and Merck's marketing of this aspect of the drug was consistent with the conclusions of their clinical trials.

2. THE VIOXX LABEL REPORTED ON THE DRUG'S GASTROINTESTINAL BENEFITS

i. THE 1999 LABEL

The Vioxx label approved by the FDA in 1999 stated: "Serious gastrointestinal toxicity such as bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, can occur at any time, with or without warning symptoms, in patients treated with nonsteroidal anti-inflammatory drugs (NSAIDs)." (DX 73, MRK-99420021422:280-82.) The label additionally cautioned that "NSAIDs should be prescribed with extreme caution in patients with a prior history of ulcer disease or gastrointestinal bleeding. . . . For high risk patients, alternate therapies that do not involve NSAIDs should be considered." (*Id.*)

Vioxx's 1999 gastrointestinal warning did not make claims about Vioxx's gastrointestinal

safety relative to other NSAIDs. (DX 73.) Rather, the label included a paragraph noting that it was "unclear" how the rates of gastrointestinal complications found with traditional NSAID usage applied to Vioxx. (*Id.* at MRK-99420021422:296-97.) The paragraph provided data about the number of "serious upper GI event[s]" in 3,357 patients who had received Vioxx in clinical trials of six weeks to one year at daily doses ranging from 12.5 mg to 50 mg and noted that "[a]pproximately 23% of these 3357 patients were in studies that required them to be free of ulcers at study entry. It is unclear if this study population is representative of the general population." (*Id.* at MRK-99420021422:304-06.) The paragraph concluded: "Prospective, long-term studies required to compare the incidence of serious, clinically significant upper GI adverse events in patients taking VIOXX vs. comparator NSAID products have not been performed." (*Id.*)

A separate section of the 1999 Vioxx label ("Special Studies") reported data from two endoscopy studies in a total of 1516 patients that compared the percentage of patients who developed endoscopically detectable gastroduodenal ulcers with Vioxx 25 mg daily, Vioxx 50 mg daily, ibuprofen 2400 mg daily, or placebo. (*Id.* at MRK-99420021418-21.) The label noted that patients receiving aspirin were not enrolled in the studies. (*Id.* at MRK-99420021418:201-02.) In addition to providing detailed tables of the study results, the label reported: "Treatment with VIOXX 25 mg daily or 50 mg daily was associated with a significantly lower percentage of patients with endoscopic gastroduodenal ulcers than treatment with ibuprofen 2400 mg daily. However, the studies cannot rule out at least some increase in the rate of endoscopic gastroduodenal ulcers when comparing VIOXX to placebo." (*Id.* at MRK-99420021418:207-10.) The evidence in the record does not support a finding that the summary of the endoscopy studies in the 2001 Vioxx label was inaccurate with regard to the drug's gastrointestinal benefits

or that the state of the ongoing research about Vioxx's gastrointestinal safety relative to traditional NSAIDs was misrepresented in the labeling.

ii. THE 2002 LABEL

The 2002 Vioxx label included a NSAID class gastrointestinal warning. (DX 273, MRK-LBL0000064.) The label stated: "Although the risk of GI toxicity is not completely eliminated with VIOXX, the results of the VIOXX GI outcomes research (VIGOR) study demonstrate that in patients treated with VIOXX, the risk of GI toxicity with VIOXX 50 mg once daily is significantly less than with naproxen 500 mg twice daily." (*Id.*) The label provided information about the VIGOR protocol and the scope of the study, including that the study had been conducted with rheumatoid arthritis patients and that patients were not allowed to use concomitant aspirin. (DX 273, MRK-LBL0000064.)

The 2002 label also stated that VIGOR demonstrated a statistically significant risk reduction for all PUBs ("PUBs and complicated PUBs") in subgroups of patients under 65 years of age, over 65 years of age, with a history adverse gastrointestinal events, without a history of adverse gastrointestinal events, positive for *H. pylori* infection, negative for *H. pylori* infection, and with concomitant steroid use. (DX 273, MRK-LBL0000063.) The label did not specify the findings for a subgroup comprised of steroid non-users. Nor did the label specify findings for any subgroup regarding the secondary endpoint of confirmed complicated PUBs. The label reported the relative risk reduction only for the subgroups in which the reduction was statistically significant. (*See* DX 2549-A; DX 273, MRK-LBL0000063; Trial Tr. 1271:25-1272:19, Apr. 20, 2010.) The evidence in the record in this case does not support a finding that results of the ongoing research about Vioxx's gastrointestinal safety relative to traditional NSAIDs was misrepresented in the 2002 label.

C. THERE ARE CARDIOVASCULAR RISKS ASSOCIATED WITH VIOXX

1. COX-2 INHIBITORS SUCH AS VIOXX DO NOT HAVE THE CARDIOPROTECTIVE PROPERTIES OF ASPRIN

COX-2 inhibitors do not share the cardioprotective properties of aspirin. Scientists have long known that aspirin, by irreversibly inhibiting COX-1 activity in blood platelets, inhibits synthesis of thromboxane, a prostaglandin that facilitates platelet aggregation (clotting) and constriction of blood vessels. (*See, e.g.*, Nies Dep. 140:18-20, Mar. 2, 2005; Nies Dep. 391:13-22, 392:13-16, Apr. 1, 2005; Trial Tr. 965:11-966:10, Apr. 19, 2010.) By suppressing synthesis of thromboxane, aspirin effectively "thins" the blood, reducing the risk of a heart attack. Studies during Vioxx development confirmed that Vioxx, designed to inhibit COX-2 but not COX-1, does not inhibit clotting or affect bleeding time relative to placebo. (DX 73, MRK-99420021414:26-31, MRK-99420021421:249-54.)

2. CLINICAL RESULTS INDICATE THAT VIOXX IS CARDIOTOXIC

In March 2000, Merck learned the preliminary results of the VIGOR trial. (Scolnick Dep. 885:25-886:4, June 1, 2005.) VIGOR was an approximately 8,000 patient trial designed to assess the incidence of serious gastrointestinal adverse events in rheumatoid arthritis patients treated with Vioxx as compared to the incidence of such events in patients treated with naproxen, a traditional NSAID. (Trial Tr. 1115:5-14, Apr. 20, 2010; Reicin Test. 2196:5-19, Sept.20, 2006.) Over treatment periods averaging nine months, half of the patients in the study took daily doses of Vioxx 50 mg (double the highest recommended dose for continuous use), while the other half took twice-daily doses of naproxen 500 mg (a common, submaximal therapeutic dose).

(Reicin Test. 2195:25-2196:19, 2198:3-7, Sept. 20, 2006.) The results of VIGOR indicated that those taking Vioxx had a greater risk of heart attack and the overall category thromboembolic events. These results were statistically significant for the subgroups of aspirin indicated (higher risk) and non-aspirin indicated (lower risk) subjects of the study. (Trial Tr. 476:24-479:23, Apr. 12, 2010; LAAG 59, MRK-NJ0071324-25.)

There is dispute over whether the higher rates of heart attacks and thromboembolic events in the Vioxx population were due to a cardiotoxic effect of Vioxx or a cardioprotective effect of naproxen.[3] (*Compare* Trial Tr. 479:24-480:4, 489:5-13, Apr. 14, 2010 *with* Nies. Dep. 455:25-456:18, Apr. 1, 2005.) But the weight of the credible evidence supports the conclusion that the increase was due to the cardiotoxic effect of Vioxx.

In April 2002, after considering additional incoming clinical trial data and analysis, the FDA approved a new label for Vioxx, which detailed the cardiovascular findings in VIGOR. (DX 273; Reicin Test. 2261:15-20, Sept. 20, 2006.) Specifically, the label stated that "[t]he VIGOR study showed a higher incidence of adjudicated serious cardiovascular thrombotic events in patients treated with Vioxx 50 mg once daily as compared to patients treated with naproxen 500 mg twice daily. . . . This finding was largely due to a difference in the incidence of myocardial infarction between the groups." (DX 273, MRK-LBL0000063.) This information

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[3]The VIGOR data was published in the New England Journal of Medicine. *See* Claire Bombardier, et al., *Comparison of Upper Gastrointestinal Toxicity of Rofexcoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 New Eng. J. Med. 1520 (Nov. 23, 2000). Approximately five years later, the Journal published an "Expression of Concern" detailing certain inaccuracies in the underlying data and raising concerns about the conclusions of the original paper. *See* Gregory D. Curfman, et al., *Expression of Concern*, 353 New Eng. J. Med. 2813 (Dec. 29, 2005). The Journal subsequently published several responses from the original authors. *See* Correspondence, *Response to Expression of Concern Regarding VIGOR Study*, 354 New Eng. J. Med. 1196 (Mar. 16, 2006).

was placed in the precautions section of the label rather than in the warnings section. Further, the "[p]recautions" section of the label stated "[t]he significance of the cardiovascular findings from these 3 studies (VIGOR and 2 placebo-controlled studies) is unknown. Prospective studies specifically designed to compare the incidence of serious CV events in patients taking VIOXX versus NSAID comparators or placebo have not been performed." (*Id.* at MRK-LBL0000065.)

In consultation with the FDA, Merck designed a study protocol (known as "Protocol 203") for systematic analysis of adjudicated cardiovascular safety data from three large scale, long-term, placebo-controlled trials designed to assess the utility of Vioxx in the prevention and treatment of colon or prostate cancer. (Reicin Test. 2297:2-8, 2298:5-2300:25, 2301:12-2303:2, Sept. 20, 2006.)

One of these trials was known as APPROVe. APPROVe was a blinded, randomized, placebo-controlled clinical trial designed to assess whether Vioxx could help prevent the recurrence of precancerous colon polyps. An external committee adjudicated the study, and found adverse events that represented potential thrombotic cardiovascular events (Reicin Test. 2309:15-2310:20, Sept. 21, 2006; Morrison Test. 1817:15-23, Nov. 8, 2006.)

On September 24, 2004, Merck learned that APPROVe's external safety monitoring board recommended that the study be terminated early in light of interim data the board had received the preceding week. (Morrison Test. 1817:24-1818:3, Nov. 8, 2006.) The monitoring board concluded that, after 18 months of continuous daily use, study participants on Vioxx 25 mg began to experience a gradually increasing rate of confirmed adverse cardiovascular events as compared to study participants on placebo. (Morrison Test. 1819:7-1821:18, Nov. 8, 2006; Reicin Test. 2309-15-2310:20, Sept. 21, 2006.) The interim results from the APPROVe study

prompted Merck to withdraw Vioxx from the market on September 30, 2004. (Reicin Test. 2313:12-16, Sept. 21, 2006.)

3. THE FDA DETERMINED THAT VIOXX IS CARDIOTOXIC, AND WOULD REQUIRE PROPER WARNINGS IF MERCK DECIDED TO PLACE IT BACK ON THE MARKET

On February 16-18, 2005, the FDA convened Special Advisory Committee hearings to obtain recommendations on future regulatory treatment for the entire class of selective COX-2 inhibitors. (LAAG 287; Trial Tr. 979:11-24, Apr. 19, 2010; Trial Tr. 1222:23-1223:5, Apr. 20, 2010.) The Special Advisory Committee consisted of 32 leading scientists and clinicians in the relevant fields from throughout the country. (Trial Tr. 979:11-980:1, Apr. 19, 2010; Trial Tr. 1223:15-23, Apr. 20, 2010; LAAG 287.) During its hearings, the Committee scrutinized the entire existing body of scientific research on coxibs, including the final APPROVe data and more recently unblinded data from long-term, placebo-controlled trials involving Celebrex and other coxibs. (Reicin Test. 2314:2-10, Sept. 21, 2006.) The Committee also examined available data on traditional NSAIDs and heard presentations from scientists, physicians, pharmaceutical companies, government regulators, and members of the public. (LAAG 287.) These experts voted 32 to 0 that "the available data support a conclusion that rofecoxib significantly increases the risk of cardiovascular events." (LAAG 287; Trial Tr. 979:11-980:8, Apr. 19, 2010). With Vioxx having already been removed from the market, the Committee members voted 17 to 15 that Vioxx's benefits outweighed its risks and the drug could be once again made available for prescription provided that a black box warning was displayed on its label. (LAAG 287; Trial Tr. 1224:12-20, Apr. 20, 2010.) To date, Merck has not sought to reintroduce Vioxx to the market.

(Trial Tr. 1338:21-23, Apr. 20, 2010.)

On April 6, 2005, FDA's Center for Drug Evaluation and Research issued a memorandum setting forth a comprehensive analysis of the available data on coxibs and traditional NSAIDs in support of the regulatory actions the agency had decided to take. (DX 338.) This memorandum was based on an analysis of all of the data provided to the February 2005 Special Advisory Committee, as well as additional data available only to the FDA, including the entire regulatory histories and data contained in the NDA files and post-marketing databases for all NSAIDs. (DX 338, 3-4; *see also* Trial Tr. at 1227:7-18, Apr. 20, 2010.)

The FDA concluded that any increased cardiothrombotic risk appeared to be a class effect common to both coxibs and traditional NSAIDs (other than aspirin and possibly naproxen), the agency required all NSAIDs on the market (other than aspirin) to include a "black box" warning about a potential increased risk of adverse cardiovascular thrombotic events. (DX 338, 13-14.) Although Merck never brought Vioxx back on the market, other coxibs such as celobrex remain available in the United States with black box warnings.

With this background in mind, the Court now turns to an analysis of the State of Louisiana's claims.

D. THE STATE OF LOUISIANA COULD NOT HAVE DENIED REIMBURSEMENT FOR VIOXX PRESCRIPTIONS UNDER THE MEDICAID PHARMACY PROGRAM

The State in essence claims that had it known that Vioxx presented cardiovascular risks it would not have approved reimbursement under the State's Medicaid program. This claim is not supported by the weight of the evidence.

1. Federal Medicaid Requirements

Medicaid, an entitlement program created in 1965 by Title IX of the Social Security Act,

is jointly funded by state and federal governments to provide health care coverage to low-income families with dependent children and to elderly, blind, and disabled individuals. 42 U.S.C.A. § 1396-1; 42 U.S.C.A. § 1396a(a)(10)(A)-(C) (West 2003 & Supp. 2009). The state and federal shares of a Medicaid program's costs depend on the state's per capita income. (Trial Tr. 663:18-664:1, Apr. 15, 2010; Trial Tr. 861:16-862:8, Apr. 16, 2010.) In Louisiana, the federal government bears approximately 70% of the Medicaid costs. (Trial Tr. 861:12-14, Apr. 16, 2010.) States create and administer their own programs, but in exchange for this federal funding, they must accept significant federal regulation of the nature, scope, and attributes of their Medicaid programs. *See* 42 U.S.C.A. §1396 *et seq.*

Under federal law, state Medicaid programs are permitted, but not required, to offer prescription drug benefits to Medicaid-eligible individuals. 42 U.S.C.A. § 1396a(a)(10); *see also* 42 U.S.C.A. § 1396d(a)(12) (West 2003 & Supp. 2009). Louisiana elected to offer prescription drug benefits in its Medicaid program. (Trial Tr. 864:19-865:2, Apr. 16, 2010.)

States that decide to provide a pharmacy benefit receive both federal funding and rebates from pharmaceutical companies under the Medicaid Drug Rebate Program. 42 U.S.C.A. §§ 1396r-8(a), (b)(West 2003 & Supp. 2009). This rebate program – created by the Omnibus Budget Reconciliation Act of 1990 ("OBRA 90") – requires a drug manufacturer to enter into a national rebate agreement with the Secretary of the Department of Health and Human Services ("HHS") in order for states to receive federal funding for coverage of its drug products for Medicaid patients. *Id.* (*See also* Trial Tr. 663:3-17, 665:16-666:1, Apr. 15, 2010.) These rebates are shared between the states and the federal government according to their respective shares of the program's cost. (Trial. Tr. at 665:16:16-661:1, Apr. 15, 2010.) In exchange for these rebates, which reduce the cost of the Medicaid programs, manufacturers are guaranteed

coverage of their drugs under Medicaid, unless a particular drug is specifically exempted from coverage by the Medicaid statute. (*Id*. at 665:16:16-661:6.) *See also* 42 U.S. § 1396r-8(d)(2) (specifying categories of drugs excluded from Medicaid coverage). States may negotiate with pharmaceutical companies for supplemental rebates in addition to those provided under the federal rebate program. (Trial Tr. 817:24-818:8, 871:13-872:10, Apr. 16, 2010.)

States that elect to provide a prescription drug benefit must reimburse for all "covered outpatient drugs" that are subject to a national rebate agreement. "Covered outpatient drugs" are prescription drugs approved as safe and effective for their intended uses under the Federal Food, Drug, and Cosmetic Act. 42 U.S.C.A. §§ 1396r-8(a)(1), (d)(1)(B), (k)(2)(A) & (k)(6).

There are only four exceptions to the Medicaid mandatory reimbursement requirement. Coverage may be denied where: (1) a prescription is not made for a "medically accepted indication"; (2) a prescription is made for a category of drugs (such as barbiturates) or for an indication (such as smoking cessation) specified in 42 U.S.C.A. § 1396r-8(d)(2) or a drug has been determined by the Secretary of HHS to be subject to clinical abuse or misuse; (3) a state has executed a special rebate agreement with the manufacturer, approved by the Secretary of HHS, specifically restricting coverage of the prescription; or (4) a state has established a formulary meeting statutory requirements and exclusion of the drug from the formulary is based on the drug's label and is for a specified population and/or condition for reasons of safety or efficacy, and the exclusion conforms with procedures set forth in the federal Medicaid statute (including making specified findings in writing and securing approval from the Secretary of HHS). 42 U.S.C.A. §§ 1396r-8(d)(1), (2), (4).

The federal Medicaid statute defines "medically accepted indications" as all uses approved by the FDA, as well as any non-approved uses supported by the compendia listed in the

statute: the American Hospital Formulary Service Drug Information, the United States Pharmacopeia-Drug Information, or the DRUGDEX Information System. 42 U.S.C.A. §§ 1396r-8(k)(6), (g)(1)(B)(i).

Although reimbursement for covered outpatient drugs is mandatory, save for the exceptions set forth above, states are permitted to subject any covered outpatient drug to a prior authorization requirement, as long as the prior authorization program meets certain standards. 42 U.S.C.A. § 1396r-8(d)(1)(A). First, to establish a prior authorization program, a state must obtain approval of the plan from the Center for Medicare and Medicaid Services and enact enabling legislation. 42 C.F.R. § 430.12(c). Second, to comply with federal law, the state's approval system must: (a) provide a response by telephone or other telecommunication device within 24 hours of the request for authorization; and (b) permit a 72-hour supply of a covered outpatient drug to be dispensed in an emergency situation (as defined by the Secretary of HHS). 42 U.S.C.A. §§ 1396r-8(d)(1)(A), (d)(5). The establishment of a prior authorization requirement for a given drug involves setting criteria for permissible use of the product. (*See* Trial Tr. 681:11-23, Apr. 15, 2010.) Prior authorization requirements are not intended to interpose the state between a doctor and patient or to deny access to a drug altogether. (*Id.*)

2. HISTORY OF LOUISIANA'S MEDICAID PHARMACY PROGRAM

Louisiana's Medicaid Program is administered by the Louisiana Department of Health and Hospitals ("LDHH"). *See* La. Rev. Stat. Ann. § 46:153.3 (2009). Prior to June 13, 2001, Louisiana law mandated that LDHH "provide reimbursement for any drug prescribed by a physician that, in his professional judgment and within the lawful scope of his practice, he considers appropriate for the . . . patient." La. Rev. Stat. Ann. § 46:153.3(B)(2) (1999).

Specifically, it required Medicaid reimbursement of all FDA-approved drugs, except for certain specified categories of drugs (such as infertility drugs). La. Rev. Stat. Ann. § 46:153.3(B) (1999). (*See also* Trial Tr. 717:3-12, Apr. 15, 2010; Trial Tr. 820:16-23, 865:20-866:1, 866:19-23, Apr. 16, 2010.) Therefore, prior to June 13, 2001, Louisiana law precluded the establishment of a Medicaid restrictive formulary[4] pursuant to 42 U.S.C.A. § 1396r-8(d)(4). La. Rev. Stat. Ann. § 46:153.3(B) (1999). During this time, Louisiana law also did not permit the establishment of a preferred drug list ("PDL") or prior authorization requirements in the Medicaid pharmacy program. La. Rev. Stat. Ann. § 46:153.3(B)(3) (1999).

On June 13, 2001, the Louisiana State Legislature modified the State's Medicaid pharmacy program. 2001 La. Acts 395, *amending* La. Rev. Stat. Ann. § 46:153.3. Pursuant to the authority conferred by Act 395, LDHH instituted a preferred drug list and a prior authorization program, which became effective on June 10, 2002 following legislative approval of the preferred drug list. *See* 2001 La. Acts 395, *amending* La. Rev. Stat. Ann. § 46:153.3; 28 La. Reg. 979-80 (May 2002) (implementing an Emergency Rule to create a prior authorization program for drugs prescribed to Medicaid recipients); *see also* 28 La. Reg. 1639, 1640 (July 2002) (Notice of Intent to promulgate final rule establishing prior authorization program for Medicaid prescription drug program). (*See also* Trial Tr. 820:24-821:3, 848:23-25, Apr. 16, 2010.) Under this program, prescription drugs placed on the preferred drug list are covered automatically, while reimbursement for drugs not on the preferred drug list is conditioned on a prior authorization. (*See* Trial Tr. 867:3-22, Apr. 16, 2010; Trial Tr. 378:21-379:10, Apr. 13,

[4] 42 U.S.C.A. § 1396r-8(d) refers simply to a "formulary." In practice and in the relevant case law, a formulary established pursuant to 42 U.S.C.A. § 1396r-8(d)(4) is referred to as a "restrictive" or "exclusive" formulary.

2010.)

Act 395 also authorized the creation of the Medicaid Pharmaceutical & Therapeutics ("P&T") Committee, which is responsible for recommending to the Secretary of LDHH which drugs to include on the preferred drug list and which drugs should require prior authorization. 2001 La. Acts 395, *amending* La. Rev. Stat. Ann. § 46:153.3(C). (*See also* Trial Tr. 822:12-16, 867:23-868:4, Apr. 16, 2010.) The Act not only specified that the Committee must have twenty-one members, but established criteria for the members. For example, Act 395 mandated that one member be a physician from Tulane with an expertise in pharmacology, while another be a practicing physician who participates in the Title XIX program as a surgeon recommended from a list of three names provided by the Louisiana Medical Society. 2001 La. Acts 395, *amending* La. Rev. Stat. Ann. § 46:153.3(C). Act 395 required that all members be appointed by the Governor and confirmed by the Senate. *Id.*

Under Act 395, the P&T Committee is "responsible for developing and maintaining a pharmacopoeia established in conjunction with a prior approval process as provided in Subparagraph (B)(2)(a) of this Section." 2001 La. Acts 395, *adding* La. Rev. Stat. Ann. § 46:153.3(C)(5)(a). Mirroring the prior authorization requirements under federal law, Act 395 required that the prior authorization program "[p]rovide for the dispensing of a minimum of a seventy-two hour supply of a covered outpatient prescription drug in an emergency situation as provided by federal rule or regulation." *See* La. Rev. Stat. Ann. § 46:153.3(B)(2)(a)(ii). Act 395 also made clear that "[t]he department shall not implement the pharmacopoeia authorized by this Subsection until the initial pharmacopoeia is submitted to and approved by the House and Senate Committees on Health and Welfare." 2001 La. Acts 395, *adding* La. Rev. Stat. Ann. § 46:153.3(C)(5)(c).

3. AT NO TIME WHILE VIOXX WAS ON THE MARKET WAS THERE A SYSTEM IN PLACE IN LOUISIANA THAT ALLOWED FOR DENIAL OF REIMBURSEMENT OF MEDICAID VIOXX PRESCRIPTIONS

Because Vioxx was a "covered outpatient drug" subject to a rebate agreement between the Secretary of HHS and Merck, LDHH was required under federal and Louisiana law to provide reimbursements for Vioxx prescriptions the entire time the drug was on the market. In 1999, when Vioxx was approved by the FDA, LDHH had an open formulary system, as discussed above, and therefore was required to cover Vioxx prescriptions automatically. (*See* Trial Tr. at 868:5-8, 896:4-6, Apr. 16, 2010.)

Following Louisiana's enactment of Act 395 and LDHH's establishment of the prior authorization program in 2002, all covered drugs were included on the preferred drug list until the P&T Committee determined whether they should be retained on the list or subjected to a prior authorization requirement. (Trial Tr. at 727:10-728:23, Apr. 15, 2010; Trial Tr. at 831:9-20, 874:7-875:18, Apr. 16, 2010.) Vioxx prescriptions thus remained automatically reimbursable until June 10, 2002, when the Secretary of LDHH adopted the P&T Committee's May 8, 2002 recommendation that Vioxx not be included on the preferred drug list, but instead require prior authorization to be prescribed. (Trial Tr. 738:9-17, Apr. 15, 2010 (COX-2 inhibitors were first considered for inclusion on the preferred drug list on May 8, 2002); Trial Tr. at 838:13-840:11, Apr. 16, 2010 (Vioxx was not recommended for the preferred drug list by the P&T Committee and required a prior authorization when the list was implemented on June 10, 2002).) As explained below this change was made for purely cost containment purposes and had nothing to do with safety concerns.

Nevertheless, LDHH's obligation to pay for Vioxx prescriptions continued even after the

implementation of the preferred drug list. When it established the prior authorization program, LDHH prohibited for six months any restriction on prescriptions written prior to June 10, 2002, the date the prior authorization program became effective. (DX 3639, 5; *see also* Trial Tr. at 418:17-420:13, Apr. 13, 2010.) After that six-month period, reimbursement of Vioxx prescriptions was conditioned on prior authorization. But while physicians were required to seek prior authorization, such authorization could not be withheld. (Biglane Dep. 93:18-94:7, Oct. 28, 2009; Trial Tr. 873:5-16, Apr. 16, 2010.) *See* also 28 La. Reg. 1639, 1640 (July 2002). The Louisiana prior authorization program has a policy of deferring to prescribing physicians and has never rejected a request for prior authorization. (Trial Tr. 823:18-824:1, Apr. 16, 2010.) No denial process has ever been created. (Trial Tr. 824:2-9, Apr. 16, 2010.)

On July 14, 2003, LDHH Secretary David Hood accepted the recommendation of the P&T Committee to place Vioxx on the preferred drug list, making it once again automatically reimbursable. (*See* Trial Tr. 749:23-750:16, Apr. 15, 2010.) In summary prior authorization was only required for Vioxx prescriptions written and filled between June 10, 2002 and July 14, 2003, and even during that time, prior authorization could not be withheld and was always granted.

E. THE STATE OF LOUISIANA DID NOT MEET THEIR BURDEN OF SHOWING THAT THEY COULD AND WOULD HAVE ESTABLISHED AN EXCLUSIVE FORMULARY AND EXCLUDED VIOXX FROM IT HAD THE STATE KNOWN DIFFERENT INFORMATION ABOUT THE DRUG

Plaintiff argues that it would have taken steps to modify its pharmacy program in order to deny reimbursement for Vioxx entirely if it had had different information about Vioxx. As previously noted, there are only four circumstances under which a state Medicaid program is entitled to deny coverage for a covered outpatient drug. The only avenue of the four potentially

applicable to the State of Louisiana was to establish an exclusive formulary. Plaintiff claimed that, had it known of different information about Vioxx, LDHH would have established an exclusive formulary pursuant to 42 U.S.C.A. § 1396r-8(d)(4) for the purpose of excluding Vioxx from the formulary, and thereby denied coverage for the drug. The credible evidence shows, however, that LDHH could not, and would not, have established such a formulary.

1. THE LOUISIANA LEGISLATURE WOULD NOT HAVE APPROVED AN EXCLUSIVE FORMULARY

As discussed above, until the Louisiana Legislature passed Act 395 on June 13, 2001, LDHH was legally prohibited from establishing an exclusive formulary. La. Rev. Stat. Ann. § 46:153.3(B) (1999). Act 395 was not self-executing. It required LDHH to get approval by the House and Senate Committees on Health and Welfare before implementing a "pharmacopoeia" or formulary. 2001 La. Acts 395, *adding* La. Rev. Stat. Ann. § 46:153.3(C)(5)(c). LDHH did not promulgate regulations to implement a prior authorization system until a year later. *See* 28 La. Reg. 979-80 (May 2002); 28 La. Reg. 1639 (July 2002). (*See also* Trial Tr. 406:18-21, 413:24-414:14, 416:24-417:2, Apr. 13, 2010.) In the interim, LDHH was required to identify P&T Committee members to be appointed by the Governor, form the Committee, establish Committee by-laws, contract with Provider Synergies to perform drug assessments, review drugs to construct the initial preferred drug list, and gain approval of the list from the legislature. (*Id.* at 417:12-418:5; Trial Tr. 728:24-730:14, Apr. 15, 2010.)

These legalities would have had to be completed for an exclusive formulary as well. *See* 42 U.S.C.A. § 1396r-8(d)(4)(A) (an exclusive formulary must be "developed by a committee consisting of physicians, pharmacists, and other appropriate individuals appointed by the Governor of the State"); La. Rev. Stat. Ann. § 46:153.3(D)(5)(d) (pharmacopoeia authorized by

Act 395 cannot be implemented until initial pharmacopoeia is submitted to and approved by the Louisiana House and Senate committees on health and welfare). Federal Medicaid law does permit a state's Drug Use Review ("DUR") Board to create an exclusive formulary if so authorized by the state (42 U.S.C.A. § 1396r-8(d)(4)(A)). Act 395 created the P&T Committee and authorized it to "develop[ ] and maintain[ ] a pharmacopoeia established in conjunction with a prior approval process." 2001 La. Acts 395, *adding* La. Rev. Stat. Ann. § 46:153.3(C)(5)(a). However, development of an exclusive formulary by the DUR Board was not authorized by Act 395 and would have conflicted with the establishment and duties of the P&T Committee.

To establish an exclusive formulary, the State of Louisiana would also have been required to file an amended state plan and seek approval from the federal Center for Medicare and Medicaid Services ("CMS"). *See* 42 C.F.R. § 430.12(c). (*See also* Trial Tr. 444:3-8, Apr. 13, 2010.)

Additionally, the evidence shows that LDHH would not have been able to gain the necessary legislative approval if it had attempted to institute an exclusive formulary. Louisiana had experimented with a closed formulary in the 1980s, and it had met with considerable opposition from physicians, pharmacists and patient advocates. (Trial Tr. 402:18-403:15, 451:19-24, Apr. 13, 2010.) Consequently the State moved to an open formulary which required the Medicaid program to reimburse for all covered prescription drugs. *See* La. Rev. Stat. Ann. § 46:153.3(B)(2) (1999).

When LDHH began to work toward passage of Act 395, the State wanted a system that would ensure that when a doctor made an individual prescribing decision, there was a mechanism in place to get the prescribed drug to the patient. (Trial Tr. 431:16-23, Apr. 13, 2010.) As Secretary Hood testified, an exclusive formulary would not have been politically "palatable."

(*Id.* at 409:15-19.) Further, the fact that Act 395 provided for a prior authorization process, but no actual denial of prescriptions, was a selling point that helped to get buy in from other actors in the political process. (Trial Tr. 824:10-17, Apr. 16, 2010.)

Legislative opposition to an exclusive formulary was evident even after Act 395 was passed. LDHH was required to return to the Louisiana House and Senate Joint Committee on Health and Welfare to gain approval of the prior authorization process and the initial formulary it had designed pursuant to the powers granted by Act 395. *See* 2001 La. Acts 395, *adding* La. Rev. Stat. Ann. § 46:153.3(C)(5)(c). (*See also* Trial Tr. 404:1-13, 406:2-25, Apr. 13, 2010.) Mr. Hood admitted that, in the course of this process, legislators expressed their opposition to any system akin to the closed formulary of the 1980s. (*Id.* at 407:3-7, 407:23-408:4.) The Chairman of the Committee declared that the legislative intent was never to institute a formulary where LDHH "could say automatically these drugs are excluded." (Rec. Doc. No. 40187-1, Testimony Before the Louisiana Health and Welfare Committee, May 9, 2002 (Ex. A to Merck's Notice of Filing of Transcript of Certain Testimony Before Legislative Committee Hearings Played During the Testimony of David W. Hood).) Rather, he insisted, the legislature "didn't do anything different other than say it's a preferred provider list." As LDHH Secretary, Mr. Hood assured the Committee that the prior authorization program would not restrict access to drugs. (Trial Tr. 407:22-408:24, 409:15-19, Apr. 13, 2010.) Specifically, he stated:

> There was brought up the concern about would this be a replay of the 1989 formulary that was put into effect. The answer is no. There was no prior authorization in 1989. That meant that it was either you use the drug on the list or you don't get the drug, period. But that's not the case now. We do have prior authorization.

(Rec. Doc. No. 40187-1.)

Given the political opposition to restricting Medicaid recipients' access to FDA-approved

drugs, it is not plausible to conclude by a preponderance of the evidence that, had LDHH received different or additional information about Vioxx, it could have garnered the necessary legislative approval to institute an exclusive formulary, radically transforming the Louisiana Medicaid pharmacy program, for the narrow purpose of trying to deny reimbursement for a single drug.

2. HAD LDHH KNOWN DIFFERENT INFORMATION ABOUT VIOXX THEY WOULD NOT HAVE SOUGHT APPROVAL BY THE LEGISLATURE FOR AN EXCLUSIVE FORMULARY

Apart from the question of whether LDHH *could* have instituted an exclusive formulary while Vioxx was on the market, Plaintiff did not carry its burden that, had the State possessed different clinical information about Vioxx, it *would* have sought to restrict Vioxx Medicaid reimbursements entirely. The record shows, in fact, that neither LDHH nor any reasonable department of health and hospitals would have attempted to establish an exclusive Medicaid formulary for the sole purpose of cutting off reimbursements for Vioxx.

David Hood was Secretary of LDHH from 1998 to February of 2004, nearly the entire time that Vioxx was on the market. (Trial Tr. 368:18-22, Apr. 13, 2010). As Secretary, David Hood had exclusive authority within LDHH to implement changes to the State's prior authorization program and preferred drug list. (*Id.* at 369:17-370:8; *see also* Trial Tr. 882:8-20, Apr. 16, 2010; Trial Tr. 741:12-19, Apr. 15, 2010). Mr. Hood admitted that, as Secretary of LDHH, he never made any decisions about a prescription drug, including Vioxx, based on his independent assessment or understanding of the drug's risks and benefits. (Trial Tr. 423:8-14, 426:21-427:5, Apr. 13, 2010.) Mr. Hood is not a medical doctor and he readily acknowledged that he was not qualified to make independent assessments of the clinical risks and benefits of prescription drugs. (*Id.* at 400:16-17, 426:7-17.) For such assessments, he relied upon the

judgment of the LDHH staff and the doctors, pharmacists and pharmacologists on the P&T Committee. (*See id.* at 423:8-14, 426:18-20, 372:10-15, 372:21-373:1, 373:12-374:2, 375:15-25; *see also* Trial Tr. at 830:24-831:2, Apr. 16, 2010.) The P&T Committee, in turn, contracted with Provider Synergies to complete clinical evaluations of drugs and make recommendations to the Committee about which products to place on the preferred drug list. (Trial Tr. 380:7-15, 432:9-20, Apr. 13, 2010; *see also id.* at 434:13-20.) Mr. Hood testified that he was aware that Vioxx carried cardiovascular and gastrointestinal risks, but he relied upon the judgment of the P&T Committee and Provider Synergies. (*Id.* at 421:17-423:14, 426:18-427:5.)

Mr. Hood testified that he was unaware of any instance in which the Louisiana P&T Committee came to a decision about the safety and/or efficacy of an FDA-approved drug that was at odds with the FDA's determination. (Trial Tr. 430:5-22, 431:8-15, Apr. 13, 2010; *see also* Trial Tr. 722:7-11, Apr. 15, 2010 (Mr. Castille testifying that the State of Louisiana does not make determinations independent of the FDA about a drug's safety and efficacy).) Mr. Hood acknowledged that FDA approval of a medicine is important to DHH and the P&T Committee as "an indication" that a product is "a safe drug." (Trial Tr. 429:20-23, Apr. 13, 2010.)

LDHH's motive in establishing a preferred drug list and prior authorization process was to save money. Toward this end, Provider Synergies is charged with providing the P&T Committee with an analysis of the comparative costs of drugs. (Trial Tr. 826:17-22, 877:23-878:10, Apr. 16, 2010.) Provider Synergies plays a critical role in reducing prescription drug costs to LDHH by securing supplemental rebate agreements from drug manufacturers. (Trial Tr. 767:9-12, Apr. 15, 2010; Trial Tr. 825:15-25, 877:10-22, 890:14-16, Apr. 16, 2010.) A pharmaceutical company's unwillingness to provide a supplemental rebate for its drugs would adversely affect the company's chances that its products would be placed on the preferred drug

list. (*See* Trial Tr. 734:5-9, Apr. 15, 2010.)

Charles Castille, the Undersecretary of DHH, testified that Merck's initial refusal to provide supplemental rebates to Louisiana was "generally the reason" that Merck's products, including Vioxx, were not included on the preferred drug list in 2002. (Trial Tr. 734:10-17, Apr. 15, 2010.) By the time the P&T Committee considered Vioxx for inclusion on the preferred drug list in 2003, Merck had offered Louisiana a supplemental rebate on its drugs. (Trial Tr. 746:5-8, Apr. 15, 2010.) The Committee decided to include Vioxx on the preferred drug list because Merck's supplemental rebate offer made Vioxx more cost-effective to the State than Celebrex. (Trial Tr. 889:10-890:13, Apr. 16, 2010.)

The P&T Committee's prioritization of cost continued throughout the time Vioxx was on the market and beyond. At the May 5, 2004 P&T Committee meeting, Provider Synergies reported that the manufacturer of Celebrex had offered an additional rebate, but that it was not sufficient to warrant putting the drug back on the preferred drug list. (DX 2119, 4; DX 2120, 25-31; Trial Tr. 754:7-755:11, 790:14-791:10, Apr. 15, 2010.)

By the August 11, 2004 meeting of the P&T Committee, however, Provider Synergies and Pfizer had negotiated an acceptable price. (*See* Trial Tr. 794:1-11, Apr. 15, 2010.) The Committee voted to follow Provider Synergies' recommendation that all three COX-2 drugs be placed on the preferred drug list. (Trial Tr. 757:7-758:7, Apr. 15, 2010.)

Because Mr. Hood made decisions about drugs in reliance on the recommendations of LDHH staff, P&T Committee members and Provider Synergies and there is no evidence in the record of what recommendations these entities would have made had they possessed different data, it is not legally sustainable to conclude that Mr. Hood would have acted to deny reimbursements for Vioxx had the State received different information about the drug.

Mr. Hood also conceded that as LDHH Secretary he never even considered restricting the State's reimbursement of an FDA-approved drug. (Trial Tr. 428:2-5, Apr. 13, 2010.) He acknowledged that, while Secretary, he did not know of any authority under which he could have instituted an exclusive formulary had he decided one was necessary on account of Vioxx. (*Id.* at 438:20-439:14, 439:24-440:7.)

Mr. Hood stated that in order to deny reimbursement for Vioxx prescriptions, he would have consulted with LDHH attorneys. (*Id.* at 381:13-382:5; *see also id.* at 440:8-21.) This is not sufficient to establish that the State would have pursued the option of an exclusive formulary. There is no factual record from which it could be inferred that Mr. Hood would have been advised that an exclusive formulary was an option. This is particularly so given the political opposition to such a formulary. Further, Charles Castille, an attorney and LDHH Undersecretary, testified that "the State could not have, for example, have done what, let's say, the FDA could do, and take a drug off the market. We obviously did not have that authority." (Trial Tr. 742:11-743:4, Apr. 15, 2010.) Taking a drug off the preferred drug list was "the most restrictive thing" LDHH could do, Mr. Castille testified. (*Id.* at 743:3-4.)

The evidence shows that the P&T Committee's decisions about which drugs to include on the preferred drug list were driven by cost, not safety concerns, such that additional information about Vioxx's potential cardiovascular risks would not have prompted the Committee to seek to deny reimbursements for Vioxx prescriptions. For safety, the P&T Committee relied on the FDA. The credible evidence supports the conclusion that the P&T Committee, and LDHH simply did not have the institutional structure, expertise, or resources to scrutinize the safety of every FDA approved drug.

3. TO DATE, LDHH HAS NOT INSTITUTED AN EXCLUSIVE FORMULARY AND CONTINUES TO REIMBURSE MEDICAID PRESCRIPTIONS FOR COMPARATOR DRUGS SUCH AS CELOBREX

One can determine what a reasonable department of health and hospitals would have done had it received different information about Vioxx by examining what LDHH actually did in a closely analogous situation. On April 6, 2005, FDA's Center for Drug Evaluation and Research issued a memorandum setting forth a comprehensive analysis of the available data on traditional NSAIDs, such as ibuprofen and diclofenac, as well as COX-2 inhibitors such as Vioxx and Celebrex. (*See* DX 338.) The memorandum concluded that there is a "class effect" for increased cardiovascular risks with all NSAIDs (except aspirin and possibly naproxen) and that it was not possible, based on available clinical trial data, to create a "rank ordering" of these drugs. (*Id.* at 10-11.) In other words, in 2005 the FDA concluded that Celebrex, Vioxx and other traditional NSAIDs (except aspirin and naproxen) carried significant cardiovascular risks. Consequently, the FDA required manufacturers of all NSAIDs -- including COX-2 inhibitors -- to place a "black box" warning on the drugs' labeling about such potential cardiovascular risks. (DX 338, 14; *see also* Trial Tr. 795:10-22, Apr. 15, 2010.)

LDHH did not institute an exclusive formulary in response to this development. Instead, it continued to keep these drugs on its preferred drug list. (*See* DX 2165.) In 2004, Celebrex, another COX-2 inhibitor, was found to carry an increased risk of cardiovascular thrombotic events and it possessed no statistically significant gastrointestinal benefit. (Trial Tr. 641:6-15, Apr. 15, 2010.) But despite these facts, and despite the addition of a black box cardiovascular warning to the Celebrex label in 2005, LDHH continued to include Celebrex on its preferred

drug list as recently as 2008. (*Id.* at 642:2-10; DX 2165.) Similarly, the NSAID diclofenac has been shown to carry a statistically significant increased cardiovascular risk, yet even after that risk was established, diclofenac remained on the Louisiana preferred drug list. (Trial Tr. at 1047:20-1050:3, Apr. 19, 2010; DX 2165.) In fact, the Louisiana preferred drug list contains a large number of drugs that carry black box warnings. (Trial Tr. 686:6-11, Apr. 15, 2010.)

F. PLAINTIFF HAD ACCESS TO LITERATURE AND CLINICAL STUDIES THAT INDICATED CARDIOVASCULAR CONCERNS OVER VIOXX

Plaintiff asserts that had it known of the cardiovascular risks of Vioxx it would have taken action. The evidence however, reveals that Plaintiff had sufficient information about these risks and did not take any action.

Following Louisiana's enactment of Act 395 and LDHH's establishment of the prior authorization program in 2002, all covered drugs were included on the preferred drug list until the P&T Committee determined whether they should remain on the list or be subject to a prior authorization requirement. (Trial Tr. 727:10-728:23, Apr. 15, 2010; Trial Tr. at 831:9-20, 874:7-875:18, Apr. 16, 2010.) Since March 19, 2002, LDHH has contracted with Provider Synergies LLC to perform clinical and economic analyses of prescription drug data for the P&T Committee, which uses that information to make recommendations about which drugs to include on the preferred drug list. (Trial Tr. 732:11-22, 766:3-10, 768:9-19, Apr. 15, 2010; Trial Tr. 878:11-879:4, 879:17-21, 880:11-19, 881:21-25, 896:15-19, Apr. 16, 2010.) Thus, the Court looks to the information that Plaintiff, specifically the P& T Committee, had available to it from 2002 on and what actions they took in response to that information.

1. THE P&T COMMITTEE RECEIVES THEIR INFORMATION ABOUT DRUGS FROM PROVIDER SYNERGIES AND BASES THEIR DECISIONS ON THAT INFORMATION

The P&T Committee relies heavily on both the FDA's and Provider Synergies' independent assessments of the clinical evidence regarding the risks and benefits of prescription drugs. (*See* Trial Tr. 429:20-23, Apr. 13, 2010; Trial Tr. at 722:7-11, 766:11-17, Apr. 15, 2010; Trial Tr. 830:9-12, Apr. 16, 2010.) Provider Synergies relies "on independent, peer-reviewed, published clinical data and FDA labeling and findings as [the] primary source of information for [its] reviews." (Trial Tr. 767:16-21, Apr. 15, 2010.) This included clinical data sponsored by Merck. Provider Synergies does not rely on marketing materials, internal emails, or formulary dossiers from pharmaceutical companies, although it does request clinical study information from manufacturers from time to time. (Trial Tr. 775:20-776:4, Apr. 15, 2010.)

Provider Synergies briefs the P&T Committee on the clinical strengths and weaknesses of the drugs the Committee considers for placement on or exclusion from the preferred drug list. (*See* Trial Tr. at 739:14-20, Apr. 15, 2010; Trial Tr. 880:11-19, Apr. 16, 2010.)

2. LDHH AND THE P&T COMMITTEE WERE PROVIDED WITH DATA AND INFORMATION THAT INDICATED CARDIOVASCULAR CONCERNS ABOUT VIOXX

In 2002, 2003, & 2004 monographs on "Selective Cyclooxygenase (COX)-2 Inhibitors" were prepared by Provider Synergies and distributed to P&T Committee members. These monographs reported the results of controlled clinical trials, including VIGOR, that tested Vioxx's safety and efficacy, as well as studies that compared the safety and efficacy of Vioxx and Celebrex. (LAAG 439; LAAG 426; DX 2118). These monographs were used by the P&T Committee at meetings to determine whether Vioxx should be placed on or taken off of the

preferred drug list. (DX2071 (Tr. of May 8, 2002 P&T Meeting); DX2095 (Tr. of May 21, 2003 P&T Committee Meeting); DX2120 (Tr. of May 5, 2004 P&T Committee Meeting).)

The 2002 monograph included a section entitled "Cardiovascular Concerns." This section summarized the findings of a meta-analysis of COX-2 inhibitors published by Dr. Steven Nissen and Dr. Eric Topol in *JAMA* in August 2001 and noted that the authors of the analysis "concluded that a prospective trial may be necessary to evaluate the potential risk of cardiovascular events with these agents." (*See* LAAG 439, 6 & 6, n.33; *see also* Trial Tr. 884:18-885:10, Apr. 16, 2010.) Reference to the *JAMA* article in the monographs indicated that the reviewers who prepared the monograph were familiar with the ongoing scientific discussion about the possible reasons for the VIGOR cardiovascular outcomes, including the possibility that Vioxx had a prothrombotic, cardiotoxic effect. (*See* Trial Tr. 942:13-944:3, Apr. 19, 2010.)

Additionally, in July of 2003, the LDHH Pharmacy Director, M.J. Terrebonne, and then-Secretary of LDHH, David Hood, received a letter from Pfizer, the manufacturer of Celebrex, requesting a review of Celebrex's exclusion from Louisiana's preferred drug list. (Trial Tr. 843:20-844:13, Apr. 16, 2010.) The Pfizer letter went to lengths to emphasize that Vioxx (unlike Celebrex) had a cardiovascular warning on its label, including a statement that Vioxx should be used with caution in patients with a history of ischemic heart disease. (*Id.* at 844:14-846:6.) Ms. Terrebonne testified that, having attended the P&T Committee meetings at which Vioxx was discussed, she already knew of the cardiovascular concerns with Vioxx raised in the July 2003 Pfizer letter. (*Id.* at 846:7-11.)

3. MERCK ATTEMPTED TO NEUTRALIZE CONCERNS THAT VIOXX WAS CARDIOTOXIC

The 2002, 2003 and 2004 monographs provided by Provider Synergies to the P& T

Committee all cited to the *Journal of the American Medical Association (JAMA)* article by Mukherjee which reported on the VIGOR results and concluded, according to Provider Synergies, "that a prospective trial may be necessary to evaluate the potential risk of cardiovascular events" with COX-2 inhibitors. (LAAG 439, 6, n.33; LAAG 426, 10, n.58; DX 2118, 13, n.62.) The monographs cautioned against the method of meta-analysis used in *JAMA* to establish cardiovascular risks (LAAG 439, 6; LAAG 426, 10; DX 2118, 13), and the 2003 and 2004 monographs included citations to the Merck sponsored Reicin and Konstam articles which further undercut the findings of the VIGOR study. (LAAG 426, 10, nn.60-61; DX 2118, 13, nn.65-66). These Merck sponsored articles were provided to Provider Synergies on April 19, 2002, in response to Provider Synergies' Valerie Taylor's request for cardiovascular information regarding Vioxx. Merck cited the Reicin and Konstam studies in response to the *JAMA* article and claimed that the Reicin article demonstrated that "no difference exists between [Vioxx], comparator non-selective NSAIDs, and placebo in the risks of cardiovascular thrombotic events."(LAAG 573.)[5] Merck stated that the Konstam article concluded, "[Vioxx] was not associated with excess CV thrombotic events compared with either placebo or non-naproxen NSAIDs." (*Id.*) They went on to re-urge the "naproxen theory" stating, "The data suggest, but are insufficient to ascertain, the cardioprotective effects of naproxen."(*Id.*)

However, despite these two articles which may have counterbalanced the VIGOR data, the 2003 and 2004 monographs provided to the P&T Committee concluded that

> The VIGOR study raised some questions regarding the cardiovascular safety of rofecoxib (Vioxx). Patients receiving rofecoxib (Vioxx) had a significantly higher risk of developing a cardiovascular thrombotic event compared to

[5]The Court reserved ruling on several trial and deposition exhibits. Upon further consideration, the Court now admits LAAG 573 into the record. Further, the remaining exhibits are not admitted.

> patients receiving naproxen. Aspirin for cardiovascular prophylaxis was not permitted in the study, which does not reflect "real world" use of the NSAIDS. Although the significance of this potential cardiovascular risk is unknown, it does raise questions.

(LAAG 426, 12; DX 2118, 15.)

The point is that since February of 2002 the P&T Committee was aware of the potential cardiovascular risks of Vioxx that were indicated in VIGOR. Further, the 2003 and 2004 monographs provided further, more extensive information to the P&T Committee regarding the controversy surrounding Cox-2 inhibitors including Vioxx and yet at no time did the P&T Committee make any recommendations to try to restrict its use. Plaintiff's protestations now ring hollow.

III. CONCLUSIONS OF LAW

To establish a claim in redhibition, the plaintiff must satisfy the following elements:

> (1) the thing sold is absolutely useless for its intended purposes, or that he would not have bought it had he known of the defect; (2) that the defect existed at the time that he purchased the thing, but was neither known nor apparent to him; and (3) that the seller was given the opportunity to repair the defect.

Alston v. Fleetwood Motor Homes of Indiana, 480 F.3d 695, 699 (5th Cir. 2007).

This Court concludes that Plaintiff's redhibition claim fails because Plaintiff did not prove causation. As such, the Court need not reach a conclusion as to whether Vioxx suffered from a redhibitory defect, whether the Plaintiff was on notice of the defect at the time of purchase, or what remedy Plaintiff may have been entitled to.

Plaintiff failed to satisfy its burden of proving causation because it did not establish at trial that: had it known different facts about Vioxx (a) the State could have established an exclusive formulary; (b) and the State would have established such a formulary and excluded Vioxx from it.

Louisiana could not have adopted an exclusive formulary before June 13, 2001. Prior to that time, Louisiana law required that LDHH "provide reimbursement for any drug prescribed by a physician that, in his professional judgment and within the lawful scope of his practice, he considers appropriate for the diagnosis and treatment of the patient." La. Rev. Stat. Ann. § 46:153.3(B)(2) (1999).

Upon the enactment of Act 395 on June 13, 2001, LDHH instituted a Medicaid pharmacy program utilizing a preferred drug list and prior authorization system -- not an exclusive formulary. *See* 2001 La. Acts 395, *amending* La. Rev. Stat. Ann. § 46:153.3; 28 La. Reg. 979-80 (May 2002) (implementing an Emergency Rule to create a prior authorization program for drugs prescribed to Medicaid recipients); *see also* 28 La. Reg. 1639, 1639-41 (July 2002) (Notice of Intent to promulgate final rule establishing prior authorization program for Medicaid prescription drug program). Under this program, prescription drugs placed on the preferred drug list are covered automatically, while reimbursement for drugs not on the preferred drug list is conditioned on prior authorization. (*See* Trial Tr. 378:21-379:10, Apr. 13, 2010.) While the prior approval procedure creates an incentive for physicians to prescribe drugs on the preferred drug list, authorization for a drug not on the list cannot be withheld. *See Edmonds v. Levine,* 417 F. Supp. 2d 1323, 1329 (S.D. Fla. 2006) ("The Medicaid Act does not authorize a state to use [this type] of prior authorization program to deny coverage for a covered drug; it can only condition reimbursement upon a prescribing doctor first calling a state pharmacist to obtain approval for the drug."); *see also Pharm. Research & Mfrs. v. Meadows*, 304 F.3d 1197, 1201, 1207 (11th Cir. 2002). Plaintiff does not dispute that under the Medicaid drug program LDHH actually adopted in 2002, reimbursements for Vioxx could not be denied.

Plaintiff has not presented any evidence that LDHH ever prepared a proposed plan amendment for submission to the Center for Medicare and Medicaid Services, whose authorization would be required before LDHH could adopt an exclusive formulary. 42 C.F.R. § 430.12. Mr. Hood admitted that neither the P&T Committee nor the State ever considered a proposal to adopt an exclusive formulary to restrict reimbursement coverage of an FDA-approved drug during the time he was Secretary. (Trial Tr. 430:5-22, Apr. 13, 2010.)

An exclusive formulary would have significantly limited the State's power to consider and negotiate drug costs, and would have frustrated the intent of the Act. No witness affiliated with LDHH testified that the State would have created an exclusive formulary which would have conflicted with the entire purpose of Act 395. This Court therefore concludes that LDHH would not have attempted to institute an exclusive formulary in June 2001 or at any other point.

IV. CONCLUSION

Based on the above findings of fact and conclusions of law, the Court rules in favor of the Defendant, Merck. P laintiff's redhibition claim is hereby dismissed with prejudice and costs.

New Orleans, Louisiana, this 29th day of June, 2010.

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United States District Judge