UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE NEURONTIN MARKETING AND SALES PRACTICES LITIGATION	
THIS DOCUMENT RELATES TO:	CIVIL ACTION NO. 04-cv-10739-PBS
KAISER FOUNDATION HEALTH PLAN, INC., et al.	
v.	
PFIZER, INC., et al.	

AMENDED FINDINGS OF FACT AND CONCLUSIONS OF LAW

August 31, 2011

Saris, U.S.D.J.

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I. INTRODUCTION

Approved by the Food and Drug Administration (FDA) in 1993 as a secondary treatment for epilepsy, Neurontin became one of the top selling drugs in the world. Sales rose from fewer than 50,000 prescriptions in 1995 to more than 1.4 million in 2004. The success of the drug was due to the illegal activities of Parke-Davis, Warner-Lambert and Pfizer, companies that undertook a nationwide effort to unlawfully market this drug for off-label uses for which there was little or no scientific evidence of efficacy. The Food, Drug and Cosmetic Act (FDCA) prohibits such off-label marketing by pharmaceutical companies. See 21 U.S.C. § 355(a).

Dubbed "snake oil" by Pfizer's own sales team, Neurontin was promoted through a publication strategy that suppressed negative clinical trials and showcased positive ones. Pfizer also sponsored continuing medical education programs and detailed doctors to promote off-label uses of the drug. Eventually Warner-Lambert pled guilty to criminal violations of the FDCA and paid civil fines and criminal penalties totaling $430 million.

This action, which was independently filed in the District of Massachusetts, is related to a larger multi-district litigation (MDL) that consolidates for pretrial purposes Neurontin-related civil lawsuits brought nationwide. One group of MDL cases consists of products liability actions claiming that

Neurontin caused someone to commit or attempt to commit suicide. Another group of cases involves lawsuits related to the sales and marketing of Neurontin. This case falls within the latter category. Pfizer previously moved for summary judgment in most of the sales and marketing cases. The Court allowed the summary judgment motion as it related to plaintiffs Guardian Life Insurance Company and Aetna, Inc., two other third party payors, because the Court found that these companies had not provided admissible evidence to create disputed fact issues with respect to reliance or causation. See In re Neurontin Mktg. & Sales Practices Litig., 677 F. Supp. 2d 479 (D. Mass. 2010).

Kaiser Foundation Health Plan and Kaiser Foundation Hospitals (collectively, "Kaiser"), bring this case against Pfizer, Inc. and Warner-Lambert Company (collectively, "Pfizer"), alleging violations of the Racketeer Influenced and Corrupt Organizations Act (RICO) and the California Unfair Competition Law ("UCL"). See 18 U.S.C. § 1962(c) (RICO); Cal. Bus. & Prof. Code § 17200 (UCL). Kaiser spent about $200 million on Neurontin from 1996 to 2004. After a five-week trial, on March 25, 2010 a federal jury found that Pfizer engaged in a RICO enterprise that committed mail and wire fraud by fraudulently marketing Neurontin for off-label conditions such as bipolar disorder, neuropathic pain, and migraine, and at doses greater than 1800 mg/day. The jury found for defendants with respect to plaintiffs' claims of

fraudulent promotion of Neurontin for nociceptive pain.[1] The jury rendered a verdict in plaintiffs' favor on the remaining claims in the amount of $47,363,092. (See Jury Verdict, Docket No. 2760.) The statute requires the Court to treble the award to $142,089,276. 18 U.S.C. § 1964(c).

Now before this Court is the question of whether that same conduct violated the UCL. During a trial that spanned five weeks, the parties presented testimony of twenty-one live witnesses and eighteen witnesses by deposition. The trial involved sixteen expert witnesses and more than 400 admitted exhibits. The Court was impressed with the caliber of most of the expert witnesses for both sides. Kaiser offered testimony from four of its executives, including the chairperson of the Southern California Pharmacy and Therapeutics Committee and the chairperson of Kaiser's Drug Information Service. Remarkably, Pfizer did not offer live testimony from any officer or employee, nor was any Pfizer representative present during the trial.

After a review of all the evidence, the Court orders entry of judgment in favor of Kaiser on its UCL claim, and finds as follows:

1. Kaiser has proven that Pfizer fraudulently marketed Neurontin by making material misrepresentations in

[1] Nociceptive pain is pain caused by injury such as "hitting your thumb nail with a hammer" or a fracture. (Trial Tr. vol. 6, 142, Mar. 1, 2010.)

advertising supplements, articles it sponsored, and direct communications to Kaiser.

2. Kaiser has proven that Pfizer fraudulently marketed Neurontin by showcasing positive information about Neurontin's efficacy in the published literature, while suppressing negative evidence from Pfizer-sponsored clinical trials about Neurontin's efficacy for bipolar disorder, neuropathic pain, migraine, and at doses greater than 1800 mg/day.

3. Kaiser has proven that there is little or no scientifically accepted evidence that Neurontin is effective for the treatment of bipolar disorder, neuropathic pain, nociceptive pain, migraine, or doses greater than 1800 mg/day.

4. Kaiser has proven that Pfizer's conduct caused it injury in the form of reimbursements for Neurontin prescriptions in excess of payments for alternative prescriptions that would have been made for more or equally effective, but less expensive medicines, in the absence of Pfizer's fraudulent marketing campaign. Kaiser is entitled to restitution in the amount of $95,286,518 in excess payments.

II. FINDINGS OF FACT

A. Kaiser Foundation Health Plan and Kaiser Foundation Hospitals

1. Kaiser's Proactive Drug Management

Kaiser is one of the largest health maintenance organizations in the United States and is a non-profit healthcare provider. (Trial Tr. vol. 5, 82, 92, Feb. 26, 2010.) It is composed of two separate corporations: the Kaiser Foundation Health Plan and the Kaiser Foundation Hospitals. Kaiser Foundation Health Plan directly provides medical coverage to beneficiaries in California and Hawaii. In addition, Kaiser Foundation Health Plan is the parent corporation of six wholly owned regional health plans: Kaiser Foundation Health Plan of Colorado; Kaiser Foundation Health Plan of Georgia, Inc.; Kaiser Foundation Health Plan of the Mid-Atlantic States, Inc.; Kaiser Foundation Health Plan of the Northwest; and Kaiser Foundation Health Plan of Ohio. Overall, the health plan and the regional subsidiaries provide medical insurance to approximately 8.6 million members. Seventy-six percent of those members are located in California. (Id. at 82-83.) The Kaiser hospitals provide facilities at which health plan members receive medical care. The hospitals also have in-house pharmacies where health plan members may fill prescriptions.

While the Kaiser Foundation Health Plan and regional subsidiaries do not directly employ physicians, they have an

exclusive contractual relationship with regional Permanente Medical Groups, which are groups of physicians who provide services to Kaiser health plan members. Kaiser and the regional Permanente Medical Groups work together to form an integrated medical care services program that operates under the trade name "Kaiser Permanente." (Trial Tr. vol. 8, 99-102, 126-27, Mar. 3, 2010.) Each regional Permanente Medical Group has its own Pharmacy and Therapeutics ("P&T") Committee that determines which drugs to place on a formulary, a list of medications approved for prescription by treating physicians. While the P&T committees are technically housed within the organizational structure of the regional Permanente Medical Groups, Kaiser personnel are involved in the development of the formulary and other P&T committee activities. The head of Kaiser's Drug Information Services and the health plan's Vice-President of Pharmacy Strategy and Operations are members of both regional P&T committees in California. In this way, the health plan collaborates with the regional PMGs to "develop, maintain, and implement" the "Kaiser Permanente" regional formularies. The health plan recognizes the P&T committees as the bodies that are authorized to make decisions regarding specific drugs. (See Carver Dep. Tr., 49-50 (played Mar. 2, 2010).)

Kaiser takes a proactive approach to managing drugs prescribed by PMG physicians. The organization utilizes its centralized Drug Information Service ("DIS") to research drugs

and disseminate information about those drugs to physicians and to the P&T Committees. DIS is part of Kaiser Hospitals, and supports both Kaiser Hospitals and Kaiser Health Plan. The DIS chairperson is a nonvoting member of the Northern and Southern California regional P&T Committees. DIS pharmacists regularly prepare monographs on new drugs or drugs for which there are emerging uses. These monographs summarize the best available evidence on the drug's safety and efficacy and provide recommendations on appropriate usage of the drug. DIS searches for publicly available evidence and requests unpublished information from pharmaceutical manufacturers. (Trial Tr. vol. 9, 46-47, Mar. 4, 2010; Trial Tr. vol. 10, 80-81, Mar. 5, 2010.) In making formulary decisions, P&T Committees rely heavily on DIS's monographs. (Trial Tr. vol. 12, 93-94, Mar. 9, 2010.) Monographs are shared with all other Kaiser regions during monthly teleconferences with formulary personnel, chaired by the head of DIS. (Trial Tr. vol. 5, 110.) Information is also shared at regular interregional P&T Committee meetings. (Trial Tr. vol. 12, 93.) In addition, DIS maintains an inquiry service that responds to direct inquiries from PMG physicians. DIS regularly contacts pharmaceutical manufacturers when researching inquiries about drugs. (Trial Tr. vol. 9, 89-90.)

As previously mentioned, Kaiser authorizes the P&T committees to make decisions regarding specific drugs. Each P&T

committee utilizes a drug formulary, which is essentially a list of medications approved to be prescribed to Kaiser members for certain medical indications. Drugs on the formulary are either listed without restrictions, with restrictions, or with guidelines. If a drug is listed without restrictions, physicians may prescribe the drug to a patient for any indication they believe is appropriate. If a drug is listed with restrictions, prescribing may be limited to a group of physicians, such as neurologists or psychiatrists. If a drug is listed with guidelines, then any physician may prescribe the drug, but guidelines for appropriate prescribing in terms of indication or alternative treatments are included in the formulary.

In order to make a change to the formulary or add a new drug, PMG physicians or individual P&T Committee members may make a request to the P&T Committee. Once a request is made, DIS prepares a monograph that includes a recommendation for the P&T Committee. (Trial Tr. vol. 9, 46.) The P&T Committee discusses the evidence provided by the monograph, considers any other evidence or information submitted to the committee, and then votes on the proposed additions or changes.

Kaiser will pay for off-formulary prescriptions. No prior authorization is required for any prescription. Nonetheless, an internal study found that 95% of prescriptions written by PMG

physicians are in compliance with the drug formulary. (Trial Tr. vol. 5, 103-04, 108-09; Trial Exhibit ("TX") 323 at 41.)

2. Placement of Neurontin on Formularies

After Neurontin was approved by the FDA for epilepsy in 1993, each regional P&T committee began to add Neurontin to its formulary. Neurontin was added to the formularies for the Northern California and Northwest regions without restriction in 1994. The Southern California and Ohio P&T committees added Neurontin to the formulary in 1994, restricted to neurologists. Neurontin was added to the Colorado regional formulary in 1995 and the Southeast regional formulary in 1996. Finally, it was added to the regional drug formulary for Hawaii in 2000. (Trial Exhibit ("TX") 840; Trial Tr. vol. 12, 95.) There is no evidence regarding Neurontin's placement on the formulary in the Mid-Atlantic States region.

In September 1997, the Southern California P&T Committee approved a request by its Chiefs of Anesthesiology to allow prescribing of Neurontin by anesthesiologists for the treatment of Reflex Sympathetic Dystrophy, a pain syndrome. (Trial Tr. vol. 9, 49-51; TX 290 at 6.) In June 1999, the Chiefs of Neurology for the Southern California region recommended removing Neurontin's prescribing restrictions and adding guidelines for use. The guidelines provided that Neurontin should be reserved for neuropathic pain patients unresponsive to, or intolerant of,

tricyclic antidepressants and other treatments. For all indications, the recommendation suggested that the initial prescription should be limited to a one month trial. (TX 557.) The P&T Committee approved the request, despite a large predicted cost impact. (Trial Tr. vol. 9, 61-63, 69-70; Trial Tr. vol. 12, 98-100.)

In September 1999, the Southern California P&T Committee voted to remove all remaining formulary restrictions on Neurontin. (TXs 327, 291.)

B. Marketing of Neurontin

Parke-Davis, the pharmaceutical company that developed the drug Neurontin, is an operating division of Warner-Lambert Company. Warner-Lambert was acquired by the pharmaceutical company Pfizer in 2000. (See, e.g., TX 143.) Pfizer is one of the largest pharmaceutical companies in the world.

1. FDA Approval of Neurontin for Epilepsy Treatment

Neurontin was developed throughout the 1980s and early 1990s by Parke-Davis as an anti-epileptic drug (AED). Its generic name is gabapentin.

The FDA approved Neurontin as an adjunctive therapy in the treatment of partial seizures in adults with epilepsy on December 30, 1993. (TX 9 at 1, 6.) The maximum dose was set at 1800

mg/day. Plaintiffs' expert, Dr. David Kessler,[2] explained that, before approving a drug for a particular indication, the FDA requires that the manufacturer submit two favorable double-blind randomized controlled trials ("DBRCTs"). (Trial Tr. vol. 2, 30, Feb. 23, 2010.) Parke-Davis fulfilled that requirement with respect to the use of Neurontin as an adjunctive therapy for partial seizures. (Id. at 33.)

In 1992, during its "medical statistical review" of Neurontin, the FDA found that certain patients taking Neurontin experienced depressive side effects, presenting safety concerns about the drug. (TX 207 at 117.) The FDA wrote that "less common but more serious [adverse] events may limit the drug's widespread usefulness," citing depression with or without suicidal ideation as one of those "more serious" adverse events. (Id.) In fact, as early as 1994, Neurontin's FDA-approved label included information about depression and "suicide gesture" as adverse events observed during clinical trials. (TX 507 at 2.)

Plaintiffs' expert, Dr. Curt Furberg,[3] testified that the

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[2] At trial, plaintiffs presented the testimony of Dr. David Kessler, an expert on how the federal Food and Drug Administration (FDA) works and how a pharmaceutical company interacts with the FDA. Dr. Kessler holds both a medical and a law degree from Harvard University. Dr. Kessler served as the Commissioner of the FDA from 1990 to 1997. (Trial Tr. vol. 1, 154-56, Feb. 22, 2010.) He is currently a professor of pediatrics, epidemiology and biostatistics and the University of California - San Francisco. (Id. at 156.)

[3] Dr. Furberg specializes in the design, conduct, analysis and reporting of clinical trials and has provided training to the

FDA's review of depressive side effects related to Neurontin suggested that the drug should be used "with caution." (Trial Tr. vol. 13, 69, Mar. 10, 2010.) Specifically, Dr. Furberg stated that, according to his review of the available data, "there was about a 65 percent increase in risk of depression with the drug compared to placebo, the sugar pill." (Id. at 71.) He added that "if you see harm in this population of epilepsy [patients], you would expect to see that in the treatment of other conditions." (Id. at 72.)

In his view, the incidence of depressive side effects is relevant to the use and marketing of Neurontin for patients with bipolar disorder because "bipolar disorder includes depression" along with a manic component. (Id. at 73.)

In January 2008, the FDA issued an "alert" about eleven AEDs, including Neurontin, that warned physicians to "[b]e aware of the possibility of the emergence or worsening of depression, suicidality, or any unusual changes in behavior." (Trial Tr. vol. 13, 82.)

2. The "Strategic Swerve" to Maximize Neurontin Profits for Off-Label Indications

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FDA on how to conduct clinical trials. He is currently a senior advisor to the dean at Wake Forest University School of Medicine, where he previously established a research center on epidemiology and biostatistics. Dr. Furberg is the co-author of Fundamentals of Clinical Trials, the leading text in the world on the design, conduct, and analysis and reporting of clinical trials. (Trial Tr. vol. 13, 60-61.)

In 1994, Parke-Davis estimated that Neurontin would generate $500 million in profits over the duration of its patent. (TX 29.) In a memorandum circulated within Parke-Davis, one executive suggested a "strategic swerve" to increase the earning potential of Neurontin. (Id.) Some of the strategies explored included marketing the drug for epilepsy monotherapy, bipolar disorder and social phobia, and neuropathic pain. (See TXs 4, 7.) Defendants adopted these new strategies, which turned out to be stunningly successful: in 2003 alone, Neurontin sales exceeded $2 billion. (TX 111 at 5.)

Beginning in 1995, Parke-Davis began developing strategies to market Neurontin for off-label conditions, that is, conditions not included on the official label approved by the FDA. The company was interested in Neurontin's potential psychiatric uses, despite the uncertainty about its efficacy in treating bipolar disorder. In a cover letter attached to Parke-Davis's 1995 bipolar marketing assessment for Neurontin, Oliver Brandicourt, a Parke-Davis employee, wrote that "[t]he results [of bipolar trials], if positive, will be publicized in medical congresses and published in peer-reviewed journals, but there is no intention to fully develop these indications at this point." (TX 4 at 20559; see also Trial Tr. vol. 5, 21.) The assessment also included a "Recommendation" section that stated: "[D]ue to the lack of scientific rationale, since Neurontin has a different mechanism of action than the mood-stabilizing antiepileptics, it

is recommended to implement only an exploratory study in outpatients with bipolar disorders with the results highlighted through a peer-reviewed publication." (TX 4 at 20564.) The marketing team forecasted that a publication strategy for bipolar disorder would generate an additional $20 to $30 million in annual sales by 1999. (Id. at 20578.)

The company also developed marketing assessments for various pain conditions, including neuropathic pain. In September 1995, Parke-Davis sponsored a consultants' meeting where they discussed marketing options for Neurontin if it were found to be "analgesic" or pain-relieving. (TX 31 at 7; Trial Tr. vol. 6, 31.) Options discussed included sponsorship of a booth at the 1996 meeting of the American Pain Society, conferences and symposia with invited physicians, continuing medical education ("CME") events, and sponsorship of "publications of seeding trials" to create "[a] drumbeat in the literature." (TX 31 at 7.) The 1995 Neurontin marketing assessment for neuropathic pain forecast potential annual sales of an additional $20 to $25 million by 1999 if a marketing strategy was adopted for neuropathic pain. (TX 7 at 15.)

3. Efforts to Expand On-Label Uses Fail at the FDA

Meanwhile, efforts to expand "on-label" uses of Neurontin hit a brick wall. In 1996, Parke-Davis submitted a supplemental new drug application to the FDA, seeking approval of Neurontin as

a monotherapy for the treatment of seizures and requesting an increase of the effective dose range to include 3600 mg/day and the maximum recommended dose range to 4800 mg/day. (TX 91; Trial Tr. vol. 2, 37-38.) However, the FDA did not approve either of these changes, stating that "[t]he evidence from controlled trials fails to provide evidence that higher doses of Neurontin are more effective than those recommended." (TX 91 at 3.)

4. The Two Marketing Partnerships

Throughout the time period at issue in this case, 1995-2004, defendants engaged in two partnerships to further their goal of marketing Neurontin for off-label indications such as bipolar disorder, neuropathic pain, and migraine, and at doses greater than 1800 mg/day. The first such venture began in 1995 and involved a partnership between Parke-Davis and a healthcare advertising agency called Cline Davis Mann (CDM). CDM joined Parke-Davis's internal Extended Neurontin Disease Team, an interdisciplinary team that had primary oversight over the marketing of Neurontin. (Knoop Dep. Tr., 231-32, 235 (played Mar. 11, 2010).) Between June 1995 and June 2000, CDM prepared marketing strategy proposals for Neurontin and then devised tactics to implement those strategies, including Parke-Davis's strategy to "Expand Emerging Uses." (See, e.g., TXs 17, 44, 75.)

After Pfizer acquired Parke-Davis in 2000, it implemented a "publications strategy" to ensure the placement of key messages

relating to off-label uses of Neurontin in medical journals. (TX 138 at 62.) In order to implement this strategy, Pfizer engaged in a second venture that involved a partnership with Medical Action Communications (MAC). The MAC partnership began in 2001 and ended in 2004. MAC and Pfizer worked together through the joint Publications Subcommittee, which developed "key messages" to be used in publications. (TX 136.) These key messages focused on the claim that Neurontin was effective for off-label uses such as bipolar disorder, neuropathic pain, migraine, and high doses. (TX 210.) These key messages were disseminated throughout the medical community through the sponsorship of CME seminars and journal publications. (TX 259 at 11617.) MAC also helped Pfizer spin, delay and/or suppress negative evidence about Neurontin. For example, MAC took the position that the negative Reckless study, discussed infra, which showed that Neurontin was not effective for neuropathic pain, should not be "pushed for publication." (TX 136 at 4.) This plan was followed, and as will be seen, the negative Reckless study was suppressed in the medical literature.

Dr. Kay Dickersin, an expert in clinical trial design from Johns Hopkins University and the director of the U.S. Cochrane Group, gave a particularly helpful overview of defendants' use of scholarly publications as a tool to provide misleading

information about Neurontin to physicians.[4] (Trial Tr. vol. 4, 14-119, Feb. 25, 2010.)

Dr. Dickersin reviewed defendants' research study protocols, research reports, internal emails and documents, and publications, when available. (Id. at 23-24.) Dr. Dickersin found that "what was in the published record didn't agree with what was actually planned or what had been done" and that there was a "failure to publish results that were known." (Id. at 24.) She reviewed twenty-one trials sponsored by the defendants, and found that each and every trial exhibited "some form of bias or deviation from the truth." (Id. at 38.) Dr. Dickersin's testimony was credible and compelling.

The failure to publish results was a particular concern in this case, because, as Dr. Dickersin testified, defendants'

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[4] Dr. Dickersin holds a Ph.D. in epidemiology and is currently the director of the Center for Clinical Trials in the School of Public Health at Johns Hopkins University. (Trial Tr. vol. 4, 15-17.) She has also served as the director of the United States Cochrane Group since the early 1990s. (Id. at 17.) The Cochrane Group is an international nonprofit organization that provides compilations of the most reliable scientific evidence available about the use of certain drugs to treat various indications. (Trial Tr. vol. 2, 121.)

Dr. Dickersin indicated that her work in this case was compensated at an hourly rate of $400, but she asked the plaintiffs to contribute that money directly to Johns Hopkins University. (Trial Tr. vol. 4, 22.) She also stated that, although she has been asked to testify as an expert many times, she never agreed to do so before this case. She agreed to participate in this litigation because she felt "that the people had a right to know the truth." (Id. at 23.) She published her findings in this case in the New England Journal of Medicine in 2009. (TX 2091.)

marketing assessments for pain, migraine, and bipolar indicated that results of clinical trials would only be published "if positive." (Trial Tr. vol. 4, 36-37; TX 4 at 20559; TX 216 at 1586.) She explained that doctors who practice "evidence-based medicine," or make diagnoses and give treatments based on evidence from research, rely on published studies in medical and scientific journals because they do not have access to unpublished research reports. (Trial Tr. vol. 4, 26-27.) Therefore, if doctors do not have access to negative reports that are unpublished, they may prescribe a drug without being fully informed of the available evidence. (Id.)

Aside from the problem of unpublished trials, Dr. Dickersin explained a concept called "publication bias," which is "a failure to publish related to the direction and the strength of the results that you get in a study." (Id. at 30-31.) One type of publication bias is "selective outcome reporting." In designing a trial protocol, an investigator defines one primary outcome to be studied in the trial (e.g. change in median pain score after seven weeks). She also defines several secondary outcomes, or measures that she is interested in but that are not as important as the primary outcome. If the results of the study are negative for the primary outcome, but positive for one of the secondary outcomes, the investigator might publish an article that describes a previously-defined secondary outcome as the

primary outcome studied. (Id. at 32-33.) This "selective outcome reporting" is viewed as problematic within the scientific community. According to Dr. Dickersin, scientists should not "cherry-pick" outcomes that support their other interests, whether academic or financial, because it increases the likelihood that the results are not accurate if they are chosen after the study has been completed.[5] (Id. at 33-34.)

Another type of publication bias described by Dr. Dickersin is "location bias" or "gray literature bias" where a company publishes a negative trial in a journal that has a smaller circulation than more well-known medical journals. (Id. at 35.) Pfizer also engaged in this type of publication bias.

These efforts to market Neurontin for unapproved uses were incredibly successful. Before Pfizer acquired Parke-Davis, a Pfizer employee sent an internal email referring to Neurontin as "the 'snake oil' of the twentieth century." (TX 479.) As the following chart illustrates, Neurontin use for epilepsy was largely static throughout the relevant time period, while off-label use skyrocketed.

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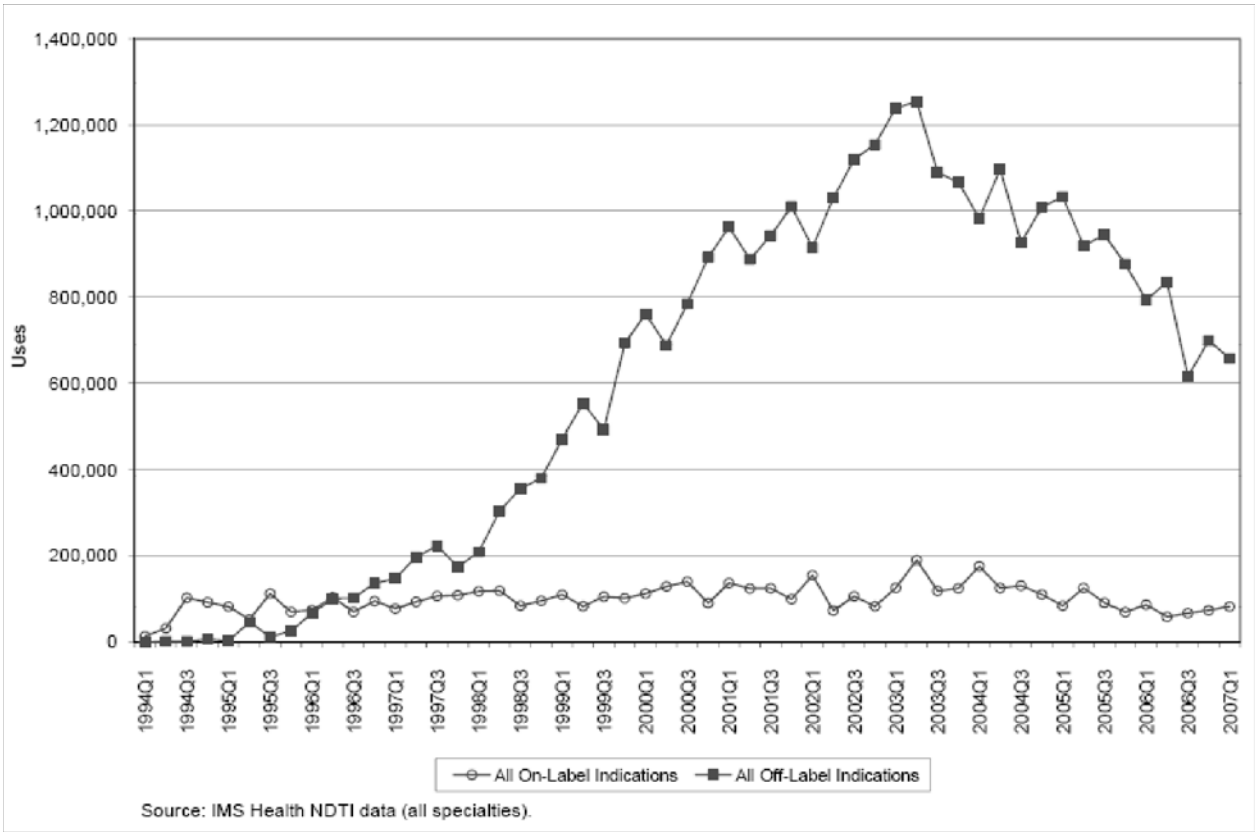
[5] "Once the data [from a clinical trial] are known, the addition or subtraction of primary outcomes can lead to the presentation of chance findings as evidence of a drug's effectiveness." (TX 2091 at 1969 (S. Swaroop Vedula, Lisa Bero, Roberta W. Scherer & Kay Dickersin, "Outcome Reporting in Industry-Sponsored Trials of Gabapentin for Off-Label Use," 361 New England Journal of Medicine 1963, 1969 (2009)).)



(TX 405-B). By the time Pfizer acquired Parke-Davis, Pfizer estimated that 87.5% of Neurontin prescriptions were for non-epilepsy indications, including 14.7% for bipolar disorder, 33% for neuropathic pain, and 3.8% for migraine. (TX 143 at 1170.)

5. Use of Medical Liaisons for Off-Label Marketing

Dr. David Franklin, the whistleblower in the initial Neurontin litigation in 1996, testified about the direct marketing of Neurontin to physicians for off-label uses. Dr. Franklin was hired in 1996 as a medical liaison for Parke-Davis. As part of his job he was provided training on off-label marketing of Neurontin. (Trial Tr. vol. 15, 35, Mar. 12, 2010

("[I]t was our job to . . . actually talk to physicians and sell Neurontin for off-label indications.").) His job was "99 percent focused on off-label promotion." (Id. at 43.)

Soon after Dr. Franklin was hired in 1996, he attended a national training for all Parke-Davis medical liaisons in Ann Arbor, Michigan. (Id. at 36.) During one session of the training meeting, two attorneys gave a presentation on FDA regulations related to off-label promotion. (Id. at 37-40.) This session was videotaped. (Id. at 38.) While the camera was recording, the two attorneys explained the FDA's rules regarding off-label promotion of drugs, although they stated their belief that these were "odd" rules. (Id.) Dr. Franklin was surprised by this presentation because "[i]t couldn't have been any more different" from what he had been doing in the field as a Parke-Davis medical liaison. (Id. at 41.) After this segment of the presentation on compliance with FDA rules, the two attorneys turned off the video camera and explained that the medical liaisons should not worry about these FDA regulations. They told the audience of medical liaisons "that it was . . . our job to sell" and "that we needed to dismiss what [was] just said and just be very careful . . . about how we went about doing [off-label marketing]." (Id. at 41-42.)

During another presentation given at the Ann Arbor training in 1996, a Parke-Davis employee named Sandra Pace handed out two notepads with the text "Ladies and Gentlemen of the Jury" and

"Your Honor, I plead." (Id. at 43-44.) She explained that these notepads were meant to emphasize the "importance of not creating a paper trail." (Id.)

Once Dr. Franklin became concerned that his activities as a medical liaison for Parke-Davis were violating the law, he recorded several phone conversations that were played in court. In one voicemail message recorded on May 23, 1996 from Parke-Davis employee Phil Magistro to all medical liaisons, Mr. Magistro said

> So what we need to do is focus on Neurontin. When we get out there, we want to kick some ass, we want to sell Neurontin on pain. And monotherapy and everything that we can talk about, that's what we want to do. 'Cause, I'm embarrassed. I don't know if you guys are embarrassed, but I'm embarrassed with where we are with Neurontin.

(TX 105 at 1-3.)

After working for the company for four months, Dr. Franklin consulted an attorney and ultimately filed a qui tam, or whistleblower, action under the False Claims Act with this Court, alleging that Parke-Davis was illegally promoting Neurontin for off-label indications. See United States ex rel. Franklin v. Parke-Davis, 147 F. Supp. 2d 39 (D. Mass. 2001); see also Trial Tr. vol. 15, 60-61. The case was sealed until January 2000. Ultimately, Dr. Franklin received a Relator's share as a result of the litigation in the amount of $24,640,000.

6. Investigation by the FDA

In July 1996, the FDA advised Parke-Davis that it was investigating the company's off-label promotion of Neurontin for chronic pain, bipolar disorder, and other indications. The FDA sought particular information from Parke-Davis concerning the company's financial relationship with certain doctors, including Dr. Gary Mellick, a paid Parke-Davis consultant who submitted a letter to the editor of a medical journal stating that Neurontin was effective in the treatment of Reflex Sympathetic Dystrophy. (TX 87; Trial Tr. vol. 2, 55-58.) Despite this warning, Parke-Davis continued its off-label marketing campaign.

7. FDA Rejection of Neurontin for Neuropathic Pain and Approval for Post-Herpetic Neuralgia (PHN)

In 2001, Pfizer (which had by then acquired Parke-Davis) attended a meeting with the FDA, during which the company discussed its planned submission of a supplemental New Drug Application ("NDA") seeking approval of Neurontin for the broad indication of neuropathic pain. During this meeting, the FDA stated:

> The general neuropathic pain indication cannot be granted for Neurontin based on the clinical trials in painful diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN). These two conditions are distinct, pathophysiological states and, therefore, will be treated as two indications. In order for a general neuropathic indication to be granted, the sponsor must provide evidence that the underlying disease process is similar for DPN, PHN, and the pain of other neuropathic disorders and/or that the drug is effective for the neuropathic pain of all (or at least

most) etiologies.

(TX 200 at 4.) In addition, the FDA gave Pfizer specific feedback about the use of Neurontin for the treatment of diabetic peripheral neuropathy: "The sponsor must provide evidence of efficacy replicated in a second study for DPN. This trial must be 12 weeks in length at fixed doses, as required for a chronically administered drug." (Id.) Pfizer filed a supplemental NDA for a broad neuropathic pain indication, but later withdrew that application. (Trial Tr. vol. 2, 46.)

After Pfizer met with the FDA to discuss a broad neuropathic pain indication in May 2001, it convened a meeting with a group of outside, non-FDA experts at the Crowne Plaza Hotel in Ann Arbor, Michigan. (Trial Tr. vol. 2, 44.) These experts concluded that the "preclinical and clinical data to date is that the evidence is not convincing to support a broad neuropathic pain claim. . . . New analyses/data not only do not support the broad claim, they provide evidence contrary to a broad indication." (TX 173 at 1.) One expert said, "You're done." (Id. at 2.)

In August 2001, Pfizer filed another supplemental NDA seeking approval of Neurontin specifically for the treatment of post-herpetic neuralgia. (TX 195.) In addition, Pfizer sought approval for doses above 1800 mg/day. (Trial Tr. vol. 2, 48.) In May 2002, the FDA approved Neurontin for the treatment of PHN,

a type of neuropathic pain associated with shingles, in adults. (TX 195.) However, the FDA did not approve the use of doses greater than 1800 mg/day, finding that there was no evidence of increased efficacy at higher doses. (Id. at 31; Trial Tr. vol. 2, 48.) The FDA required that the Neurontin label include the phrase "[a]dditional benefit of using doses greater than 1800 was not demonstrated." (TX 195 at 32.)

8. Warner-Lambert Guilty Plea

On May 13, 2004 the Department of Justice filed a criminal information charging Warner-Lambert with illegal off-label promotion of Neurontin. (TX 366.) The same day, Pfizer caused Warner-Lambert (which it owned) to plead guilty to two felony counts of marketing Neurontin for various unapproved uses, including painful diabetic neuropathy, bipolar disorder, reflex sympathetic dystrophy (RSD), and migraine headaches. (TX 371 ¶ 1 (stating that "Warner-Lambert expressly and unequivocally admits that it committed the crimes charged in the Information. Warner-Lambert agrees that the facts set forth in the Information are true.").) As a result of its guilty plea, Warner-Lambert agreed to pay a $240 million criminal fine. (Id.) The guilty plea included an admission that the company promoted the sale and use of Neurontin for the off-label indications of neuropathic pain, bipolar disorder, and migraine through the use of sales representatives, medical liaisons, advisory board meetings,

consultants meetings, and teleconferences. (TX 366 ¶¶ 9, 20-22, 23-24, 25-32, 33-36.)

In addition to the $240 million criminal fine, Pfizer paid an additional $190 million in civil fines to the government. (Trial Tr. vol. 15, 75.)

A year after the guilty plea was entered, Kaiser brought this lawsuit against Pfizer in the District of Massachusetts.[6]

C. Target: Kaiser

As early as 1994, Parke-Davis identified Kaiser as a potentially lucrative target for its marketing campaign. The marketing team listed Kaiser Health Plans second on its list of "Top 10 HMOs Targeted for Neurontin" in 1994. (TX 90 at 11.)

Defendants' focus on Kaiser continued throughout the relevant period. For example, in 2004 Pfizer developed an "Operating Plan" specifically for marketing to Kaiser. (TX 250.) This plan listed the following Kaiser-specific marketing

[6] On December 4, 2009, a little over two months before the trial date, the defendants moved to transfer the case to California pursuant to 28 U.S.C. § 1404. (See Docket No. 2193.) The Court declined to transfer the case for a number of reasons, including the late nature of the motion to transfer. The California-based plaintiffs did not wish to transfer venue. In addition, this Court presides over MDL cases and has developed expertise in the area, while any transferee judge would need a significant amount of time to familiarize herself with the case before holding a trial. This case has been pending for five years and the Court did not wish to create further delay. Moreover, the fact that videotaped trial depositions were already completed by December 2009 minimized any potential disadvantage to the defendants.

strategies for Neurontin: (1) "[i]dentify and build relationship [sic] with the P&T members;" (2) [p]rovide clinical and outcomes information to the Drug Information Coordinators on a regular basis;" (3) "develop relationships with [P&T members] who are not considered 'whistle blowers;'" (4) "maintain and improve the existing relationships and develop new relationships with physicians, Drug Education Coordinators (DECs), Drug Information, Kaiser research entities and brokers;" and (5) "support and attend the Kaiser conferences." (Id. at 25, 26, 29.)

Pfizer had significant contacts with PMG physicians, not only through detailing but also through the employment of PMG doctors to serve on speakers' bureaus and publish articles. According to Dr. Ambrose Carrejo, the pharmaceutical contracting leader for Kaiser, Pfizer detailed PMG physicians and drug information specialists about Neurontin throughout the relevant time period. (Trial Tr. vol. 5, 97-98.) It also recruited and paid prominent PMG physicians to serve on its Neurontin speakers' bureau. (Trial Tr. vol. 8, 120-22; TXs 276, 278, 279.) For example, Dr. William McCarberg, a PMG pain specialist, worked for Pfizer as a "pain mentor" and a Neurontin speaker. (TXs 276, 279.) He also reached out to Pfizer while writing an article with another PMG author to request information that would help dissuade his co-author from writing about "the overuse of Neurontin for questionable pain conditions." (TX 278.) In the final article, published in American Family Physician in February

2005, Dr. McCarberg and his co-author cast Neurontin in a positive light with respect to pain conditions and did not disclose that Dr. McCarberg used information from the company while developing the article. (TX 795.)

D. The Marketing Fraud

Defendants conducted marketing largely through three tactics: direct marketing to physicians, publication of positive Neurontin articles in medical journals and suppression of negative trials, and the sponsorship of CME events attended by physicians.

The Court finds that fraudulent marketing activities took place during the following time periods for each indication: (1) bipolar disorder: July 1998 through December 2004; (2) neuropathic pain: November 1997 through December 2004; (3) migraine: April 1999 through December 2004; and (4) doses greater than 1800 mg/day: November 1997 through December 2004.

1. Bipolar Disorder

To backtrack, Parke-Davis's internal documents suggest an initial reluctance among its marketing team to pursue a bipolar indication. In 1995 the company's internal recommendation stated: "[D]ue to the lack of scientific rationale, since Neurontin has a different mechanism of action than the mood-stabilizing antiepileptics, it is recommended to implement only an exploratory study in outpatients with bipolar disorders with

the results highlighted through a peer-reviewed publication." (TX 4 at 20564.) Pfizer conducted numerous scientific studies, none of which provided evidence that Neurontin was effective for treating bipolar disorder. I briefly describe these studies, which will be reviewed in greater depth later in the opinion, before addressing defendants' marketing activities with respect to bipolar disorder.

The first DBRCT to examine Neurontin's efficacy in the treatment of bipolar disorder was the Pande trial, conducted from March 1996 through July 1997, by Dr. Atul Pande, a Parke-Davis employee. (Trial Tr. vol. 4, 128; TX 383 at 1.) The results of the Pande trial showed that the placebo outperformed Neurontin in treating patients with bipolar disorder. Parke-Davis was aware of these results as early as July 1998. (Trial Tr. vol. 4, 130-31; TX 383 at 1, 8.)

The Frye trial was an independent DBRCT conducted between 1997 and 1999 that compared Neurontin to the drug Lamotrigine and placebo in the treatment of refractory, or difficult to treat, bipolar disorder. (Trial Tr. vol. 4, 132-33; TX 1477.) The Frye trial found that Lamotrigine outperformed both Neurontin and placebo, and that there was no statistically significant difference between Neurontin and placebo. (TX 1477 at 610-11.) Interim results of the study were presented at the American Psychiatric Association meeting as early as 1997, and the final results of the study were published in the Journal of Clinical

Psychopharmacology in 2000. (Id. at 607.)

The Guille trial was also a DBRCT that compared Neurontin to placebo in treating refractory bipolar disorder. (TX 211 at 63.) The trial investigators found no significant difference between Neurontin and placebo for treatment of bipolar disorder, and presented their results at the 1999 annual meeting of the American Psychiatric Association. (Id.; TX 1335.)

The Vieta trial was a DBRCT funded by defendants that compared Neurontin to placebo. It was completed in February 2004. (TX 398.) The Vieta trial showed no difference between Neurontin and placebo in the "intention-to-treat" (ITT) population, meaning the entire population of study participants who were included in the trial. (Trial Tr. vol. 4, 138-40; TX 398 at 4.) However, the study investigators did find a statistically significant difference between Neurontin and placebo in the "per protocol" (PP) subpopulation, or those patients who were healthier and more compliant than others in the group. (Trial Tr. vol. 4, 138-40.)

Finally, the Mokhber trial was a study, published in 2008, that compared Neurontin to Lamotrigine and Tegretol in the treatment of dysphoric mania, which is a state of bipolar disorder in which a patient presents both manic and depressive symptoms. (TX 2004 at 227.) The Mokhber trial showed improvements in both mania and depressive symptoms by those patients taking gabapentin, but there was no placebo group used

to control the study. (Id. at 227; Trial Tr. vol. 18, 112-16, Mar. 19, 2010.)

(i) Direct Marketing to Physicians

Despite the fact that the scientific evidence just described did not support the use of Neurontin for the treatment of bipolar disorder, defendants nonetheless marketed the drug for that indication. As early as April 1996, Parke-Davis medical liaisons were trained to tell physicians that Neurontin was "highly effective" for bipolar disorder, and they failed to disclose both that there was no scientific support for that indication and that the FDA had found an associated increased risk of suicide and depression for Neurontin patients. (Trial Tr. vol 15, 55-56.) Dr. Franklin, for example, was trained to talk to physicians about Neurontin's supposed effectiveness in treating bipolar disorder:

> For depression, what I was trained to do was explain to physicians that 50 percent of people initially described or diagnosed with depression were actually bipolar. And so that even their patients who were diagnosed with depression, they - they needed to consider Neurontin for those patients also for the effectiveness in bipolar.

(Id. at 55.) While Pfizer protests that Dr. Franklin worked only in the northeast region, his testimony described a national program for medical liaisons. His testimony, particularly about his training at a national conference, supports the reasonable inference that the same strategy of direct marketing was being

employed nationwide.

(ii) Publication Strategy

In addition to directly detailing doctors at their offices, defendants also pursued a publication strategy to create a buzz about the use of Neurontin for bipolar disorder. An article co-authored by a group of physicians, pharmacists, and researchers[7], published in the Journal of Psychiatric Practice in March 2008, explained that the extensive use of Neurontin in bipolar disorder was due to widespread positive reports in journals that created an "echo chamber" effect:

> The large number of case series and case reports reported encouraging results that were not confirmed by the later small randomized trials. The number of reports and their distribution in a number of journals created a type of "echo chamber" effect, through which the sheer number of publications and citations may have given legitimacy to the practice of using gabapentin for bipolar disorder.

(TX 1995 at 19-20.)

In February 1996, three members of Parke-Davis's department of Central Nervous System Clinical Research and Development

[7] This article was co-authored by Timothy S. Carey, M.D., M.P.H.; John W. Williams, Jr., M.D., M.H.S.; John M. Oldham, M.D., M.S.; Francine Goodman, Pharm.D., BCPS; Leah M. Ranney, Ph.D.; Lynn Whitener, Dr.P.H., MSLS; Laura C. Morgan, M.A.; Cathy L. Melvin, Ph.D., M.P.H. Carey, Ranney, Whitener, Morgan and Melvin are employed by the Cecil G. Sheps Center for Health Services Research at the University of North Carolina at Chapel Hill. Williams is employed by Duke University School of Medicine. Oldham is employed by the Menninger Department of Psychiatry and Behavioral Sciences at the Baylor College of Medicine. Goodman is employed by the Veterans Health Administration Pharmacy Benefits Management Strategic Healthcare Group.

published an article entitled "Effect of Gabapentin (Neurontonin® [sic]) on Mood and Well-Being in Patients with Epilepsy" in the journal Progress in Neuro-Psychopharmacology and Biological Psychiatry ("Dimond Article"). (TX 1158; Trial Tr. vol. 13, 73-75.) The Dimond Article examined the same five epilepsy trials that the FDA had examined in its 1992 medical statistical review, and claimed that Neurontin had beneficial effects on mood. However, the authors failed to reference the FDA's findings that Neurontin increased the risk of depression with or without suicidal ideation. (TX 1158; Trial Tr. vol. 13, 73-76; Trial Tr. vol. 16, 146-48, Mar. 15, 2010.)

In 1998, Parke-Davis sponsored the publication of a supplement to the Cleveland Clinic Journal of Medicine that reported the results of a symposium held July 24, 1998.[8] The supplement, titled "New Treatment Strategies in Psychiatry: Role of Anticonvulsants," discusses several case reports indicating that Neurontin is effective for the treatment of bipolar disorder

[8] A supplement to a medical journal is typically a "non-peer-reviewed . . . compendium of a discussion" and is not Level 1 evidence. (Trial Tr. vol. 5 at 24.) Scientists and physicians use the concept of levels of evidence to assign different weights to different types of evidence. Level 1 evidence "is evidence that results from double-blinded randomized controlled clinical trials" and is considered to be the best type of evidence. Level 2 evidence "is evidence that results from clinical trials . . . that are not necessarily well controlled. They can be unblinded. They could be nonrandomized." Level 3 evidence is "the result of a clinical judgment" such as case reports or anecdotal evidence. (Trial Tr. vol. 2, 24-26.)

and concludes that "[t]he data presented here indicate that gabapentin holds promise for treatment of bipolar disorder." (TX 110 at S1-11.) However, at the time the supplement was published in the fall of 1998, Parke-Davis was aware of the negative results of the Pande trial, which found that Neurontin was worse than a placebo for the treatment of bipolar disorder. The negative Pande trial results, disclosed to investigators on July 28, 1998, were not included in the supplement. (Trial Tr. vol. 5, 25.) The supplement, which was distributed to 43,000 psychiatrists, purported to gather the available evidence about the use of Neurontin in the treatment of bipolar disorder. I find that this supplement was intentionally misleading by only publishing half-truths.

The next year, an article written by Parke-Davis employee Leslie Magnus was published in a supplement to the journal Epilepsia. This article discussed several case studies, case series, and even a single-patient case report, but did not disclose the negative results of the Pande trial. (TX 2079 at S68-S69; Trial Tr. vol. 5, 26-27.) At this point, Pfizer likely knew about the Frye study as well. The article, published in 1999, concluded that

> [g]abapentin, a novel AED, has a unique mechanism of action. Its favorable safety profile and lack of drug interactions make it an attractive alternative for use in a wide array of neurologic and psychiatric conditions. The usefulness of gabapentin has been demonstrated in neuropathic pain syndromes, bipolar disorder, movement disorders, migraine prophylaxis, and

cocaine dependence.

(TX 2079 at S71.) The circulation was to 5,000 physicians. (Trial Tr. vol. 5, 27.) Similar to the Cleveland Clinic supplement, this article was intentionally misleading and is factually untrue in light of the Frye and Pande studies.

Also in 1999, Dr. Atul Pande, a Parke-Davis employee and the lead author of the negative bipolar DBRCT completed in 1998, published an article in the Journal of Clinical Psychopharmacology entitled "Treatment of Social Phobia with Gabapentin: A Placebo-Controlled Study."[9] This article stated that "[i]n clinical studies of patients with epilepsy, gabapentin produced improvements in mood and general well-being." (TX 1324 at 342.) The footnote supporting this statement only lists the Dimond article, which the Court has found to be problematic in its own right. It does not mention the negative results of Dr. Pande's earlier DBRCT, completed the year before this article was published, in which a placebo outperformed Neurontin in the treatment of bipolar disorder. (TX 1324 at 347; Trial Tr. vol. 5, 28-29.) Dr. Pande's article on social phobia was distributed by Parke-Davis to 25,150 psychiatrists. In addition, 125,850

[9] Social phobia is a disease where people are very afraid of social situations. It "is a potentially disabling condition where patients may not be able to interact [with others]." (Trial Tr. vol. 5, 28.) Social phobia is distinct from bipolar disorder, but may in some patients be comorbid (meaning co-existing) with bipolar disorder. (Id. at 29.)

copies of the article were printed and given to sales representatives, who visited psychiatrists and distributed the article in person. (Trial Tr. vol. 5, 29-30.) Pfizer's failure to disclose the results of Dr. Pande's other study (as well as the results of the Frye and Guille studies) to these psychiatrists constitutes a fraudulent half-truth.

Moreover, despite publishing the positive social phobia study by Dr. Pande in 1999, defendants suppressed the negative results of Dr. Pande's original bipolar study in 1998, completed in 1997, until October 2000, when the study was published in the journal Bipolar Disorders, a "fairly narrow" and "small journal" with a circulation of only 455 physicians.[10] (TX 1393; Trial Tr. vol. 4, 131-32.) The article blamed the negative results of the study on poor study design and failed to cite the negative results of two other Parke-Davis DBRCTs conducted by Drs. Frye and Guille, which were sponsored by defendants and the results of which were available at the time of publication. This placement of the negative Pande article in a small, lesser-known journal is an example of "location bias" as described by Dr. Dickersin.

To sum up, Parke-Davis sponsored two publications that contained intentional misrepresentations about the efficacy of

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[10] The Court notes that Dr. Pande did present the negative results of his study at the Third International Bipolar Conference in June 1999. (Trial Tr. vol. 3, 90-96.) Defendants presented evidence that ten physicians who have prescribed Neurontin to Kaiser health plan members attended that conference. (Id.; see also TXs 571, 923.)

Neurontin for the treatment of bipolar disorder: the Cleveland Clinic supplement in 1998 and the Epilepsia supplement in 1999. In addition, it detailed psychiatrists to sell Neurontin for biopolar without disclosing to doctors the information about the negative clinical studies. Finally, it suppressed the negative Pande study for three years, and completely suppressed the negative Guille and Frye studies.

(iii) Sponsorship of Continuing Medical Education (CME)

Defendants funded the development of several CME events attended by large numbers of psychiatrists and other physicians.

In 1998, Parke-Davis sponsored a CME titled "New Frontiers in Social Phobia and Bipolar Disorders" that was attended by 5,645 physicians in thirty cities, including Los Angeles, San Diego, and San Francisco. (TX 360.) Thirty-three PMG physicians from four different Kaiser regions attended this CME. (TXs 360, 923.)

Later that year, on November 21, 1998, Pfizer sponsored another CME called "New Options in Bipolar Disorder." During that conference, attendees were shown a slide that indicated Neurontin was an effective add-on treatment for bipolar disorder, citing a study by Dr. Trevor Young that was completed in 1997. (Trial Tr. vol. 2, 116-18.) However, the slide did not indicate that the Young study was sponsored by Pfizer, only included 15 people, and was not a randomized controlled trial but rather an

open-label study.[11] (Id. at 116, 119; TX 1197.) Nor did the slide indicate that the Pande study, the results of which were disclosed to investigators in July 1998, found that Neurontin was "significantly inferior to a sugar pill." (Trial Tr. vol. 2, 116.) As this CME purported to provide information from various sources about the use of Neurontin in treating bipolar disorder, the slide constitutes an intentional misrepresentation.

In 1999, Parke-Davis sponsored a CME event titled "New Frontiers in Anxiety, Substance Abuse and Bipolar Disorders" that was presented to 8,500 doctors, predominantly psychiatrists, across the country. (TX 63 at 3; Trial Tr. vol. 5, 31.) The slides prepared for the bipolar disorder segment of this CME include a slide titled "Gabapentin: Advantages and Disadvantages" that lists "reports and open-label data suggesting efficacy" as an advantage and "need for controlled studies" as a disadvantage. (TX 63 at 42.) Nowhere in the slide deck is the negative Pande or Frye trial for bipolar disorder mentioned. (Id.; Trial Tr. vol. 5, 31-32.) In addition, the materials for this CME recommend a dosing range of 900-3600 mg per day (sometimes higher) for gabapentin, which exceeds the maximum dose on the FDA label of 1800 mg/day. (TX 63 at 42.) In fact, in 1996 the FDA

[11] An open-label study a type of clinical trial where both the study investigators and the study participants know which treatment (i.e. an active drug or a placebo) is being administered.

rejected Parke-Davis's request to increase the maximum dose due to a lack of evidence of increased efficacy. The information presented at this CME involved fraudulent half-truths.

In June 2000, Pfizer prepared an internal strategy document titled "Neurontin: 2001 Situation Analysis" that stated the following: "Currently bipolar disorder represents over half of all psychiatric drug uses for Neurontin. . . . The increased use comes despite the results of the "Gabapentin in Bipolar Disorder" trial (945-209) [Pande] which showed no significant improvement when compared to placebo." (TX 213 at 19-20.) Despite the company's express acknowledgment of the negative trial results, the same document contains a Neurontin marketing plan for psychiatry that includes meetings and symposia at gatherings of the American Psychiatric Association and other organizations, half-day courses on anxiety and bipolar disorders, dinner meetings, and publications. (Id. at 28-29.) The document also states that "Parke-Davis plans to continue to support educational initiatives in the psychiatric arena that will discuss the broad utility of AEDs in a range of medical conditions such as bipolar disorders, anxiety states and substance abuse (alcohol withdrawal and cocaine treatment)." (Id. at 19.)

(iv) Communications with the Cochrane Review

In July 2003, Dr. Karine Macritchie of the Cochrane Review, an internationally recognized review organization, contacted

Pfizer about development of a protocol focused on Neurontin for the treatment of bipolar disorder and requested all data "published and unpublished, complete or ongoing, which would meet our inclusion criteria." (TX 236 at 1.) In response to an internal Pfizer email chain discussing what information to send to the Cochrane Review, Bruce Parsons, a Pfizer employee, wrote "I would not send unpublished Neurontin data to anyone outside Pfizer." (TX 159 at 1.) After repeated requests for data went unanswered, Cochrane abandoned its plans to complete a protocol on the use of Neurontin for bipolar disorder in April 2007. (Trial Tr. vol. 2, 123-24.) By referring the Cochrane Review researchers to positive, published articles about the use of Neurontin for the treatment of bipolar disorder without disclosing the negative, unpublished trials known to the defendants, Pfizer committed fraud.

(v) The Bottom Line

Beginning in July 1998 when Parke-Davis obtained (and began to suppress) the negative results of the Pande trial, the defendants engaged in the fraudulent marketing of Neurontin for the treatment of bipolar disorder. In addition to fraudulent detailing, Pfizer sponsored at least two fraudulent supplements, engaged in a fraudulent publication strategy by publishing only positive information and suppressing negative; conducted at least two fraudulent continuing medical education programs; and made a fraudulent misrepresentation, through a half-truth, to the

Cochrane Review.

2. "Kick Ass" on Neuropathic Pain

Defendants focused a significant portion of their marketing efforts on neuropathic pain because they recognized it as a potentially enormous market for Neurontin. Pfizer conducted numerous scientific studies to analyze the efficacy of Neurontin in the treatment of neuropathic pain. I briefly describe several of the studies that are relevant to the defendants' marketing strategies before addressing the marketing activities related to neuropathic pain. Again, the Court will revisit these studies in its discussion of the scientific proof of the efficacy of Neurontin.

1. Gorson Trial - Completed in 1997, the Gorson trial was funded by Parke-Davis and showed that Neurontin was no more effective than placebo in the treatment of painful diabetic neuropathy. This study was never published as a full article.
2. Backonja Trial - Also completed in 1997, the Backonja trial was a Parke-Davis study that concluded that Neurontin was effective in the treatment of painful diabetic neuropathy. The Backonja trial was published in JAMA in December 1998. This study involved issues of potential "unblinding" that compromised the integrity of its results. The article falsely stated that it was "the first trial to evaluate

gabapentin's efficacy" for neuropathic pain. (TX 1250 at 1832.) It also omitted any reference to the negative results of the Gorson study. (Id. at 1836.)

3. Reckless Trial - This study, which included three times as many patients as the Backonja study, was a Parke-Davis DBRCT completed in late 1999 that concluded that Neurontin was not effective for the treatment of painful diabetic neuropathy. The Reckless trial was never published.

4. POPP Trial - The POPP trial was sponsored by Pfizer and completed in November 2001. The investigators released their research report in 2003. This study concluded that Neurontin was not effective, on the study's primary measure, for the treatment of postsurgical or traumatic nerve injury pain. The POPP trial was not published until 2008.

5. Morello Trial - The Morello trial was published in 1999, and compared Neurontin with a tricyclic antidepressant to compare the drugs' efficacy for the treatment of painful diabetic neuropathy. The study found the drugs to be comparable.

6. Serpell Trial - This study, sponsored by Pfizer and completed in 2002, examined Neurontin's efficacy in treating people with a wide variety of neuropathies, including postherpetic neuralgia and painful diabetic neuropathy. The study found Neurontin to be effective. However, when those

patients with postherpetic neuralgia (for which Neurontin has been approved by the FDA) were removed from the study's results, the drug was no longer shown to be effective.

The marketing of Neurontin for neuropathic pain was accomplished through the use of direct marketing by sales representatives and medical liaisons, through a publication strategy, and through the sponsorship of CME events for physicians.

(i) Publication Strategy

In the mid-1990s, eager to get into the pain market, Parke-Davis sponsored a DBRCT conducted by Dr. Kenneth Gorson to study the effectiveness of Neurontin in the treatment of painful diabetic neuropathy. In August 1997, Dr. Gorson faxed Parke-Davis his manuscript from the study, which found that Neurontin "at a dose of 900 mg/day, is probably no more effective than placebo in the treatment of painful diabetic neuropathy." (TX 19 at 3.)

The manuscript of the Gorson trial that was later circulated among the study's investigators and Parke-Davis's marketing department by Phil Magistro, a Parke-Davis employee, put forth the conclusion that "[g]abapentin may be effective in the treatment of painful diabetic neuropathy. Our results suggest that further studies evaluating higher dosages of gabapentin are warranted." (TX 30 at 2.) As justification for this positive gloss, the modified manuscript focused solely on the randomized

group that received Neurontin, and compared patients' pain outcomes at the beginning of the study with the outcomes at the end. The patients did improve. However, the comparison to the placebo group was omitted. That comparison showed that the Neurontin group's improvement was statistically insignificant and that the evidence did not support a finding of efficacy. (Trial Tr. vol. 2, 143-45.)

Parke-Davis never published a full article with the findings of the Gorson study, but it did publish an "abstract" about the study in the April 1998 issue of Neurology.[12] The "conclusions" of the abstract mirrored the altered Magistro manuscript, stating that Neurontin "may be effective" in treating diabetic neuropathy. (TX 1271; see also Trial Tr. vol. 4, 56-58.) I find that the Neurology abstract about the Gorson study, published in 1998, was an intentional misrepresentation in that it specifically changed the lead investigator's primary conclusion.

In November 1997, Parke-Davis sponsored the publication of a supplement to the journal Internal Medicine entitled "Managing the pain of diabetic neuropathy." (TX 40 at 1.) A supplement in a medical journal is "a common vehicle to . . . avoid expert

[12] In 1999, Dr. Gorson published a letter to the editor in the Journal of Neurology, Neurosurgery & Psychiatry stating that "[t]he results of this study suggest that gabapentin is probably ineffective or only minimally effective for the treatment of painful diabetic neuropathy at a dosage of 900 mg/day." (TX 1379.)

independent review by people who might have disagreed with the conclusions . . . . Typically, for example, a company might sponsor a meeting . . . and the proceedings of the meeting would then be published as a supplement to a journal." (Trial Tr. vol. 7, 34-35, Mar. 2, 2010 (testimony of Dr. Thomas Perry).) In this particular article, the author, who is unnamed, describes the treatment of some neuropathies as a "trial and error" process, and the article explores the use of the anticonvulsant class of medications as a possible treatment option. (TX 40 at 12.) The author concludes that "Gabapentin can be used as a first-choice anticonvulsant, added as a second agent, or reserved for cases in which carbamazepine and phenytoin have been unsuccessful." (Id. at 14.) At the time this article was published in November 1997, the defendants had the results of the negative Gorson trial, but that information was neither discussed nor disclosed in this supplement. (Trial Tr. vol. 7, 37-38.) As an article that purports to gather available evidence on the use of Neurontin for the treatment of neuropathic pain, the Internal Medicine supplement was an intentional misrepresentation because it omitted the negative Gorson study available to Parke-Davis at the time.

During the same time period, Parke-Davis also sponsored a DBRCT led by Dr. Miroslav Backonja that studied the effectiveness of Neurontin in treating painful diabetic neuropathy. (Trial Tr.

vol. 3, 21, Feb. 24, 2010.) Completed in 1997, the study was published in the Journal of the American Medical Association (JAMA) in 1998 and concluded that "[g]abapentin monotherapy appears to be efficacious for the treatment of pain and sleep interference associated with diabetic peripheral neuropathy." (TX 1250 at 1831.) The study compared the results for the group of patients receiving Neurontin to a group receiving a placebo. Neurontin often caused central nervous system (CNS) side effects in patients such as sleepiness or dizziness. Those patients experiencing CNS side effects were potentially "unblinded," meaning that they were able to determine that they were receiving Neurontin as opposed to the placebo. The potential unblinding decreased the reliability of the study's results.[13]

Parke-Davis was aware of the potential unblinding effect present in the Backonja study. An attachment to an email sent to various Parke-Davis employees dated July 1, 1998 described the potential unblinding: "[A]t a pain experts' meeting, it was proposed that we should look for a correlation of maximum CNS-related Adverse Event severity with mean pain score, assuming that patients with more severe AEs tend to believe that they are

[13] This was not an inevitable result of any DBRCT studying Neurontin. Some articles produced close to the time of the JAMA publication suggested that clinical trials of drugs involving CNS side effects should utilize active placebos or comparators, which would cause sleepiness or dizziness in the placebo group as well and would thereby prevent unblinding. (TX 1282; Trial Tr. vol. 3, 18-25.)

on a study drug (which probably would be a good guess) and therefore tend to have better efficacy data, thus unblinding and corrupting the study." (TX 108 at 2; see also TX 107.)

Parke-Davis hired a public relations firm, Makovsky and Company, to publicize the 1998 Backonja JAMA article through video and radio news releases, advertisements on airline in-flight entertainment systems, and other forms of media. In total, the public relations campaign generated more than "85 million impressions." (TX 71 at 4.)

During the months before the Backonja JAMA article was published in December 1998, Parke-Davis sought to capitalize on the publication of the article by planning various outreach activities, some of which were described in an email sent from Parke-Davis employee Tammy Martin to the CNS Marketing Managers. The email stated that "[t]he [Customer Business Units] will band together for the CME teleconferences and Dinner Meetings. The plan would include a core faculty content development meeting in November and a faculty training meeting for December." (TX 102 at 1.) The email continued: "For the CME Teleconferences and Dinners each CBU needs to submit five potential thought leaders for the core faculty from the specialties of Neurology (pain management), Anesthesiology, Endocrinology and Immunology." (Id.) In the document attached to Tammy Martin's email, a section labeled "Strategy" states

Central marketing will focus efforts on the mailing of

> articles to all key specialists, coordinate development of the core slide kit and direct the PR efforts. CBUs will direct the sales force efforts to disseminate the studies to the physicians' offices. They will also coordinate teleconference sessions and local advisory board and plan dinner meetings for roll-out in [the first quarter of 1999]. The PR campaign will seek to maximize the exposure of the clinical data to both the professional audience and consumers.

(Id. at 7.)

In 1998, after the Backonja JAMA article was accepted for publication but not yet in print, Parke-Davis sponsored another supplement article, this time to the Cleveland Clinic Journal of Medicine. (TX 110.) This supplement included a section written by Dr. Edward Covington who wrote that "[d]espite few controlled studies on the efficacy of gabapentin in human pain management, this new drug has become the anticonvulsant of choice among many pain specialists." (Id. at SI-24.) The article cites to a case report written by Dr. Gary Mellick, a paid Pfizer consultant, and to various animal studies, but does not reference the negative Gorson trial. (Trial Tr. vol. 7, 39-41.) The article does, however, reference the positive Backonja trial, which had not yet been published in JAMA, indicating that Dr. Covington, the author, had access to Pfizer's unpublished trial data. (TX 110 at SI-29 n.44.) Because this supplement states that "there is substantial documentation for the clinical efficacy of [Neurontin] in the treatment of neuropathic pain syndromes" without referencing the negative Gorson trial, this supplement is

an intentional misrepresentation.

The next year, in March 1999, Defendants mailed a journal supplement entitled "Pharmacology of Painful Peripheral Neuropathies" to all neurologists practicing in the United States. (See TX 139 at 11657 (listing as a "1999 Key Strateg[y]" the mailing of "Dannemiller CME pain supplements" to "universe of Neurologists and Anesthesiologists"); see also TX 80 (listing Dannemiller Memorial Educational Foundation as the sponsor of the supplement). The supplement cited the Backonja article as supporting Neurontin's use as a "first line therapy for the treatment of painful peripheral neuropathies," without disclosing either the unblinding problem with Backonja or the negative results of the Gorson study. (Trial Tr. vol. 7, 51; TX 80.) This was an intentional misrepresentation.

A study conducted by Dr. Reckless, completed in late 1999 with results presented to Pfizer in February 2000, found that Neurontin was not effective in treating painful diabetic neuropathy. (TX 382 at 12.) Dr. Reckless, the lead author on this study, was "keen to publish" the results of this study. (TX 203 at 2.) However, Parke-Davis chose to "delay[] the publication for as long as possible" and refused to allow Dr. Reckless to write up the manuscript himself. (TX 183 at 1; see also TXs 185, 136, 109.) This strategy was successful, and the Reckless study was never written up as a stand-alone manuscript.

(Trial Tr. vol. 6, 30.) Despite the fact that the Reckless study included three times as many patients as the Backonja study, defendants suppressed the negative results of the Reckless study because of a desire "NOT to publish anything that damages Neurontin's marketing success." (TX 109; Trial Tr. vol. 3, 32.) Although the defendants never published Reckless as a full article, four years later they bundled the Reckless trial into a non-systematic review article that concluded that Neurontin was not only effective for neuropathic pain, but also that it was more effective at doses above 1800 mg/day. (TX 1660.)

In March 2000, Parke-Davis sponsored a supplement to Neurology Reviews titled "Management of Neuropathic Pain Syndromes." (TX 82 at 1.) The article concludes that "[o]f the new anticonvulsants, gabapentin was shown to be effective in the treatment of [diabetic neuropathy] in a double-blind, placebo-controlled, eight-week dose-titration trial using doses from 900 to 3,600 mg/d." (Id. at 11 (citing the Backonja JAMA article).) However, the article in the supplement does not discuss the negative results of either the Gorson trial or the Reckless trial, both of which were sponsored by Parke-Davis and studied diabetic neuropathy. (Trial Tr. vol. 7, 52.) Because this article reports on results of the Backonja trial without disclosing the results of the negative Gorson and Reckless trials, it is a fraudulent misrepresentation.

In the middle of 2001, Pfizer engaged a company called

Medical Action Communications (MAC) to market Neurontin for off-label indications. (Trial Tr. vol. 3, 40-41.) In conjunction with MAC, Pfizer sponsored the publication of a review article in which one of the key messages was that Neurontin is effective for the treatment of neuropathic pain. (Id. at 41.) Remember that at the time this article was being developed, Pfizer also held a meeting with its own pain experts at the Crowne Plaza hotel in Ann Arbor, Michigan on September 6, 2001 where the experts opined that the science did not support the development of neuropathic pain as an indication. (Id. at 40.) Once the article was ready to be published, a Pfizer employee sent an email to "Neurontin Product Champions" and wrote: "Because this is a key publication for NEURONTIN, information from this study should be used in all neuropathic pain initiatives, subject to your local regulations. Examples of such activities include: Promotional detail aids, Speakers programs, Regional promotional and scientific meetings, and Public relations programs (materials attached). If you are thinking about organizing any local PR activities please don't initiate them until the end of January (once the paper is published)." (TX 209 at 1-2.)

The review article, authored by Dr. Backonja and a Pfizer physician, Dr. Glanzman, was entitled "Gabapentin Dosing for Neuropathic Pain: Evidence from Randomized, Placebo-Controlled Clinical Trials" and was published in the journal Clinical

Therapeutics in 2003. (TX 1660.) The article concluded that Neurontin "is effective and well tolerated in the treatment of adults with neuropathic pain." (Id. at 82.) It intentionally does not cite to either the negative Gorson or the negative Reckless trial. (See, e.g., TX 262 at 1 (email from David Cooper, the Medical Director of MAC, to a marketing employee at Pfizer, stating that "[t]he real issue is deciding how to justify only reviewing 4 of the 6 randomized placebo controlled studies and the rationale for why Dr. Backonja [the author of the article] has access to unpublished papers and Pfizer data on file.").) As a review article that purports to gather available evidence but selectively omits negative evidence, the Clinical Therapeutics article was an intentional misrepresentation by Pfizer.

(ii) Direct Marketing and Sponsorship of CMEs

In June 1997, Defendants sponsored a symposium in Boston in connection with the 57th Annual Meeting of the American Diabetes Association. Dr. Gorson, who worked in Boston, was not asked to present the results of his negative study. Defendants instead selected Dr. Vera Bril as a speaker. When Parke-Davis learned that Dr. Bril would not recommend the use of Neurontin for neuropathic pain, its marketing partner, Cline Davis Mann, planted pre-written questions in the audience to "reverse the message that was delivered." (TX 43 at 3.)

In 2001, Pfizer's Global Operating Plan included a section titled "Developing the [Neuropathic] Pain Market" that listed as a strategy "Create New Standard of Care for NeP Treatment."[14] (TX 219 at 15.) This goal was to be accomplished by "educat[ing] PCPs and specialists on diagnosis and treatment" and "increas[ing] Neurontin field force presence in PCP and specialist offices." (Id. at 18.)

In Pfizer's 2003 "Neurontin Operational and Tactical Plan," it listed as one of its global strategies to "grow NePain market with NEURONTIN." (TX 239 at 24.) It also included a slide titled "Global Neuropathic Pain Positioning" that showed only the following text: "NEURONTIN is an ideal first-line therapy for neuropathic pain with proven efficacy, excellent safety and tolerability, favorable onset of action and ease of use, thereby restoring patients' quality of life." (Id. at 27.) The evidence does not indicate whether this slide was presented outside of Pfizer.

To sum up, as part of its publication strategy, Pfizer published half-truths and intentionally misleading information, submitted the April 1998 abstract about the Gorson trial that was published in Neurology, published the November 1997 supplement to Internal Medicine, mailed the March 1999 supplement to all

[14] "NeP" is an abbreviation for neuropathic pain. (Trial Tr. vol. 3, 44.)

neurologists in the United States, sponsored a 2000 supplement to Neurology Reviews, and sponsored an article in the journal Clinical Therapeutics in 2003. During the years at issue in this case, Pfizer deliberately suppressed publication of negative studies concerning many types of neuropathic pain, including DPN. (Tive Dep. Tr., 650-51, 666-67, 723-25 (played 3/11/10); see also TXs 136, 175, 183, 203.) Those trials suppressed included negative studies referred to as the Gorson, Reckless, and POPP studies. In addition, defendants published a positive study by Dr. Miroslav Backonja, but failed to disclose the unblinding problems with the trial design in promotional activities and advertisements related to the Backonja JAMA article. Pfizer also published a trial called the Serpell study without acknowledging that its positive results were attributable to patients suffering from post-heuretic neuralgia ("PHN"), a condition for which Neurontin had been approved by the FDA.

(iii) Detailing Doctors

Despite an admitted lack of reliable scientific evidence of efficacy, and a rejection by the FDA in 2001, defendants continued to aggressively and successfully market Neurontin to doctors as an effective treatment for the broad indication of neuropathic pain. (See, e.g., Trial Tr. vol. 3, 32-34, 40-41.)

Defendants' focus on detailing doctors to encourage use of Neurontin for neuropathic pain is perhaps best exhibited through the voicemail left for Parke-Davis medical liaisons by marketing

employee Phil Magistro in 1996:

> What we'd like you to do is, any time you're called out just make sure that your main focus out of what you're doing is on Neurontin. . . . So what we need to do is focus on Neurontin. When we get out there, we want to kick some ass, we want to sell Neurontin on pain. And monotherapy and everything that we can talk about, that's what we want to do. 'Cause I'm embarrassed. I don't know if you guys are embarrassed, but I'm embarrassed with where we are with Neurontin. We've got to take it into our own hands and really kick some ass on it, all right?

(TX 105 at 1-3.)

(iv) The Bottom Line

Beginning in November 1997 with the publication of the Internal Medicine supplement, defendants engaged in the fraudulent marketing of Neurontin for the treatment of neuropathic pain through the sponsorship of fraudulent publications.

3. Migraine

(i) Publication Strategy

Pfizer conducted a DBRCT (protocol 879-200) in the 1980s to investigate Neurontin's use in treating migraine. Defendants published interim results in 1987 in a supplement to An International Journal of Headache, pointing out positive outcomes. (Trial Tr. vol. 3, 56-57; Trial Tr. vol. 4, 46-49; Trial Tr. vol. 6, 23-24; TX 1056.) By June 1990, however, defendants were aware that the study demonstrated that Neurontin was no more effective than a placebo for migraine prophylaxis,

which means the prevention of migraine onset. They never published or otherwise disclosed the study's outcome. (TX 37; Trial Tr. vol. 6, 22-24; Trial Tr. vol. 3, 56-58.) Despite this evidence, Dr. Franklin credibly testified that Parke-Davis medical liaisons routinely informed physicians that Neurontin was effective for migraine without disclosing the negative results of the DBRCT.[15] (Trial Tr. vol. 15, 55, 63.) Such statements made by medical liaisons to physicians were intentional misrepresentations.

In September 1995, Parke-Davis sponsored a consultants' meeting where they discussed marketing options for Neurontin if it were found to be "analgesic" or pain-relieving. (TX 31 at 7; Trial Tr. vol. 6, 31.) Options discussed included sponsorship of a booth at the 1996 meeting of the American Pain Society, conferences and symposia with invited physicians, CME events, and sponsorship of "publications of seeding trials" to create "[a] drumbeat in the literature." (TX 31 at 7.) According to plaintiffs' migraine expert, Dr. Douglas McCrory, a seeding trial refers to a marketing tool involving "placement of peer reviewed articles in the literature to keep the message in the forefront." (Trial Tr. vol. 6, 32.)

In 1996, Parke-Davis distributed a memorandum to the Parke-

[15] In fact, according to Dr. Franklin, the medical liaisons were never informed about the negative 879-200 trial. (Trial Tr. vol. 15, 55.)

Davis Neurontin Marketing Group that described the Marketing Assessment for Neurontin in migraine prophylaxis. (TX 216.) With respect to Parke-Davis's intention to conduct further clinical studies, the memorandum states, "The results, if positive, will therefore be publicized in medical congresses and published in peer-reviewed journals." (Id. at 1586.)

Study 945-217, a Parke-Davis DBRCT, looked again at Neurontin's effectiveness in preventing migraines. Completed in early 1999, it found that Neurontin was not effective as a migraine prophylaxis. (TX 397 at 67; Trial Tr. vol. 3, 63.) In a document titled "Neurontin: 2001 Situation Analysis," the following text describes this DBRCT: "The B.I.D. Study (Migraine Study 217) did not show statistical significance in mean reduction in headaches . . . . The team has delayed posting or dissemination of results and they have not been presented at any scientific meetings to date." (TX 213 at 22.)

The Mathew Trial was conducted by the defendants from 1996 to 1998. (TX 396 at 1; Trial Tr. vol. 6, 28-29.) The trial results showed no statistically significant difference between Neurontin and placebo "with respect to 4-week migraine headache rates or proportion of patients with reduction of 50% or greater in migraine headache rates." (TX 396 at 4.) An article about the Mathew trial was published in the journal Headache in 2001. It claimed that "gapabentin is an effective prophylactic agent for patients with migraine." (TX 612 at 119.) The discrepancy

between the research report and the published article is not explicitly mentioned; however, the positive published results were achieved by using a "modified" intent-to-treat population and by focusing on outcomes identified as secondary in the research report. Moreover, the article did not disclose the negative results of trials 879-200 or 945-217. I find that the conclusions of the Mathew article were intentional misrepresentations.

In March 2002, the Cochrane Review requested data from Pfizer about the use of Neurontin for migraine prophylaxis. (TX 122 at 3.) In an email chain among Pfizer employees in early 2002, Elizabeth Mutisya wrote, "We would not be able to provide them with our databases which is what they are ultimately interested in." (Id. at 2.) In response to Ms. Mutisya's email, Leslie Tive wrote: "If they are looking for unpublished data, I would be reluctant to send it. I would not even send actual articles." (Id.) Cochrane's review, first published in July 2004, concluded, "The evidence derived from trials of gabapentin suggests a beneficial effect in migraine prophylaxis, but this drug needs further evaluation." (TX 2086 at 9.) The Cochrane article cites to the positive Di Trapani study, a trial unaffiliated with Parke-Davis and completed in 2000 (see Trial Tr. vol. 6, 76-77; TX 1478), and to the positive results of the Mathew trial as published in 2001. It does not refer to either of Pfizer's negative migraine prophylaxis DBRCTs, or to the

unpublished data indicating that the Mathew trial did not show statistical significance in the primary outcome identified in the study's protocol. (TX 2086 at 10-11; Trial Tr. vol. 3, 65.) Because of defendants' suppression of negative DBRCTs, the Cochrane Review researchers concluded that Neurontin was effective for migraine prophylaxis. (TX 2086.)

In 2003, a doctor of pharmacy named Alicia Mack published an article in the Journal of Managed Care Pharmacy titled "Examination of the Evidence for Off-Label Use of Gabapentin." (TX 349 at 559.) Essentially, Mack reviewed the available literature about the use of Neurontin in treating off-label indications such as diabetic neuropathy, migraine prophylaxis and bipolar disorder. (Id.) With respect to migraine prophylaxis, Mack included two DBRCTs: the 2000 Di Trapani study and the Mathew article published in 2001. Mack's article concluded that "there are clinical trials of gabapentin in migraine prophylaxis" but cautioned that "outstanding questions remain regarding the drug's utility in clinical practice." (Id. at 565.) Mack's review of the literature did not include two unpublished negative DBRCTs or the unpublished negative data from the Mathew trial, all of which was in Pfizer's possession. (Trial Tr. vol. 3, 68.)

(ii) Sponsorship of CME Events

Beginning in April 1999, Dr. Ninan Mathew, the lead investigator of the Mathew trial, led a CME titled "Advances in the Preventive Treatment of Migraine." In the outline provided

to physicians participating in the CME program, gabapentin is listed as one of the "[f]irst-line options for migraine prophylaxis." (TX 245 at 2.) This CME was sponsored by Parke-Davis. (TX 248 at 5.) Dr. Mathew was paid $20,000 for his participation in this CME. (Id. at 8-9.) Because the materials used for this CME do not reference the negative studies 945-217 or 879-200, both of which were completed by early 1999, the statement made in the CME materials constitutes an intentional misrepresentation.

To sum up, beginning in April 1999, the defendants engaged in fraudulent marketing of Neurontin for migraine prophylaxis through the sponsorship of a CME that included a fraudulent statement and the sponsorship of the misleading Mathew article in 2001. Parke-Davis medical liaisons also made misrepresentations regarding the efficacy of Neurontin in treating migraines in detail visits to physicians as early as April 1996, (see Trial Tr. vol. 15, 63-64).[16]

4. Nociceptive Pain

Plaintiffs allege that defendants fraudulently promoted Neurontin for nociceptive pain. They have not presented any documents that directly reference a marketing strategy to promote Neurontin for the treatment of nociceptive pain. Because certain

[16] However, Kaiser's damages expert did not provide the Court with migraine damage amounts for 1996, 1997 or the first three quarters of 1998. (TX 408-I.)

documents refer to pain in an ambiguous manner, plaintiffs contend that there is sufficient evidence of fraudulent promotion of Neurontin for the treatment of nociceptive pain. The jury found for defendants on this claim of fraudulent off-label marketing for nociceptive pain.

Dr. David Franklin testified that Parke-Davis medical liaisons, during the time he was employed in 1996, were trained to promote Neurontin to physicians for the treatment of pain. (Trial Tr. vol. 15, 63.) In a voicemail recorded by Dr. Franklin in 1996, Parke-Davis employee John Ford told medical liaisons: "If we are going to market Neurontin effectively, we have to do it for monotherapy, for epilepsy, also for pain and bipolar and other psychiatric uses. And, how, you know, that's a labeling issue, and ultimately what that means is that the liaisons have to be the ones that primarily do that." (TX 105 at 498-99.) In another voicemail, Parke-Davis employee Lisa Kellett urges medical liaisons to promote Neurontin to doctors "even if [they] treat[] garden variety pain." (Id. at 601.)

In a memorandum distributed by Parke-Davis to participants in a "Consultants Meeting" held in 1995, one consultant wrote that Neurontin "may be effective in more than neuropathic pain," citing Dr. Mellick's case reports. (TX 31 at 4.) In the same memorandum, another consultant suggested that Parke-Davis "study low back pain because of large incidence in population . . . . Could do pilot studies in areas other than neuropathic pain."

(Id. at 5.)

Based on the paucity of this evidence, the Court concludes that plaintiffs have not proven that defendants fraudulently marketed Neurontin for nociceptive pain. Compared to the other off-label conditions for which there are marketing documents and publications that explicitly promote Neurontin based on half-truths or actual misrepresentations, the evidence presented for nociceptive pain seems to represent internal discussions and use of imprecise language more than an actual fraudulent marketing scheme. The jury reached the same conclusion. (See Docket No. 2760.)

5. Doses Greater than 1800 mg/day

In 1996, the FDA rejected Parke-Davis's request to increase the effective dose range listed on Neurontin's label to 3600 mg/day, stating that "the evidence from controlled trials fails to provide evidence that higher doses of Neurontin are more effective than those recommended." (TX 91 at 3.) In 2002, the FDA rejected Pfizer's proposed marketing materials regarding high doses because "additional benefits of using doses greater than 1800 mg/day were not demonstrated." (TX 190 at 2.)

Although Parke-Davis did sponsor clinical studies where Neurontin was forcibly titrated to doses greater than 1800 mg/day or where one group of patients received high doses, none of those trials indicated that Neurontin was more effective at a higher

dose than at a lower dose. (See, e.g., TX 1250 (Backonja Trial); TX 382 (Reckless Trial).) In the 1999 Reckless trial, for example, one group of patients received 2400 mg/day of Neurontin, but that group did not have results that were statistically significantly better than the placebo group. (TX 382 at 12.) Despite the FDA's rejection of two requests to increase the maximum dose of Neurontin for its on-label indications due to lack of evidence of increased efficacy, defendants consistently disseminated the message that Neurontin was safe and effective at doses greater than 3,600 mg/day and claimed that this was supported by clinical studies. (Glanzman Dep. Tr., 343-44 (played 3/12/10) (testimony from a Pfizer employee stating that he approved a marketing "key message" in 2001 stating that "Gabapentin is safe and effective at high doses greater than 3,600 milligrams".) This was a fraudulent misrepresentation.

In 1997, Parke-Davis sponsored a CME where physicians were told that Neurontin can be used in doses up to 4800 mg/day to treat patients with bipolar disorder. (Trial Tr. vol. 2, 127.) This was an intentional misrepresentation.

In November 1997, Parke-Davis sponsored the publication of a supplement to Internal Medicine that claimed Neurontin was effective in treating diabetic peripheral neuropathy, but that "[a] daily total [dose] of 1,800-3,600 mg may be needed." (TX 40 at 14.) By representing that high doses may be necessary when

studies had not shown any additional efficacy for any indication at doses over 1800 mg/day, this supplement made an intentional misrepresentation.

The 5,645 physicians who attended the 1998 CME series entitled "New Frontiers in Social Phobia and Bipolar Disorders," including 33 PMG physicians, were instructed to titrate Neurontin to 3600 mg (sometimes higher), without any disclosure of the fact that no additional benefits above 1800 mg/day had been demonstrated in clinical trials. (TX 360; Trial Tr. vol. 5, 32.) These statements were intentional misrepresentations.

In March 1999, defendants mailed a copy of a supplement to the journal Progress in Neurology to all neurologists practicing in the United States. (TX 80; TX 139 at 11657.) This supplement stated that some patients require 3600 mg/day of Neurontin. (TX 80 at 6.) Because there is no scientifically reliable evidence showing increased efficacy at higher doses, this was an intentional misrepresentation.

In 2000, Parke-Davis sponsored the publication of a supplement to the journal Neurology Reviews. This supplement cited to the Backonja trial, published in JAMA in 1998, and said that "gabapentin was shown to be effective in the treatment of [diabetic neuropathy] . . . using doses from 900 to 3,600 mg/d." (TX 82 at 11.) While the Backonja trial did titrate patients up to 3600 mg/day, this statement is a fraudulent half-truth because

it does not disclose that no additional efficacy was found for those patients titrated to high doses. (Id.; see also TX 195 at 31-32 (FDA's 2002 statement that there is no evidence of additional efficacy at high doses).)

In 2003, Pfizer worked with Dr. Miroslav Backonja and Dr. Robert Glanzman, a Pfizer employee, to develop a review article on Neurontin dosing for neuropathic pain. (TX 1660 at 81.) Despite the fact that the FDA had approved the maximum dose of Neurontin at 1800 mg/day, the review article concluded that "[a]t doses of 1800 to 3600 mg/d, gabapentin was effective and well tolerated in the treatment of adults with neuropathic pain." (Id. at 82.) This conclusion was published despite the fact that the authors, and Pfizer, had access to the results of the Reckless study, which found that Neurontin was not effective in doses greater than 1800 mg/day. (Trial Tr. vol. 3, 54; Trial Tr. vol. 7, 27-28 (stating that in the Reckless trial, "[t]here was no difference at the higher dose of 2,400 milligrams compared with either of the lower doses or placebo.").) The Reckless study was not cited in this review article. (TX 1660 at 101-04.) Because this article was a review article, purporting to gather all available evidence on Neurontin, the statements regarding dosing were intentional misrepresentations.

To recapitulate, beginning in November 1997 with the publication of the Internal Medicine supplement, defendants

engaged in fraudulent marketing of Neurontin at doses greater than 1800 mg/day through the sponsorship of four publications and two continuing medical education programs that contained fraudulent statements about Neurontin's efficacy.

E. Kaiser's Reliance on Pfizer's Misrepresentations

From 1994 through 2004, Kaiser spent almost $200 million on Neurontin. (Trial Tr. vol. 5, 91-92.) As discussed earlier, Kaiser has a centralized Drug Information Service that develops drug monographs for the P&T Committees. It independently researches and analyzes pharmaceutical products before placing them on the drug formulary. Neurontin was initially placed on Kaiser's regional formularies in 1994 as an AED approved by the FDA. In the case of Kaiser's Southern California region, its use was limited to neurologists.

Throughout the time period relevant to this case, the Southern California P&T Committee reviewed Neurontin's formulary restrictions three times. Prior to each review, DIS prepared an updated drug monograph and gave a recommendation as to the appropriate prescribing of Neurontin. As Dr. Mirta Millares, the chairperson of Kaiser's DIS, testified, the Neurontin monographs were circulated among all the Kaiser regions through national teleconferences and interregional P&T Committee meetings. (Trial Tr. vol. 5, 110.) The P&T Committees and PMG doctors relied on DIS's research. (Trial Tr. vol. 12, 94.)

In September 1997, the Southern California P&T Committee approved a request by the Chiefs of Anesthesiology to allow anesthesiologists to prescribe Neurontin for the treatment of Reflex Sympathetic Dystrophy (RSD), a neuropathic pain syndrome. (Trial Tr. vol. 9, 49-51; TX 290.) In approving the request for an expansion, both DIS and the P&T Committee relied on two letters to the editor published in scientific journals that touted successful use of Neurontin in the treatment of RSD. (TX 322; Trial Tr. vol. 9, 51-52.) Both of these letters to the editor were written by Dr. Gary Mellick, a paid Parke-Davis consultant. (See TXs 23-25, 27, 322.) Parke-Davis became aware of the negative results of the Gorson study by August 23, 1997. (TX 19.) However, DIS prepared the RSD drug monograph in April 1997, prior to the internal release of the Gorson results. (TX 322.) At that point, Pfizer did not have any scientific evidence to support the use of Neurontin for the broad neuropathic indication, but neither did it have any of the negative studies yet. There is no evidence that Kaiser's DIS relied on any misrepresentation in the 1997 monograph.

In June 1999, the Southern California P&T Committee received a request by the Chiefs of Psychiatry to relax the restrictions on Neurontin to allow psychiatrists to prescribe Neurontin for the treatment of mood disorders, including bipolar disorder. (TX 311.) The P&T Committee approved the request despite a

"significant" predicted cost impact because Neurontin was an expensive drug in comparison with alternative treatments.[17] (TX 543; Trial Tr. vol. 9, 62-63, 69-71.) DIS relied on a "personal communication" with Parke-Davis when making a recommendation to the P&T Committee. (TX 311 at 6.) The letter that a Parke-Davis employee sent to Kaiser in response to this communication did not disclose the negative Pande study, which Parke-Davis had known about since at least 1998. (TX 301; Trial Tr. vol. 9, 67-69; Trial Tr. vol. 10, 81-83, 84.) Instead, the letter disclosed only the Dimond article that interpreted the epilepsy studies as proof that Neurontin had a beneficial effect on mood. Had the defendants disclosed the 1997 and 1998 negative studies, that information would have been reflected in the monograph and DIS probably would not have recommended relaxing the restrictions on Neurontin. (Trial Tr. vol. 9, 66-71.) In addition, Dr. Dale Daniel, the Chair of the P&T Committee, would not have voted to relax the restriction if he had known about the negative Pande study. (Trial Tr. vol. 12, 100-01.)

In September 1999, the Southern California P&T Committee voted to remove the remaining formulary restrictions on

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[17] Gabapentin was predicted to cost $1,172-$1,900 per patient per year as compared to Lithium Carbonate at $22-$44, Carbamazepine at $146-$175, and Valproic Acid (Depakote) at $694-$1,077. Altogether, Kaiser predicted a cost impact of $457,000 to $740,000 per year if gabapentin were used as an adjunct therapy in 10% of patients taking valproic acid or carbamazepine. (TX 543.)

Neurontin. (TX 327, 291.) At the time the restrictions were removed, there were multiple lower-cost drug options on the formularies utilized by PMG physicians for the treatment of diabetic neuropathy; removing restrictions on Neurontin had a significant cost impact. (Trial Tr. vol. 9, 72-76; TX 327.)

In preparing an updated drug monograph and recommending the removal of all restrictions in August 1999, DIS relied on a communication with a Parke-Davis employee. (TX 327 at 9.) This communication failed to disclose (1) complete information about the negative Gorson trial and (2) complete information about the potential unblinding of the Backonja trial. (Trial Tr. vol. 9, 76-80; Trial Tr. vol. 12, 101-07.) Although DIS did have access to a letter to the editor published in the Journal of Neurology, Neurosurgery & Psychiatry about the Gorson trial which disclosed the negative results of the trial (see TX 1379), Millares thought it was "funky" that a DBRCT would only be published as a letter to the editor, rather than in a peer-reviewed journal.[18] Accordingly, Dr. Millares stated that DIS gave the Gorson letter less weight than the Level I evidence presented by the Backonja DBRCT. (TX 544; Trial Tr. vol. 9, 79.) Dr. Millares credibly testified that, had DIS been aware of the undisclosed information

[18] While DIS did review the Gorson letter to the editor, it does not appear that DIS was aware of the Gorson "abstract" published in Neurology that touted the study as having positive results. (See TX 1271.)

about Backonja, it would not have recommended that the P&T Committee lift the restrictions on Neurontin. (Trial Tr. vol. 9, 88.) A different recommendation from DIS would have been material to the P&T Committee in making its decision, and Dr. Dale Daniel, the chair of that committee testified that, had he known about the withheld information, he would not have voted to lift the formulary restrictions. (Trial Tr. vol. 12, 104.) In fact, he specifically testified that he gave the Gorson letter less weight than the Backonja JAMA article because it was not a full article and had not been peer-reviewed. (Id. at 103-04.)

Thus, plaintiffs have proved that Kaiser relied on Pfizer's misrepresentations and omissions during the development of drug monographs in both June and September 1999.

Kaiser also directly relied on statements by Pfizer through its inquiry service. DIS maintains an inquiry service that responds to inquiries from PMG physicians. DIS regularly contacts pharmaceutical manufacturers when researching inquiries about drugs. (Trial Tr. vol. 9, 89-90.) DIS made multiple inquiries throughout the relevant period about the proper usage of Neurontin. Defendants' responses failed to disclose DBRCTs that demonstrated Neurontin was ineffective for particular indications and falsely indicated that Neurontin was effective in dosages greater than 1800 mg/day. (Id. at 91-97; TXs 292, 294, 296, 309.) In particular, in August 2000 Pfizer faxed DIS a

document stating that the dose used for one of its studies was "3600 mg/day regardless of efficacy achieved at the lower dosage." (TX 296.) In December 2000, Pfizer told DIS that "the maximum dose that they have seen is for 6,000 mg/day in non-Parke-Davis studies." (TX 294.) Throughout the relevant time period, defendants also provided misleading information directly to Kaiser healthcare professionals through misleading standard response letters that omitted key negative studies. (Trial Tr. vol. 9, 97-100; TX 432 at 13.)

PMG physicians attended CME conferences where Neurontin was promoted for off-label uses. Kaiser conducted an internal analysis looking at how the prescribing decisions of PMG physicians were affected by attendance at a CME where Neurontin was promoted. This analysis was based on a May 1999 CME that was attended by a group of PMG physicians. The internal analysis, completed in 2003, found that new starts of Neurontin increased by 62% soon after the 1999 CME. In addition, Kaiser's internal analysis showed a continuing effect, with 100% more new starts in early 2003 than in early 1999. (TX 286.) However, the evidence introduced at trial does not indicate whether these analyses were restricted to new starts by those physicians attending the CME in 1999.

In March 2000 defendants sent a letter to a PMG physician named Dr. Barbara Livermore in response to a request for

information. (TX 432; TX 461-A at 5; Trial Tr. vol. 9, 98-99.) The letter purportedly summarizes the evidence for Neurontin's use for a number of indications, including neuropathic pain and migraine. The letter omitted any reference to the Gorson and Reckless studies, which were both negative. The letter also failed to mention the negative results from the three migraine DBRCTs sponsored by Parke-Davis. (TX 432; Trial Tr. vol. 9, 97-98.)

The Court found the testimony of Dr. Millares and Dr. Daniel to be credible. The publication strategies and the other communications between Pfizer and Kaiser directly affected =decisions about Neurontin's placement on formulary without restrictions. In addition, the direct communications to PMG physicians caused Kaiser injury because it reimbursed for Neurontin rather than less costly alternatives. Because Kaiser has a 95% compliance rate with its formulary, formulary restrictions necessarily affect the number of prescriptions written for any given drug. I find that Kaiser was injured as a result of its reliance on Pfizer's intentional misrepresentations and omissions.

The Court finds that Kaiser relied on defendants' fraudulent marketing activities during the following time periods for each indication: (1) bipolar disorder: June 1999 through December 2004; (2) neuropathic pain: September 1999 through December 2004;

(3) migraine: September 1999 through December 2004; and (4) doses greater than 1800 mg/day: September 1999 through December 2004.

F. Kaiser's DUAT and DRUG Campaigns

Pfizer contends that Kaiser did not do enough to prevent PMG physicians from prescribing Neurontin for off-label indications once it became aware of defendants' fraud. It is true that Kaiser did not remove Neurontin from its formulary or impose restrictions. Indeed, Pfizer introduced the embarrassing fact that favorable information about Neurontin for the treatment of neuropathic pain stayed on the Kaiser website until the week before trial. Still, Pfizer unfairly demeans Kaiser's efforts to mitigate its injury. Kaiser did vigorously pursue an information campaign to reduce off-label prescribing once it became aware of the off-label marketing campaign by Pfizer.

By September 1999, Kaiser's formularies did not include any restrictions on Neurontin, and prescribing increased dramatically. Dr. Ambrose Carrejo, the pharmaceutical contracting leader for Kaiser, testified that "[t]he genie was out of the bottle. It just took off. It was quarter over quarter utilization growing in 10 percent, quarter over quarter, there was a dramatic increase." (Trial Tr. vol. 5, 110-11.) This dramatic increase in utilization raised red flags for some Kaiser regions and led them to examine their members' use of Neurontin. (Id. at 111-13.) As a result, the Northern

California region did two things. First, by the spring of 2002 it made Neurontin a nondetailable product, meaning that Pfizer drug representatives were not permitted to visit or contact PMG physicians with respect to Neurontin. Second, Northern California's Drug Utilization Group ("DRUG") began a campaign to promote appropriate use of the drug. (Id. 113-15; TX 273 at 5; Trial Tr. vol. 8, 102-05.) Other regions joined the effort. (Trial Tr. vol. 5, 113-15; TX 273 at 5; Trial Tr. vol. 8, 102-05.)

In late 2002, Kaiser learned about the whistleblower suit brought by Dr. David Franklin, a former medical liaison of Parke-Davis. Kaiser learned that "exaggerated or false claims about the safety and efficacy" of Neurontin had been made by its manufacturers. At that point, Kaiser escalated its efforts to promote appropriate prescribing of the drug. (Trial Tr. vol. 5, 115-17; TX 319; Trial Tr. vol. 8, 107-09; TX 355; TX 344.) Those efforts focused on neuropathic pain, bipolar disorder, migraine, and nociceptive pain. (Trial Tr. vol. 5, 120-23; TX 352-353.) The Neurontin materials produced by DRUG and its Southern California counterpart, the Drug Utilization Action Team ("DUAT"), were shared with all Kaiser regions. (Trial Tr. vol. 8, 103-04, 111-12, 130-32.)

Kaiser's efforts to promote appropriate Neurontin prescribing involved a "significant number of [PMG] physicians and pharmacists [and] dedicated a lot of resource[s] to coming up

with the appropriate alternatives" to Neurontin. (Trial Tr. vol. 5, 128.) The efforts of the DRUG and DUAT teams, along with teams from other regions, were successful, resulting in a 33-34% decrease in new starts of Neurontin and a similar decrease across all specialties. Meanwhile, Neurontin use continued to increase nationally. On January 8, 2004, DRUG reported a 50% decrease in new starts of Neurontin in Kaiser's Northern California region. By June 2004, a 34% decrease in Neurontin utilization was experienced in Kaiser's Southern California region. (Trial Tr. vol. 5, 124-26; Trial Tr. vol. 8, 114-15; TX 340 at 2, 6; TX 272 at 3.)

Kaiser employees testified that the company learned about the scope of defendants' fraud through (i) the discovery and resulting expert reports produced in this litigation and (ii) the publication of Dr. Kay Dickersin's article in the New England Journal of Medicine in November 2009. (Trial Tr. vol. 5, 136-37; Trial Tr. vol. 7, 60-62, 111, 113; Trial Tr. vol. 8, 16-18, 141; Trial Tr. vol. 9, 126; Trial Tr. vol. 13, 55-56.) The recent publication of the Dickersin article reinvigorated Kaiser's efforts to educate PMG physicians and Kaiser members about appropriate prescribing of Neurontin. (Trial Tr. vol. 8, 123-24, 143-44; Trial Tr. vol. 10, 95-96; Trial Tr. vol. 12, 131.)

G. <u>Injury/Damages</u>

Although Kaiser has introduced persuasive evidence of its

direct reliance on Pfizer's misrepresentations and omissions and of its injury, plaintiffs had a difficult challenge in quantifying the number of prescriptions that were actually caused by defendants' misconduct because the prescribing decisions of physicians are influenced by a wide range of factors, including their own clinical experience and the clinical experience of their colleagues. (Trial Tr. vol. 8, 27; Trial Tr. vol. 17, 34-35, 45-47, Mar. 16, 2010.) Of significance, no individual physician testified in this case (or in the MDL litigation as a whole) that he or she prescribed Neurontin as a result of fraudulent off-label promotion. The analysis is further complicated by the fact that during the relevant time period Kaiser did not track Neurontin prescription data by medical indication. (Trial Tr. vol. 8, 99-100.)

To meet its burden of proving causation, plaintiffs offered the testimony of Professor Meredith Rosenthal, who gave an expert opinion quantifying the impact of defendants' conduct in promoting Neurontin on units of Neurontin paid for by Kaiser. Dr. Rosenthal holds a Ph.D. in health economics from Harvard University and is currently on the faculty at the Harvard School of Public Health. (Trial Tr. vol. 10, 104-05.) She has previously testified before Congress and in state legislatures on matters concerning health insurance and health care payment, in addition to publishing in such journals as the New England Journal of Medicine and JAMA. (Id.) She has also been qualified

as an expert in federal litigation. (Id. at 106.) See also In re Pharm. Indus. Average Wholesale Price Litig., 491 F. Supp. 2d 20, 36-37 (D. Mass. 2007). I find that she is a qualified expert.

The easy part of the analysis was linking national data on Pfizer's promotional spending with sales. Dr. Rosenthal explained that "the standard practice in these types of analyses is to use aggregate data and statistical approaches to link patterns in promotional spending to patterns in prescribing for the drug." (Trial Tr. vol. 11, 16, Mar. 8, 2010.) This method of analysis "looks at patterns of actual behavior, aggregate patterns of promotion, and makes the connection between the two, both to assess whether there was exposure and its impact." (Id. at 17.) Using these methods, she "estimate[d] and calculate[d] a time series model that . . . quantif[ied] the specific contribution of promotion to sales."[19] In addition, she gave an opinion quantifying "the share of prescriptions [for each indication] that were caused by the alleged fraud." (Trial Tr. vol. 10, 144-45; TX 405-K.)

[19] The data on promotional spending used by Dr. Rosenthal included spending on detailing of doctors, advertisements in professional journals, and the retail value of samples. (Trial Tr. vol. 10, 133-35.) The evidence was unclear as to whether or not the category of promotional spending on advertisements in professional journals encompassed money spent by defendants on supplements to professional journals.

To perform her analysis, Dr. Rosenthal used "gold standard" national data on Neurontin and other anti-epileptic drugs from IMS Health and Verispan. (Trial Tr. vol. 10, 115, 117, 118-21.) She then calculated percentages of affected prescriptions applicable to Kaiser, based on the reasonable assumption that Kaiser's patient population and physician distribution are similar to the national mix.[20] (Id. at 25, 50-51.)

Defendants criticize Professor Rosenthal's analysis because it assumes that the promotional spending on off-label marketing was the same as the promotional spending on fraudulent off-label marketing.[21] This leap is less obvious because, in some circumstances, off-label marketing can be truthful. However, based on the compelling evidence in this case, I conclude that the assumption is reasonable, given the pervasive nature of the

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[20] Defendants challenge the reliability of Dr. Rosenthal's calculations of percentages of total Neurontin prescriptions filled for each off-label indication. They point in particular to a 2003 chart review of 20,429 Neurontin prescriptions paid for by Kaiser which found that prescriptions for bipolar disorder comprised 4% of total Neurontin prescriptions, as opposed to the 16% found by Dr. Rosenthal. (Compare TX 692 with TX 408-F.) Dr. Ambrose Carrejo, who conducted the chart review, testified credibly that the chart review was inaccurate because Kaiser didn't have the ability to "hard code a prescription to a diagnosis." (Trial Tr. vol. 8, 58-59.) The Court finds that it was reasonable for Dr. Rosenthal to apply the national percentages to Kaiser. Indeed, the 16% bipolar estimate used by Dr. Rosenthal is quite close to Pfizer's own estimate in 2000 (14.7%) of the percentage of Neurontin prescriptions written to treat bipolar disorder. (TX 143 at 14.)

[21] Professor Rosenthal did not attempt to measure the impact of the alleged publication strategy.

publication fraud that infected the nationwide sources of information available to all physicians, including PMG physicians, and to Kaiser's DIS. I find that Pfizer designed the national strategy of off-label marketing (by promotional spending on detailing doctors and sponsorship of CME conferences) to implement its fraudulent publication strategy.

Based on the regression analyses, Dr. Rosenthal concluded that the following numbers represented the percentage of Neurontin prescriptions that were caused by Pfizer's fraudulent marketing of Neurontin: (1) bipolar: 99.4%; (2) neuropathic pain: 70%; (3) migraine: 27.9%; (4) doses over 1800 mg/day: 37.5%. (TX 405-K.)

In order to convert Dr. Rosenthal's percentages into dollar amounts useful for the Court's damages analysis, plaintiffs offered the testimony of Dr. Raymond Hartman, who holds a Ph.D. in economics from the Massachusetts Institute of Technology and currently is the "president and director of an economic consulting firm that does statistical and econometric research." (Trial Tr. vol. 11, 131-32.)

To determine the price paid for Neurontin, Dr. Hartman used the total dollar amount that Kaiser spent on Neurontin, combined with the total number of prescriptions, to calculate a price for an average prescription of Neurontin. (Id. at 146.) He then multiplied the quantity of allegedly affected prescriptions paid

for by Kaiser (by quarter) by the average weighted price per prescription (by quarter) to determine Kaiser's damages. (Id.)

Dr. Hartman's results, excluding interest, totaled $69,384,202. That number includes $22,662,575 for bipolar; $41,813,611 for neuropathic pain; $1,312,098 for migraine; and $3,599,348 for doses greater than 1800 mg/day. (TX 408-F.) These numbers only represent the time periods during which the Court finds that defendants engaged in fraudulent conduct upon which plaintiffs relied. See supra p. 72.

However, because PMG physicians would have almost certainly prescribed alternative medication to their patients had they not prescribed Neurontin, Dr. Hartman also calculated plaintiffs' damages as the difference between the cost of Neurontin and the cost of the cheaper and more optimal drug that would have been prescribed. To do this, Dr. Hartman relied on information provided by Dr. Mirta Millares, a doctor of pharmacy and the chairperson of Kaiser's DIS. This information included a list drugs that, based on efficacy, safety and cost, were more appropriate for each off-label indication than Neurontin. (TX 365; Trial Tr. vol. 9, 89.) To develop this list of medications, Dr. Millares "looked at what agents were FDA approved for those indications and what agents [Kaiser] had on formulary." (Trial Tr. vol. 9, 89.) She consulted with colleagues at Kaiser and other people involved in formulary management to develop the

list. (Id.) Dr. Millares was a reliable source of information about alternative medications.

Using the average cost of these alternative medications for each indication, Dr. Hartman calculated that Kaiser's damages (not including the cost of alternative treatment) totaled $62,457,082. This includes the following amounts for each indication: (1) bipolar disorder: $17,822,647; (2) neuropathic pain: $39,774,623; (3) migraine: $1,260,464; (4) doses greater than 1800 mg/day: $3,599,348.

H. Neurontin's Efficacy for Off-Label Conditions

One of defendants' primary theories of defense is that Pfizer made no material misrepresentations because Neurontin is actually effective for the off-label indications at issue in this case: bipolar disorder, neuropathic pain, migraine, and doses over 1800 mg/day. The Court finds that there is no reliable scientific evidence that Neurontin is effective for bipolar disorder, migraine, or at high doses. With respect to some kinds of neuropathic pain, there is some scientific evidence of efficacy. However, as the FDA found, there is no reliable scientific evidence to support a broad indication of neuropathic pain. Defendants do not contend that Neurontin is effective for nociceptive pain.

In determining whether a drug is effective in treating a particular indication, the FDA and physicians first look to the

results of DBRCTs. (Trial Tr. vol. 1, 175-76; Trial Tr. vol. 2, 24, 26-27; Trial Tr. vol. 4, 127.) These types of trials are considered to be the "gold standard" in the medical and scientific communities. (Trial Tr. vol. 1, 175-76.) Other types of trials (open or unblinded trials, or trials not controlled by placebo), in addition to anecdotal evidence (case reports, case series, or clinical experience), can be useful to physicians in making prescribing decisions, but are not sufficient to determine efficacy to a reasonable degree of scientific certainty. (Id. at 167-68; Trial Tr. vol. 2, 25-27; Trial Tr. vol. 13, 79.) The Court has written previously on this point:

> DBRCTs are the "gold standard" of scientific evidence. See David H. Kaye & David A. Freedman, Reference Guide on Statistics, in Federal Judicial Center, Reference Manual on Scientific Evidence 91-92, 338 (2d ed. 2000) (stating that "controlled experiments are ideal for ascertaining causation" and "inferences based on well-executed randomized experiments are more secure than inferences based on observational studies"). Experts must accord appropriate weights to different levels of evidence, i.e. a randomized, controlled trial, as the "gold standard" of evidence, must be accorded greater weight than observational, non-controlled studies or case reports. See id. at 93 ("Inferences based on well-executed randomized experiments are more secure than inferences based on observational studies."); see also Norris v. Baxter Healthcare Corp., 397 F.3d 878, 882 (10th Cir. 2005) ("While the presence of epidemiology [as opposed to anecdotal evidence] does not necessarily end the inquiry, where epidemiology is available, it cannot be ignored."); In re Bextra & Celebrex Mktg. Sales Practices & Prods. Liab. Litig., 524 F. Supp. 2d 1166, 1175-76, 1179 (N.D. Cal. 2007) (holding that experts may not "cherry-pick[ ]" observational studies to support a conclusion that is contradicted by randomized controlled trials, meta-analyses of such trials, and

> meta-analyses of observational studies and excluding an expert who "ignores the vast majority of the evidence in favor of the few studies that support her conclusion"); Casey v. Ohio Med. Prods., 877 F. Supp. 1380, 1385 (N.D. Cal. 1995) (holding that, while case reports may provide anecdotal support, they are no substitute for controlled studies or trials).

In re Neurontin Mktg. & Sales Practices Litig., No. 04-cv-10981 (Docket No. 2488), 2010 WL 559108, at *1 (D. Mass. Feb. 12, 2010). The FDA requires two DBRCTs to prove the efficacy of a drug because it is important to be able to duplicate positive results. (Trial Tr. vol. 2, 30.) The Court finds this is a reliable standard followed by the scientific community. (Id. at 169 (explaining that the FDA's standards have been adopted and are "well understood" by the industry).)

Pfizer has taken the position that plaintiffs must prove that the drug is not effective for the treatment of any patient. That is not the standard adopted by the FDA or the standard generally accepted by the scientific community. Accordingly, I reject the proposed standard under Daubert. See Daubert v. Merrell Dow Pharms., 509 U.S. 579 (1993).

1. Bipolar Disorder

Bipolar disorder is a "cyclical mood disorder." A person with bipolar disorder vacillates between an upper manic phase and a depressive phase. (Trial Tr. vol. 4, 122-23.) While bipolar disorder cannot be cured, there are approximately ten FDA-approved medications to treat bipolar disorder, including

Lithium, Depakote, Lamotrigine and Tegretol. (Id. at 124.) Neurontin was not approved by the FDA for bipolar disorder, but was marketed by Pfizer for that off-label indication beginning in at least April 1996.

The available DBRCTs that studied the efficacy of Neurontin in the treatment of bipolar disorder are described below.

(i) Pande Trial

The Pande trial was conducted by lead investigator Atul Pande, who was an employee of Parke-Davis at the time of study. (Trial Tr. vol. 4, 128; TX 383 at 1.) This trial was conducted from March 1996 through July 1997, and a research report was presented to Pfizer on March 26, 1999.[22] (TX 383 at 1.) The Pande trial sought to determine whether Neurontin was effective in the treatment of bipolar disorder as compared to a placebo. The 117 study participants were simultaneously being treated with Lithium or Depakote, or a combination of the two. (Trial Tr. vol. 4, 128; TX 383 at 4.)

The Pande trial measured patient outcomes on two rating scales: the Young mania rating scale (YMRS) and the Hamilton depression rating scale (Ham-D). (Trial Tr. vol. 4, 129.) The results of the trial showed that the placebo outperformed Neurontin on the YMRS, or mania, scale, and showed no

[22] The study was completed in July 1997, and Dr. Pande wrote a letter to the study's investigators detailing the study results on July 28, 1998. (Trial Tr. vol. 4, 130-31; TX 383 at 1, 8.)

statistically significant difference between Neurontin and placebo on the Ham-D, or depression, scale. (Id. at 129; TX 383 at 9.)

The Pande trial was published in the journal Bipolar Disorders in 2000, and concluded that the study "did not demonstrate that gabapentin is an effective adjunctive treatment when administered to outpatients with bipolar disorder." (TX 1393 at 259.)

(ii) Frye Trial

The Frye trial was an independent crossover study conducted between 1997 and 1999 that compared Neurontin to the drug Lamotrigine and placebo in the treatment of refractory, or difficult to treat, bipolar disorder using the Clinical Global Improvement (CGI) scale. (Trial Tr. vol. 4, 132-33; TX 1477.) The Frye trial found that Lamotrigine outperformed both Neurontin and placebo, and that there was no statistically significant difference between Neurontin and placebo. (TX 1477 at 610-11.)

Interim results were presented, in part, at meetings of the American Psychiatric Association in 1997 and 1998. (Id. at 607.) The Frye trial was published in the Journal of Clinical Psychopharmacology in 2000.

(iii) Guille Trial

The Guille trial was also a DBRCT that compared Neurontin to placebo in treating refractory bipolar disorder. (TX 211 at 63.) Using the YMRS and Ham-D scales to measure outcomes, the trial

investigators found no significant difference between Neurontin and placebo for treatment of either mania or depression. (Id.)

The Guille trial was presented at the 1999 annual meeting of the American Psychiatric Association. (Id.; TX 1335.)

(iv) Vieta Trial

The Vieta trial, a DBRCT comparing Neurontin to placebo, was funded by the defendants and was completed in February 2004. (TX 398.) Like the Pande trial, the Vieta trial involved patients who were also being treated with Lithium, Tegretol, or a combination of the two. (Trial Tr. vol. 4, 137.) The Vieta trial showed no difference between Neurontin and placebo in the "intention-to-treat" (ITT) population, meaning the entire population of study participants who were included in the trial. (Id. at 138-40; TX 398 at 4.) However, the study investigators did find a statistically significant difference between Neurontin and placebo in the "per protocol" (PP) subpopulation, or those patients who were healthier and more compliant than others in the group. (Trial Tr. vol. 4, 138-40.)

The Vieta trial was published in the Journal of Clinical Psychiatry in March 2006. The published article falsely stated that the trial showed efficacy in the treatment of bipolar disorder using the ITT population. (TX 1865 at 473-74.) However, the article included data and analysis only for those 25 patients in the PP subpopulation. (Trial Tr. vol. 4, 142-44.)

As Dr. Dickersin explained, the reason that it is important

to use the ITT population in a DBRCT is that

> as soon as you take people out because let's say they didn't finish the study, you have a nonrandomized study. You're back to the place where you could assign patients to this treatment or that. And so our rule in analyzing a randomized trial is, the first analysis includes everybody in the group to which they were originally assigned, and then your second analysis can include people who finish the study or who complied. And what this study did is, they did not do that intention-to-treat analysis; and, as a matter of fact, they chose a very different group for analysis than was originally assigned to each group.

(Id. at 54-55.) In the case of the Vieta study, the published results did not disclose that the study population used for analysis was not the ITT population, but rather the PP population. (Id. at 55.)

(v) Mokhber Trial

The Mokhber trial compared Neurontin to Lamotrigine and Tegretol in the treatment of dysphoric mania, which is a state of bipolar disorder in which a patient presents both manic and depressive symptoms. (TX 2004 at 227.) The Mokhber trial showed improvements in both mania and depressive symptoms by those patients taking gabapentin, but there was no placebo group used to control the study. (Id. at 227; Trial Tr. vol. 18, 112-16.) This trial was published in Neuropsychiatric Disease and Treatment in 2008. (TX 2004 at 227.) The Mokhber study used an active comparator, as opposed to a placebo control, which can be acceptable in some DBRCTs. (See Trial Tr. vol. 3, 19, Feb. 24, 2010.) However, in the Mokhber trial, the authors cautioned that

"in the absence of a parallel placebo control group we cannot conclude that this effectiveness [shown in the study] is equivalent to efficacy." (TX 2004 at 231.) The authors also stated that limitations of the Mokhber trial included "lack of a control group" and the fact that the authors could not "monitor the blood levels of the drugs due to local hospital limitations." (Id. at 232-33.) In trials using carbamazepine (Tegretol) and lamotrigine, which were the active comparators in the Mokhber trial, it is essential to monitor blood levels. (See Trial Tr. vol. 17, 56, Mar. 16, 2010; Trial Tr. vol. 18, 147.) Because blood levels could not be monitored here, the comparison of gabapentin's effectiveness with that of carbamazepine and lamotrigine is called into question.

In support of their claim that Neurontin is not effective for the treatment of bipolar disorder, plaintiffs introduced the expert testimony of Dr. Jeffrey Barkin, a board certified psychiatrist who is in private practice in Maine and is the chairperson of the Maine's Drug Utilization Review Board. (Trial Tr. vol. 4, 119-20, 122.) Dr. Barkin reviewed all of the available DBRCTs studying the use of Neurontin for the treatment of bipolar disorder and concluded that "reasonable physicians would not prescribe Neurontin for bipolar disorder." (Trial Tr. vol. 5, 34.) The DBRCTs in evidence, described supra, demonstrate that there is no generally accepted scientific

evidence that Neurontin is effective for the treatment of bipolar disorder. There is some evidence, however, that Neurontin is effective for the treatment of social phobia. People with social phobia are very afraid of social situations. (See TX 1324 (Atul Pande, "Treatment of Social Phobia with Gabapentin: A Placebo-Controlled Study," Journal of Clinical Psychopharmacology).) Social phobia "is a potentially disabling condition where patients may not be able to interact [with others]." (Trial Tr. vol. 5, 28.) It is distinct from bipolar disorder, but may in some patients be comorbid with bipolar disorder. (Id. at 29.)

Defendants offered the expert testimony of Dr. Andrew Slaby, a board-certified psychiatrist who also holds a Ph.D. in epidemiology from Yale University. He has published more than 100 articles on issues related to psychiatry and has an active clinical practice. (Trial Tr. vol. 18, 89-90.) Dr. Slaby testified that he believes "Neurontin is an effective add-on, adjunctive treatment, and in some instances a primary treatment for . . . various forms of bipolar illness." (Id. at 90.) Dr. Slaby conceded that the Frye and Pande studies that looked at the use of Neurontin to treat bipolar disorder produced negative results. However, he discounted their value because these studies involved "refractory" bipolar patients, or "patients who were least likely to respond to any drug." (Id. at 99.) In addition, he relied heavily on two separate studies conducted by Dr. Pande, one in panic disorder and one in social phobia, both

of which were positive. He also relied on the 2006 Vieta study, and claimed that it had positive results based on a measure that was not the primary outcome identified before the trial was conducted. (Id. at 99-104, 107.) Dr. Slaby did not appear to consider the negative Guille trial.

Dr. Slaby's conclusion that Neurontin is effective for the treatment of bipolar disorder seems to be based primarily on four pieces of evidence: (1) the Pande study on social phobia; (2) the Pande study on panic disorder; (3) a secondary outcome in the Vieta study; and (4) his clinical experience. The Court does not find his opinion persuasive because he gave such great weight to two studies that do not purport to draw conclusions about Neurontin's efficacy in treating patients with bipolar disorder, while simultaneously dismissing the relevance of two studies that directly dealt with bipolar disorder. In addition, the omission of the negative Guille study leads the Court to believe that Dr. Slaby's opinion was not based on a comprehensive review of all available evidence. Moreover, reliance on positive results from a secondary measure in the Vieta study is misplaced. As Dr. Dickersin testified at trial, "selective outcome reporting" or reliance on outcomes other than the primary outcome is not considered to be good science because it increases the likelihood that the results are not accurate if they are chosen after the study has been completed. (Trial Tr. vol. 4, 33-34; see also TX 2091 ("Once the data are known, the addition or subtraction of

primary outcomes can lead to the presentation of chance findings as evidence of a drug's effectiveness.").)

Accordingly, the Court does not accept Dr. Slaby's opinion on efficacy. After a review of five DBRCTs and Dr. Barkin's testimony, the Court finds that there is no scientifically acceptable evidence that Neurontin is effective in the treatment of bipolar disorder.

2. Neuropathic Pain

Neuropathic pain is pain caused by damage to the nerves. (Trial Tr. vol. 6, 143-44.) A common example of neuropathic pain is diabetic neuropathy, whereby "many people who have had [diabetes] for years get damaged nerves, particularly in their feet." This nerve damage can cause patients to lose sensation, have numbness, and experience a burning sensation. (Id.) There are many types of neuropathic pain, including postherpetic neuralgia, diabetic peripheral neuropathy, and cancer pain. While there are certain drugs approved by the FDA for the treatment of particular neuropathic pain categories, there is no drug that is FDA approved for the treatment of all neuropathic pain categories. (Trial Tr. vol. 17, 26.)

I briefly describe the DBRCT evidence presented at trial related to various neuropathic pain indications.

(i) Gorson Trial

In August 1997, Dr. Kenneth Gorson completed a DBRCT

studying Neurontin in the treatment of painful diabetic neuropathy. (TX 19 at 1.) This trial was funded by Pfizer. (See id. at 2; TX 7 at 7.) Dr. Gorson concluded that "[g]abapentin, at a dose of 900 mg/day, is probably no more effective than placebo in the treatment of painful diabetic neuropathy." (TX 19 at 3.)

The Gorson trial was never published as a full article in a peer-reviewed journal.

(ii) Backonja Trial

The Backonja trial, which sought to determine whether Neurontin was effective for the treatment of painful diabetic neuropathy, was a Pfizer DBRCT completed in 1997. (Trial Tr. vol. 3, 21.) This study was designed to use forced titration, or gradually increasing doses, of Neurontin up to 3,600 mg/day, regardless of whether the patient was experiencing symptomatic relief at a lower dose. (Id. at 22.)

The Backonja trial showed that Neurontin was effective in treating painful diabetic neuropathy. (Id.) However, there was potential "unblinding" in the DBRCT among patients who experienced central nervous system side effects such as sleepiness and dizziness and likely concluded that they were receiving gabapentin as opposed to the placebo. (Id. at 22-23.) When those patients who experienced side effects, and therefore were potentially unblinded, were removed from the study results, there was no statistical significance found between Neurontin and

the placebo. (Id. at 24-25 (testimony of Dr. John Abramson); Trial Tr. vol. 6, 117 (testimony of Dr. Nicholas Jewell); TX 416B.)

The Backonja trial was published in JAMA in December 1998 and concluded that the potential unblinding did not affect the statistical significance of the study's results. (TX 1250 at 1831, 1835.) To reach this conclusion, the study's investigators removed from the data all of the "sleepy" participants who were potentially unblinded and found that the outcomes remained the same. They then separately removed the data from all of the "dizzy" participants who were potentially unblinded and found that the outcomes were not affected. (Id.; Trial Tr. vol. 6, 106-07 (testimony of Dr. Jewell).) They did not remove both cohorts (sleepy and dizzy patients) to determine whether outcomes were different.

Plaintiffs offered the expert testimony of Dr. Nicholas Jewell, a biostatistician who holds a Ph.D. in mathematics. He is currently a professor of biostatistics at the School of Health and in the statistics department at the University of California at Berkeley, where he previously served as the vice provost. (Trial Tr. vol. 6, 96-97.) Dr. Jewell is the author of a book titled Statistics for Epidemiology and has received the Snedecor Award for lifetime achievement in biostatistics. (Id.) Dr. Jewell analyzed the data from the Backonja trial to determine the results of the study once all of those patients who were

potentially unblinded were removed from the data pool. (Trial Tr. vol. 6, 103-04.) He found that when he removed both the patients experiencing dizziness and the patients experiencing sleepiness from the study results, the difference between the change in pain scores for the Neurontin and placebo groups at the end of the study was 0.15 on an 11-point pain scale, as opposed to a difference of 1.2 points as reported in the Backonja JAMA article. (TX 416B; Trial Tr. vol. 6, 118.) A difference of 0.15 on an 11-point pain scale is not statistically significant or clinically important. (Trial Tr. vol. 6, 118.)

(iii) Reckless Trial

The Reckless trial was a Pfizer DBRCT conducted from 1998 to 1999 that also studied the use of Neurontin in treating painful diabetic neuropathy. (Trial Tr. vol. 3, 28-29.) The study design involved a total of 248 patients, divided into three groups of patients, each of which received a different dose of Neurontin (600, 1200, and 2400 mg/day) and an additional placebo group. (Id. at 29.) The Reckless trial found that "none of the gabapentin treatment groups was shown to be effective for the treatment of painful diabetic neuropathy." (TX 382 at 12.) These findings were presented to Pfizer in February 2000. (Trial Tr. vol. 3, 30.)

The Reckless trial was never published. (Id. at 33-34.)

(iv) POPP Trial

The POPP trial was a Pfizer DBRCT studying Neurontin in the treatment of postsurgical or traumatic nerve injury pain. (Trial Tr. vol. 3, 35.) The POPP study was completed in November 2001 and the authors released their research report in 2003. (Id.)

The primary outcome defined by the POPP study was a decrease in patients' Mean Pain Intensity Score. The results of the study showed that Neurontin did not statistically significantly reduce the Mean Pain Intensity Score compared with placebo. (TX 192 at 5.) Nonetheless, the study's authors concluded that "gabapentin may be of benefit for patients with neuropathic pain," largely because there was statistical significance in several secondary outcomes such as the Mean Sleep Interference Score. (Id.)

The POPP study was not published until 2008, seven years after completion. (Trial Tr. vol. 3, 35-36.)

(v) Tamez-Pérez Trial

The Tamez-Pérez trial was published in Spanish in 1998 (TX 1275), and Dr. Bird testified that it was a positive DBRCT of Neurontin for the treatment of DPN. (Trial Tr. vol. 18, 25-26.) However, a full copy of the study was not introduced into evidence.

(vi) Morello Trial

The Morello trial was a "comparator" study of Neurontin and a tricyclic antidepressant, amitriptyline hydrochloride, in the

treatment of diabetic peripheral neuropathy. (TX 1332; Trial Tr. vol. 18, 26.) The study, published in Archives of Internal Medicine in 1999, found that "although both drugs provide pain relief, mean pain score and global pain score data indicate no significant difference between gabapentin and amitriptyline. Gabapentin may be an alternative for treating diabetic peripheral neuropathy pain, yet does not appear to offer considerable advantage over amitriptyline and is more expensive." (TX 1332 at 1931.)

(vii) Serpell Trial

The Serpell trial, sponsored by Pfizer, was "a study of people with many different kinds of painful neuropathy" that "tested the efficacy of Neurontin against placebo in people who were symptomatically suffering from neuropathic pain rather than having a specific diagnosis." (Trial Tr. vol. 3, 36; TX 1552 at 557.) This DBRCT was completed in 2002. (Trial Tr. vol. 3, 37.)

When the study's authors published the Serpell trial in 2002, they concluded that the "study show[ed] that gabapentin reduces pain and improves some quality-of-life measures in patients with a wide range of neuropathic pain syndromes." (TX 1552 at 557.) In fact, the study's authors stated that they "found . . . that there were no differences in treatment effect among the various pain syndromes studied, with all types of pain showing responsiveness to gabapentin." (Id. at 564.) The raw data from the Serpell trial, however, did not support the

published article's conclusions. In fact, improvement among patients suffering from PHN, an indication for which Neurontin received FDA approval, accounted for the vast majority of the improvement that was seen in the Serpell study. (Trial Tr. vol. 3, 37-38.)

(viii) Bone Trial

The Bone trial, published in Regional Anesthesia and Pain Medicine in 2002, was a DBRCT of Neurontin for the treatment of postamputation phantom limb pain, which is a type of neuropathic pain. (TX 1546.) The trial found that, "[a]fter 6 weeks, gabapentin monotherapy was better than placebo in relieving postamputation phantom limb pain." (Id. at 481.)

(ix) Tai Trial

The Tai trial, published in the Journal of Spinal Cord Medicine in 2002, was a DBRCT looking at the use of Neurontin to treat neuropathic pain after spinal cord injury. (TX 1553 at 100.) This study was positive. (Id.; Trial Tr. vol. 18, 35.)

(x) Levendoglu Trial

The Levendoglu trial, published in the journal Spine in 2004, was a DBRCT that found that Neurontin was effective in the treatment of neuropathic pain after spinal cord injury. (TX 1683 at 743.)

(xi) Van de Vusse Trial

The Van de Vusse trial, published in the journal BMC Neurology in 2004, looked at the use of Neurontin in the

treatment of Complex Regional Pain Syndrome type I, which is a type of neuropathic pain. (TX 1727 at 1.) This DBRCT found that "[g]abapentin had a mild effect on pain in CRPS I. It significantly reduced the sensory deficit in the affected limb. A subpopulation of CRPS patients may benefit from gabapentin." (Id.)

(xii) Parsons Trial

The Parsons Trial, sponsored by Pfizer, was a DBRCT studying the use of Neurontin for the treatment of DPN. This trial was never published, but the research report was sent to Pfizer in 2005. (TX 2069.) The primary measure of efficacy, as defined by investigators prior to the study, was the change in median weekly pain score. Patients in both the Neurontin and placebo groups experienced improvement in pain scores over the course of the study. However, the difference between the change in the Neurontin group and the change in the placebo group was only 0.765 on an 11-point scale, which is not clinically important. (TX 2069 at 45; Trial Tr. vol. 18, 68-69.)

Defendants' expert, Dr. Shawn Bird, testified that the Parsons trial "was positive on the primary end points and also very positive" on the secondary outcomes. (Trial Tr. vol. 18, 31.) However, on cross-examination, he agreed that the primary outcome showed a difference of less than one point on an 11-point pain scale between the Neurontin group and the placebo group.

Plaintiffs claim that Neurontin is ineffective for the treatment of neuropathic pain, other than postherpetic neuralgia.[23] They presented the testimony of Dr. Thomas Perry, a general internist who practices and teaches at University Hospital in Vancouver, British Columbia. He is certified by the American Board of Internal Medicine. (Trial Tr. vol. 6, 134-36.) Dr. Perry works with the University of British Columbia Therapeutics Initiative, which performs evidence-based assessments of new drugs in order to explain their uses to doctors and pharmacists. (Id. at 136.) He has also served as a peer reviewer for the Cochrane Collaboration, in addition to other medical journals. (Id.)

Dr. Perry performed a meta-analysis of all available DBRCTs related to the use of Neurontin in treating neuropathic pain. (See Trial Tr. vol. 6, 134-51; Trial Tr. vol. 7, 21-96.) A meta-analysis is a compilation of all available clinical trial data for the purpose of analyzing a drug's efficacy. (Trial Tr. vol. 6, 150-51.) Based on this meta-analysis, which involved the consideration of 25 DBRCTs, Dr. Perry "did not consider [Neurontin] effective for treating neuropathic pain." (Trial Tr.

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[23] As stated earlier, Neurontin is approved by the FDA for the treatment of post-herpetic neuralgia, or pain caused by shingles. (TX 195 at 1.) Plaintiffs' claims in this case only involve the use of Neurontin for the treatment of neuropathic pain other than post-herpetic neuralgia. Accordingly, this opinion does not discuss the DBRCTs studying the use of Neurontin to treat PHN.

vol. 7, 26.)

In rebuttal, defendants offered the expert testimony of Drs. Shawn Bird and Gary Brenner. Dr. Bird is a board certified physician in neurology with experience in testing for diseases of the peripheral nerve, or those nerves in the extremities of the body such as the legs, hands and feet. (Trial Tr. vol. 18, 16, 23.) He is currently a professor at the University of Pennsylvania and is the program director of the Clinical Neurophysiology Program there. He also has an active medical practice and has served as the principal investigator in a number of clinical trials in peripheral neuropathy. (Id. at 15-16.) Dr. Bird testified that Neurontin is an effective, safe, and well-tolerated treatment for neuropathic pain in some patients. He based this opinion on his own clinical experience with the drug, along with a review of the available DBRCTs. The Court was impressed with Dr. Bird's credentials and credits his testimony that some patients with neuropathic pain benefit from Neurontin. Dr. Bird's eye view that Neurontin is effective for the broad indication of neuropathic pain, however, is not supported by the weight of the scientific evidence. He failed to address the following five areas of particular concern.

First, Dr. Bird discussed the Backonja DPN trial's positive results, but he did not address or rebut the plaintiffs' expert's opinion about "unblinding" that, when all patients experiencing CNS-related side effects (like sleepiness and dizziness) were

removed from the study, the trial results were no longer positive.

Second, Dr. Bird relied on the Gorson DPN study, the results of which he interpreted to be positive based on a secondary outcome. His testimony, however, did not address the assertion made by many of plaintiffs' efficacy experts and by Dr. Dickersin that it is not good science to rely on secondary outcomes in clinical trials when evaluating efficacy.

Third, Dr. Bird relied on the Parsons DPN study, stating that the results of the trial were positive on the primary outcome, and very positive on the other outcomes. However, the primary outcome in the Parsons trial showed a difference of less than one point on an eleven-point Likert pain scale between Neurontin and the placebo. Earlier in his testimony, when discussing the Gorson trial, Dr. Bird stated that "the patient doesn't really care if there's a 1-point change on their Likert scale." (Trial Tr. vol. 18, 28.) In addition, reliance on secondary outcomes is misplaced.

Fourth, Dr. Bird relied on the Rice and Rowbotham studies, which were positive for the use of Neurontin to treat post-herpetic neuralgia. However, plaintiffs do not dispute that Neurontin is effective for the treatment of PHN.

Fifth, Dr. Bird relied on the positive results of the Serpell study, which included patients with a variety of neuropathic pain conditions, but did not acknowledge the fact

that the results were positive largely due to the population of PHN patients included in the study. Nonetheless, Dr. Bird dismissed the negative results of the POPP study, which also included participants with a variety of neuropathies, due to the fact that the study involved a "mixed group of patients." (Id. at 38.)

Defendants also presented the testimony of Dr. Gary Brenner. Dr. Brenner is a board certified physician in both anesthesiology and pain medicine who also has a Ph.D. in immunology and neuroscience. He is currently an assistant professor of anesthesia at Harvard Medical School and has an active pain medicine practice at Massachusetts General Hospital. (Trial Tr. vol. 17, 6.) Like Dr. Bird, Dr. Brenner testified credibly that Neurontin is an effective, safe, and well-tolerated treatment for some kinds of neuropathic pain in some patients. (Id. at 13-14, 19-21, 28, 62-63.) Dr. Brenner did not discuss each DBRCT separately, but instead relied on systematic reviews of Neurontin used for the treatment of neuropathic pain. In particular, Dr. Brenner's opinion was based on the 2005 Cochrane Review of Neurontin for neuropathic pain. The Cochrane Review found that "looking at the literature as a whole . . . there is adequate evidence to support that there's efficacy of gabapentin for the treatment of neuropathic pain." (Id. at 34.) However, Dr. Brenner did not address the evidence as presented at trial and by

Dr. Perry that the Cochrane Review's neuropathic pain report on Neurontin was deficient because the reviewers did not have access to unpublished trials like Reckless and POPP and because they did not have access to the complete data for published trials like Backonja, Gorson, and Serpell. (See Trial Tr. vol. 6, 147-48.)

After a review of 12 DBRCTs studying the use of Neurontin in the treatment of neuropathic pain, and a careful consideration of the expert testimony, the Court finds that there is no generally accepted scientific evidence that Neurontin is effective in the treatment of neuropathic pain as a broad category or indication. This is a closer call because, unlike migraine and bipolar disorder, there are four DBRCTs that concluded that Neurontin was better than placebo for treating certain narrow indications like postamputation phantom limb pain, neuropathic pain after spinal cord injury, and Complex Regional Pain Syndrome I. (TXs 1546, 1553, 1683, 1727 (Bone, Tai, Levendoglu, and Van de Vusse trials).) In addition, some trials studying the use of Neurontin to treat diabetic peripheral neuropathy found that, using some secondary outcomes (i.e. not outcomes designated as the primary outcome to determine success of the trial before the trial was conducted), Neurontin outperformed placebo. (TXs 1250, 192, 2069 (Backonja, POPP, and Parsons trials).) Pfizer also points out that fifty countries have approved Neurontin for pain (although it is unclear what scientific standard these countries applied).

However, using the generally accepted standard of scientific efficacy followed by the FDA and the scientific community (requiring two DBRCTS that demonstrate efficacy), the Court is persuaded that there is insufficient reliable evidence of the efficacy of Neurontin with respect to the broad indication of neuropathic pain. While Drs. Bird and Perry credibly testified that they have had clinical success with some patients, these anecdotal accounts cannot overcome the lack of DBRCT evidence to support efficacy in the treatment of neuropathic pain as a broad indication. Moreover, even with the narrower indication of DPN, there were serious issues with trial design in all of the trials with positive results. Remember, as well, that the FDA rejected the evidence of efficacy with respect to DPN. While this is a closer call, plaintiffs have proven that Neurontin is not generally effective for neuropathic pain, with the exception of PHN.

3. Migraine

Kaiser claims that Neurontin is ineffective for the preventive treatment of migraine headache. Migraine "is a neurovascular disorder characterized by attacks of headache variable in intensity, frequency and with autonomic and neurological accompanying symptoms." (TX 1478 at 145.) Plaintiffs presented the expert testimony of Dr. Douglas McCrory, a board certified physician in internal medicine who is a tenured

faculty member at Duke University Medical Center. Dr. McCrory has an active internal medicine clinic at the Durham V.A. Hospital and spends a significant amount of his time conducting systematic reviews of clinical trial evidence for new drugs. (Trial Tr. vol. 6, 16, 17.) He is currently the lead editor for reviews on headache in the Cochrane Collaboration. (Id. at 18.) Dr. McCrory has also published more than 20 articles regarding migraine headache in medical journals.

Dr. McCrory reviewed the data from all available DBRCTs studying the use of Neurontin for migraine prophylaxis, or migraine prevention. (Trial Tr. vol. 6, 20-21.) After performing a meta-analysis of all published and unpublished trial data, Dr. McCrory concluded that "Neurontin was not an effective drug for migraine prophylaxis." (Id. at 20, 22.)

Defendants rebutted this claim by offering the testimony of Dr. Robert Gibbons, a professor of statistics at the University of Illinois at Chicago, where he is also the Director of the Center for Health Statistics. (Trial Tr. vol. 16, 35.) Dr. Gibbons is one of a handful of statisticians worldwide who has been elected to the Institutes of Medicine of the National Academy of Sciences. (Id. at 37.) Dr. Gibbons also reviewed clinical trial data for the use of Neurontin for migraine prophylaxis, and concluded that the trials show there is a "trend in the direction of increased benefit" for migraine patients using Neurontin. (Trial Tr. vol. 16, 70.) However, when the

Court directly asked Dr. Gibbons if Neurontin is "effective or not effective for migraine," he responded that "there's a trend toward effectiveness . . . [but] I can't say statistically that it is [effective]." (Id. at 65.)

Although there may be a trend in the direction of increased benefit, the clinical trials completed to date do not show that Neurontin is effective for migraine prophylaxis under the standard used by the FDA and adopted by this Court for the purposes of this efficacy analysis.

(i) Trial 879-200

Trial 879-200 was conducted by Parke-Davis during the late 1980s, and was a DBRCT of "gabapentin (900 mg/day) as prophylactic treatment in patients with standard therapy-resistant common migraine." (TX 374 at 2; Trial Tr. vol. 6, 23-24.) The investigators of the 879-200 trial concluded that the trial did not provide data "sufficient to permit conclusions regarding efficacy." (TX 374 at 5.)

Dr. McCrory testified that 879-200 "didn't find that there was a statistical[ly] significant effect of Neurontin compared with placebo." (Trial Tr. vol. 6, 23.)

(ii) Trial 945-217

Trial 945-217 was conducted from 1997 to 1999, and was a "large, well-designed trial comparing Neurontin and placebo" for the treatment of migraine prophylaxis. (TX 397 at 1-2; Trial Tr. vol. 6, 27.) The results of the trial showed no statistically

significant difference between Neurontin and placebo. (TX 397 at 5; Trial Tr. vol. 6, 27.)

(iii) Mathew Trial

The Mathew Trial was conducted by the defendants from 1996 to 1998, and had a similar trial design to 945-217. (TX 396 at 1; Trial Tr. vol. 6, 28-29.) The trial results showed no statistically significant difference between Neurontin and placebo "with respect to 4-week migraine headache rates or proportion of patients with reduction of 50% or greater in migraine headache rates." (TX 396 at 5.)

The study was published in the journal Headache in 2001, and claimed that "gabapentin is an effective prophylactic agent for patients with migraine." (TX 612 at 119.) The discrepancy between the research report and the published article is not explicitly mentioned; however, the positive published results are achieved by using a "modified" intent-to-treat population and by focusing on outcomes identified as secondary in the research report and initial protocol. Moreover, the article did not disclose the negative results of trials 879-200 or 945-217.

(iv) Di Trapani Trial

The Di Trapani trial, an Italian study conducted in the late 1990s, was a DBRCT studying the efficacy of Neurontin for migraine prophylaxis. (TX 1478 at 145; Trial Tr. vol. 6, 39; Trial Tr. vol. 16, 67-68.) The results of the trial showed Neurontin "to have an effective therapeutic action in the

prophylactic treatment of migraine." (TX 1478 at 145.) This trial was published in the journal Clinica Terapeutica in 2000. (Id.; TX 1401.)

4. Doses Greater than 1800 mg/day

Neurontin was approved by the FDA in 1993 for doses up to 1800 mg/day. (TX 9 at 14-15.) Plaintiffs have proven that Pfizer marketed Neurontin at doses greater than 1800 mg and contend there is no evidence supporting additional efficacy at doses greater than the FDA limit.

The FDA twice rejected defendants' applications to increase the maximum dose for Neurontin. (See TX 91 at 3 (noting that "the evidence from controlled trials fails to provide evidence that higher doses of Neurontin are more effective than those recommended"); TX 190 (rejecting proposed marketing materials regarding high doses because "additional benefits of using doses greater than 1800 mg/day were not demonstrated"); Trial Tr. vol. 2, 37-38, 49, 53 (testimony of Dr. David Kessler).)

In addition, the Reckless trial, a DBRCT discussed previously in the context of neuropathic pain, involved titrations to doses greater than 1800 mg/day without exhibiting increased efficacy. (See, e.g., TX 382 at 12; Trial Tr. vol. 7, 27-28.) Defendants' experts testified that Neurontin offers enhanced benefits at doses above 1800 mg/day, and that the proper dose for individual patients is determined through the process of

"titrating to effect." They also contend that the practice of titrating to effect is consistent with the FDA label. (See Trial Tr. vol. 18, 44-45 (Testimony of Dr. Bird); Trial Tr. vol. 17, 47-55 (Testimony of Dr. Brenner).) Dr. Abramson testified that the Reckless trial's fixed-dose, parallel group design is the best research design to measure effects at a given dose. (Trial Tr. vol. 3, 31-32.) While it may well be that titrating to effect is the best way to determine the proper dose for an individual patient, the Court finds the FDA's determination of lack of efficacy at higher doses persuasive.

There is no reliable evidence that Neurontin provides patients with additional benefit when administered in doses greater than the FDA-approved maximum of 1800 mg/day.

III. CONCLUSIONS OF LAW

After the jury verdict, plaintiffs' only remaining claim is brought under California Business and Professional Code § 17200, more commonly known as the California Unfair Competition Law ("UCL"). "A UCL action is equitable in nature; damages cannot be recovered." Korea Supply Co. v. Lockheed Martin Corp., 29 Cal. 4th 1134, 1144, 63 P.3d 937, 943 (2003). Accordingly, UCL claims are decided by the Court rather than a jury.

The UCL defines "unfair competition" to include "any unlawful, unfair, or fraudulent business act or practice." Cal. Bus. & Prof. Code § 17200. Its coverage is "sweeping, embracing

'anything that can properly be called a business practice and that at the same time is forbidden by law.'" Rubin v. Green, 847 P.2d 1044, 1052, 4 Cal. 4th 1187, 1200 (1993) (quoting Barquis v. Merchants Collection Ass'n, 496 P.2d 817, 830, 7 Cal. 3d 94, 113 (1972)).

Plaintiffs argue that defendants have violated the UCL under each of its three prongs: unlawful, unfair, and fraudulent conduct. Because the Court finds that defendants' conduct violated the "fraudulent" conduct prong of the UCL, it is unnecessary to discuss the "unlawful" and "unfair" prongs.

A. Fraudulent Business Acts or Practices

The Court impaneled an advisory jury to render a verdict on Kaiser's claim that Pfizer's conduct constituted fraudulent business acts or practices under the UCL. On March 25, 2010, the jury returned a verdict for Kaiser on this particular claim, finding that defendants engaged in fraudulent business acts or practices with respect to all off-label indications except nociceptive pain. The jury also found that those fraudulent acts or practices caused Kaiser damages with respect to all off-label indications except nociceptive pain. (See Docket No. 2760.) The Court agrees with the jury's conclusion. See Lucent Techs., Inc. v. Gateway, Inc., 580 F. Supp. 2d 1016, 1061 (S.D. Cal. 2008) (stating that a district court has discretion to impanel an advisory jury, but "the ultimate determination of [the] issues

rests with the Court"), rev'd on other grounds, 580 F.3d 1301 (Fed. Cir. 2009).

The California Supreme Court recently stated that "[t]o state a claim under either the [fraud prong of the] UCL or the false advertising law, based on false advertising or promotional practices, it is necessary only to show that members of the public are likely to be deceived." In re Tobacco II Cases ("Tobacco II"), 207 P.3d 20, 29, 46 Cal. 4th 298, 312 (2009). Amendments to the UCL have imposed "an actual reliance requirement on plaintiffs prosecuting a private enforcement action under the UCL's fraud prong." Id. at 39.

Defendants contend that they had no duty to disclose negative information about Neurontin's efficacy. Under California law, nondisclosure or concealment may constitute actionable fraud "when the defendant makes partial representations but also suppresses some material facts."[24]

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[24] Federal courts have recognized that fraudulent half-truths can form the basis of fraud actions. The First Circuit has said that "the locus classicus of fraud is a seller's affirmative false statement or a half-truth, i.e., a statement that is literally true but is made misleading by a significant omission." Bonilla v. Volvo Car Corp., 150 F.3d 62, 69 (1st Cir. 1998) (citing Emery v. Am. Gen. Fin., Inc., 71 F.3d 1343, 1348 (7th Cir. 1995)); see also United States v. Autuori, 212 F.3d 105, 119 (2d Cir. 2000) ("[A]n omission can violate a fraud statute only in the context of a duty to disclose; but a fiduciary duty is not the sine qua non of fraudulent omissions. . . . A duty to disclose can also arise in a situation where a defendant makes partial or ambiguous statements that require further disclosure in order to avoid being misleading."); United States v. Keplinger, 776 F.2d 678, 697 (7th Cir. 1985)

LiMandri v. Jenkins, 60 Cal. Rptr. 2d 539, 543 (Cal. Ct. App. 1997).

In a related context, the Supreme Court recently held that pharmaceutical manufacturers, who have "superior access to information about their drugs, especially in the postmarketing phase as new risks emerge," are under a special duty to investigate and report adverse effects of their drugs. Wyeth v. Levine, 129 S. Ct. 1187, 1202, 1219 (2009) ("After the FDA approves a drug, the manufacturer remains under an obligation to investigate and report any adverse events associated with the drug."); see also 21 C.F.R. § 314.80 (placing responsibility for post-marketing surveillance of drugs on the manufacturer).

In one recent UCL case, the court held:

> [A] claim that a business practice is (or was) 'fraudulent' under Section 17200 can be based upon representations that deceive because they are untrue as well as representations that may be accurate on some level but nonetheless tend to mislead or deceive. As such a perfectly true statement couched in such a manner that it is likely to mislead or deceive the consumer, such as by failure to disclose other relevant information, is actionable under Section 17200.

Gutierrez v. Wells Fargo Bank, __ F. Supp. 2d __, 2010 WL 3155934

("[O]missions or concealment of material information can constitute fraud cognizable under the mail fraud statute, without proof of a duty to disclose the information pursuant to a specific statute or regulation."); United States v. Townley, 665 F.2d 579, 585 (5th Cir. 1982) ("[U]nder the mail fraud statute, it is just as unlawful to speak 'half-truths' or to omit to state facts necessary to make the statements made, in light of the circumstances under which they were made, not misleading.").

at *47 (N.D. Cal. Aug. 10, 2010) (finding that a bank committed fraudulent acts under the UCL through its undisclosed use of a "bookkeeping device" designed to maximize the overdraft fees imposed on customers). Misleading omissions may form the basis of a "fraudulent acts and practices" claim under the UCL.

Here, Pfizer had a duty to disclose scientific data demonstrating the lack of efficacy of Neurontin for off-label uses. This duty arose because Pfizer was marketing the drug for unapproved uses by disclosing positive information about the drug while suppressing negative information in its possession. Indeed, the FDA actually rejected requests for expanded labeling of Neurontin in the area of DPN and at increased doses. Pfizer's failure to disclose lack of efficacy is particularly outrageous in the area of bipolar disorder where there was not a scrap of evidence supporting efficacy and where there were actual negative side effects of depression for certain segments of the population.

With respect to bipolar disorder, neuropathic pain, migraine, and use of Neurontin at doses greater than 1800 mg/day, defendants intentionally suppressed material negative information concerning Neurontin's efficacy, rendering defendants' positive statements about Neurontin's efficacy in treating these conditions misleading, and factually false. This information would likely have been material to any PMG physician in determining how best to prescribe Neurontin for the treatment of

patients. Because it is legal for physicians to prescribe drugs off-label, it is imperative that they have accurate scientific information about the medication in the published medical literature. As Dr. Dickerson said, health care professionals practicing evidence-based medicine must rely on the integrity of the published literature to determine whether a pharmaceutical product is effective. Moreover, this information was material to a TPP or health plan like Kaiser trying to manage its drug formulary.

Accordingly, the intentional material misrepresentations and omissions found by this Court constitute fraudulent business acts or practices under the California Unfair Competition Law because they would likely deceive a reasonable health plan or reasonable physician; and actually did so in the case of Kaiser.

B. Pfizer's Legal Defenses

1. Standing

At the end of trial, defendants claimed for the first time that Kaiser Foundation Hospitals lacked independent standing to sue under the UCL because it did not pay for any Neurontin prescriptions during the relevant time periods. Screaming that it had been sandbagged, plaintiff complains that Kaiser had no prior notice that this would be an issue and thus did not introduce at trial evidence of Kaiser Hospital's standing.

However, defendants do not challenge the standing of Kaiser

Foundation Health Plan to sue under the California UCL. Because the health plan has standing to bring this case, the Court need not determine whether Kaiser Hospitals independently has standing. See Liberty Prop. Trust v. Republic Props. Corp., 577 F.3d 335, 339 n.1 (D.C. Cir. 2009) (in a case involving two affiliated plaintiffs, a limited partnership and a trust, holding that "[b]ecause the limited partnership has standing to maintain the action and a remedial award to the partnership would also make the trust whole, in the limited circumstances of this case we need not determine whether the trust independently has standing . . . . [T]he trust and the limited partnership 'both are pieces of a single operating business.'").

Still, I have no evidence that Kaiser Hospitals had any damages apart from the Health Plan. As such, any award of restitution will be to Kaiser Foundation Health Plan.

2. Statute of Limitations

A thornier issue is whether Kaiser's UCL claims are barred by the four year statute of limitations. The complaint in this case was filed on February 1, 2005.

(i) Tolling Under American Pipe

As a threshold matter, plaintiffs argue that the related class action complaint (filed on May 14, 2004) tolled the UCL statute of limitations under American Pipe & Construction Co. v. Utah, 414 U.S. 538, 552-53 (1974). Defendants respond that this

is a pipe-dream. In its view, because Kaiser filed its own action, it cannot be considered part of the class, and American Pipe does not toll the action. The Court does not need to reach this legal question because the class action complaint did not make claims for relief under the California UCL. (See Third Amended Class Complaint, Docket No. 580.) In fashioning the American Pipe rule, the Supreme Court reasoned that the filing of a class action would protect the policies underlying the statute of limitations by providing defendants with notice of a plaintiff's claim. Id. at 554-55. Because the class complaint did not make claims under the UCL, the defendants were not on notice of Kaiser's UCL claims. Accordingly, American Pipe is inapplicable and the statute of limitations was not tolled under that theory.

(ii) The Discovery Rule

Defendants argue that many of the claims are time-barred because the complaint was filed more than four years after the alleged fraudulent activities took place. Plaintiffs argue that defendants fraudulently concealed the facts underlying Kaiser's claims.

The law is unsettled in California as to whether the discovery rule applies to the statute of limitations for UCL claims. Grisham v. Philip Morris U.S.A., Inc., 151 P.3d 1151, 1157 n.7, 40 Cal. 4th 623, 634 n.7 (2007) ("We assume for

purposes of this discussion that the delayed discovery rule applies to unfair competition claims. We note that this point is currently not settled under California law, and we do not address it.") (citations omitted). Generally, UCL claims "are subject to a four-year statute of limitations which [begins] to run on the date the cause of action accrued, not on the date of discovery." Karl Storz Endoscopy-America, Inc. v. Surgical Tech., Inc., 285 F.3d 848, 857 (9th Cir. 2002). However, in circumstances where fraud is alleged, California courts apply the "discovery" rule to UCL cases. In Broberg v. Guardian Life Ins. Co., 90 Cal. Rptr. 3d 225, 231 (Cal. Ct. App. 2009), for example, the court held:

> At least in the context of unfair competition claims based on the defendant's allegedly deceptive marketing materials and sales practices, which is simply a different legal theory for challenging fraudulent conduct and where the harm from the unfair conduct will not reasonably be discovered until a future date, we believe the better view is that the time to file a section 17200 cause of action starts to run only when a reasonable person would have discovered the factual basis for a claim.

Id. at 231 (citing April Enters., Inc. v. KKTV, 195 Cal. Rptr. 421, 434 (Cal. Ct. App. 1983) ("[The] nature of the right sued on, not the form of the action . . . determines the applicability of the statute of limitations.")).

In addition, California courts have applied the doctrine of fraudulent concealment in cases brought under the UCL. See, e.g., Snapp & Assocs. Ins. Servs., Inc. v. Malcolm Bruce Burlingame Robertson, 117 Cal. Rptr. 2d 331, 334-35 (Cal. Ct.

App. 2002) (discussing the fraudulent concealment doctrine in a UCL case and stating that the doctrine "applies to any type of case") (citations omitted). California case law describes this doctrine:

> The doctrine of fraudulent concealment, which is judicially created, limits the typical statute of limitations. 'The defendant's fraud in concealing a cause of action against him tolls the applicable statute of limitations.' In articulating the doctrine, the courts have had as their purpose to disarm a defendant who, by his own deception, has caused a claim to become stale and a plaintiff dilatory. . . . It was early extended to be available 'in all cases.'

Regents of Univ. of Cal. v. Superior Court, 976 P.2d 808, 822-23, 20 Cal. 4th 509, 533 (1999) (internal citations omitted).

The fraudulent concealment doctrine "does not come into play, whatever the lengths to which a defendant has gone to conceal the wrongs, if a plaintiff is on notice of a potential claim." Rita M. v. Roman Catholic Archbishop, 232 Cal. Rptr. 685, 690 (Cal. Ct. App. 1986). "A plaintiff is under a duty to reasonably investigate, and a suspicion of wrongdoing, coupled with a knowledge of the harm and its cause, commences the limitations period." Snapp & Assocs., 117 Cal. Rptr. 2d at 335 (citing Jolly v. Eli Lilly & Co., 751 P.2d 923, 928, 44 Cal. 3d 1103, 1112 (1988)).

For bipolar disorder, plaintiffs have proven that defendants fraudulently concealed the facts underlying plaintiffs' UCL claims. In 1999, Kaiser's DIS prepared a monograph on the use of

Neurontin for the treatment of bipolar disorder. In making its recommendation to expand Neurontin's formulary status to permit prescription by psychiatrists, DIS relied on a personal communication from a Pfizer employee who did not disclose the negative Pande trial. (TX 301.) In August of 2000, defendants responded to an inquiry from Kaiser with a letter that "concluded that gabapentin appears to be effective in the milder segment of the bipolar universe" and that the "low side effect profile associated with gabapentin gives it a favorable risk to benefit ratio." (TX 309.) This letter did not disclose the negative results of the Pande, Frye, or Guille trials on bipolar, all of which were available to defendants prior to 2000. (Id.) In addition, Pfizer suppressed these negative results in the medical literature. These actions amount to fraudulent concealment that prevented Kaiser from learning about the existence of negative data from clinical trials with respect to Neurontin's use for the treatment of bipolar disorder, all the while reinforcing the claim that Neurontin was a safe and effective treatment for mood disorders.

For neuropathic pain, defendants suppressed negative evidence about the use of Neurontin to treat neuropathic pain and sponsored publication of positive evidence in scientific journals. In 1998, Parke-Davis sponsored an "abstract" in the journal Neurology, spinning the Gorson trial as positive when the author's own manuscript interpreted the trial results as

negative. (TX 1271 ("Gapapentin may be effective in the treatment of painful diabetic neuropathy.").) In November 1997, defendants sponsored the publication of a supplement in Internal Medicine that claimed Neurontin was effective in treating neuropathic pain, while suppressing the negative Gorson trial results. (TX 40.) In 1998, defendants sponsored a supplement to the Cleveland Clinic Journal of Medicine that also touted Neurontin as a treatment for neuropathic pain while suppressing the negative Gorson results. (TX 110.) Beginning in 1999, the defendants actively prevented Dr. Reckless from presenting or publishing the negative results of his neuropathic pain trial. (TX 183 at 1; see also TXs 185, 136, 109.) In 2000, defendants sponsored a supplement to Neurology Reviews that suppressed the negative Gorson and Reckless trials. (TX 82.)

In connection with plaintiffs' development of a 1999 drug monograph, DIS contacted the defendants to request all available information about the use of Neurontin to treat neuropathic pain. (Trial Tr. vol. 9, 76-81.) In these communications, defendants did not disclose the complete story about the potential unblinding of the Backonja trial or provide the full research report of the Gorson trial. (Trial Tr. vol. 9, 76-80; Trial Tr. vol. 10, 84-85; Trial Tr. vol. 12, 102-06.) Finally, defendants also fraudulently concealed facts concerning efficacy through communications that were part of DIS's Inquiry Service. (See TXs

296, 309.) For example, in August 2000, DIS contacted Pfizer to inquire about dosing of Neurontin. Pfizer did not indicate that the Reckless trial had not shown increased efficacy at doses greater than the 1800 mg/day limit imposed by the FDA, but instead advised DIS that tolerability had been shown up to 3600 mg/day. (TX 296.) Dr. Joel Hyatt, a PMG physician who is a co-chair of the DUAT initiative, explained that had he known in 2003 the full extent of the evidence, he would not have written that Neurontin is effective for certain forms of neuropathic pain, and instead "would have made a statement that gabapentin, Neurontin, is not effective in neuropathic pain, period." (Trial Tr. vol. 8, 107-08.)

For migraine, defendants fraudulently concealed the facts underlying plaintiffs' UCL claim by suppressing the negative results of the Mathew study and subsequently publishing the study with positive results in Headache in 2001. They also sent a letter in 2000 to a PMG physician that claimed Neurontin was effective for the treatment of migraine headaches, but that did not disclose the negative results of trials 879-200, 945-217 or the Mathew study. (TX 432.) These actions prevented plaintiffs from learning the truth about Neurontin's efficacy for the migraine prophylaxis and the truth about defendants' fraud.

For high doses, defendants fraudulently concealed the underlying facts from plaintiffs through similar methods: i.e. suppression of negative studies, fraudulent publications, and

direct communications with Kaiser that contained fraudulent information. In particular, Kaiser presented several DIS Inquiry Service documents showing that, in 2000, Parke-Davis represented to Kaiser that high doses of Neurontin were more effective than low doses. (See TXs 294, 296, 309.) In one communication, Parke-Davis stated that 3600 mg/day is the maximum dose, but states that some non-Parke-Davis studies have seen doses up to 6000 mg/day. (TX 294.) It did not disclose that the results of the Reckless study, for example, showed no additional efficacy at higher doses.

Defendants claim that Kaiser was put on notice by an article titled "Warner-Lambert Neurontin Promotions Under Investigation by U.S. Attorney" in a publication called The Pink Sheet that was published on April 3, 2000. (TX 506 ("Investigation could help define limits of government authority to regulate off-label promoting.").) Although Dr. Millares, the chair of Kaiser's DIS, testified that she reads The Pink Sheet, she did not recall reading this particular article. (Trial Tr. vol. 10, 54-55.) While this article may have suggested to Kaiser that defendants were violating FDA rules about off-label promotion, there is nothing in the article that supports an inference that Neurontin might not be effective for certain off-label indications for which it was widely used. (See TX 506.)

In addition, defendants argue that the unsealing of the Franklin case in 2000 should have put defendants on notice of

their potential injuries and claims. See United States ex rel. Franklin v. Parke-Davis, No. 96-cv-11651. The unsealing of a case in Massachusetts, unaccompanied by extensive press coverage, cannot be viewed as sufficient notice, particularly to a California corporation.

Plaintiffs argue that their claims accrued in 2002 after defendants' fraud became nationally publicized. In 2002, plaintiffs were put on notice when press reports surfaced about Dr. David Franklin's whistleblower suit and the potentially fraudulent claims of efficacy made by the defendants. (See TX 319 (Kaiser "Rx Update" referencing Wall Street Journal and New York Times articles published in 2002 that discussed off-label marketing of Neurontin to physicians); Trial Tr. vol. 5, 115 (testimony of Dr. Ambrose Carrejo) (stating that in 2002 "the whole story is starting to unfold").) See also United States ex rel. Franklin v. Parke-Davis, 210 F.R.D. 257 (D. Mass. 2002) (modifying protective order governing pretrial discovery after newspapers and television networks sought to intervene in the case). After 2002, Kaiser investigated its potential injuries and engaged in serious efforts to curb inappropriate prescribing of Neurontin through its DRUG and DUAT campaigns. Kaiser's claims are not barred by the UCL's statute of limitations.

3. Prescriptions Written Outside California

Defendants argue that Kaiser cannot recover under the UCL for Neurontin prescriptions written outside California. This contention raises choice-of-law issues, and both parties agree that Massachusetts choice-of-law rules should apply to the Court's analysis because the suit was filed in Massachusetts.

Massachusetts applies a "functional approach" to choice-of-law questions, which is "explicitly guided by the Restatement (Second) of Conflict of Laws (1971)." Levin v. Dalva Bros., Inc., 459 F.3d 68, 74 (1st Cir. 2006). "Section 148 of the Restatement spells out the choice of law analysis for misrepresentation claims, indicating that the law of the state where the representations were made, received, and relied upon should govern unless another state has a closer connection to the parties or the occurrence." First Marblehead Corp. v. House, 473 F.3d 1, 9 (1st Cir. 2006); see also Restatement (Second) of Conflict of Laws § 148(1) (1971). Thus, under the choice of law rules in Massachusetts for fraud and misrepresentation, the law of the state in which a plaintiff took action in reliance on a defendant's representations applies. Bushkin Assocs., Inc. v. Raytheon Co., 393 Mass. 622, 632, 473 N.E.2d 662 (1985); see also First Marblehead Corp., 473 F.3d at 9.

Plaintiffs argue that these Massachusetts choice of law rules require the application of California law to all of their claims because Kaiser's Drug Information Service (DIS) is located

in California and DIS was the entity that primarily gathered information on Neurontin and corresponded with Pfizer about Neurontin.

Pfizer disagrees, arguing that California law should only apply to Kaiser's claims concerning prescriptions written in California. California law does have a "presumption against the extraterritorial application of its statutes," Meridian Project Sys., Inc. v. Hardin Constr. Co., 404 F. Supp. 2d 1214, 1225 (E.D. Cal. 2005) (citing Diamond Multimedia Sys., Inc. v. Superior Court, 968 P.2d 539, 554, 19 Cal. 4th 1036, 1060 n.20 (1999)), and courts have held that the UCL does not apply to conduct occurring outside California. See id. (dismissing UCL claims of Canadian firm against California competitor because it involved a plaintiff that was a Canadian corporation, the plaintiff's injuries occurred in Canada, and the only specific misconduct identified in the complaint occurred in Illinois); Van Slyke v. Capital One Bank, No. C 07-00671, 2007 WL 3343943, at *14 (N.D. Cal. Nov. 7, 2007) ("California courts have been highly critical of attempts to apply the [UCL] outside California borders for transactions that do not affect California residents and did not take place within the state.")

California courts have permitted the certification of nationwide class actions under the UCL where some, or most, class members were non-California residents. See Wershba v. Apple Computer, Inc., 110 Cal Rptr. 2d 145, 159-60 (Cal. Ct. App.

2001); Wash. Mut. Bank v. Superior Court, 15 P.3d 1071, 1080, 24 Cal. 4th 906, 919-20 (2001). Accordingly, there is no bar against the application of the California UCL to prescriptions of Neurontin filled outside California, so long as Kaiser shows that it relied, in California, on misrepresentations made by defendants.

The Kaiser Foundation Health Plan maintains its headquarters in California and Kaiser Foundation Hospitals is a not-for-profit California corporation. The majority of Kaiser's members and the bulk of Kaiser's operations, including the Drug Information Services, are located in California. (Trial Tr. vol. 5, 82-83, 92-93; Trial Tr. vol. 9, 43; Trial Tr. vol. 10, 92-93.) DIS surveys the best available evidence on a drug and often, as it did for Neurontin, contacts the drug manufacturer to learn more about the drug. (Trial Tr. vol. 9, 46, 89-97; Trial Tr. vol. 10, 80-81; TXs 461, 461-A at 22, 296, 309 at 2-4, 294, 292.) DIS then creates drug monographs summarizing its findings and regional P&T Committees rely heavily on these monographs. (Trial Tr. vol. 9, 43-46; Trial Tr. vol. 12, 94.) The monographs are shared with all Kaiser regions during monthly teleconferences with formulary personnel and at interregional P&T Committee meetings. (Trial Tr. vol. 5, 110; Trial Tr. vol. 9, 43-46 (describing the interregional formulary subcommittee at which all monographs are shared and evidence is discussed).) Kaiser employees testified that, given this cross-pollination and information-sharing, the

formularies across Kaiser regions are very similar, and certain formularies, like Kaiser's Medicare formulary, are identical across all regions. (Trial Tr. vol. 5, 112-13.) "[A]ll of the P&T committees across Kaiser Permanente rely on the same evidence, rely on the [DIS] review of that evidence, rely on the same literature, and they make decisions on the products." (Trial Tr. vol. 10, 93.) This was specifically true concerning Neurontin, which was on-formulary across all Kaiser regions. (Trial Tr. vol. 5, 109-13; Trial Tr. vol. 10, 93; Trial Tr. vol. 12, 95; TX 840.)

In addition, Pfizer's marketing teams specifically targeted Kaiser in an effort to increase off-label Neurontin prescriptions. As Dr. Millares, the manager of Kaiser's DIS, explained:

> [PMG physicians] depended on, you know, we're an evidence-based organization . . . and they depended upon the literature, what was out in the literature, they depended upon [DIS], and we depended upon the evidence, and so we came to wrong conclusions, and then they depended on the P&T committee and they depended on what we said and we depended on the literature, and so we've had . . . these lies basically that have permeated all this information, and now our physicians are convinced that [Neurontin] . . . has evidence to support it.

(Trial Tr. vol. 10, 94-95.) In other words, DIS relied on Pfizer's misrepresentations in California, and then disseminated the mis-information to the various P&T Committees.

Based on this evidence admitted at trial, the Court finds that Pfizer's misrepresentations about Neurontin's use for off-label conditions were made, received and relied on primarily in California. More than 75% of Kaiser's members are located in California. Therefore, most of the Kaiser members who were prescribed Neurontin filled their prescriptions in California. Second, the Kaiser P&T Committees outside California relied on drug monographs prepared by the California DIS in making formulary decisions about Neurontin. Accordingly, there was sufficient reliance on misrepresentations in California such that Massachusetts choice of law rules require a finding that the California UCL apply to all Neurontin prescriptions paid for by Kaiser.

4. Causation

California law describes the causation requirements under the UCL by stating that "[t]he court may make such orders or judgments . . . as may be necessary to restore to any person in interest any money or property, real or personal, which may have been acquired by means of such unfair competition." Cal. Bus. & Prof. Code § 17203.

The most difficult issue in this case involves causation. The Court has written extensively on the issue of causation requirements for a RICO claim. See In re Neurontin Mktg. & Sales Practices Litig., 677 F. Supp. 2d 479, 493-96 (D. Mass. 2010).

Defendants argue that the First Circuit's recent opinion in Rule v. Fort Dodge Animal Health, Inc., 607 F.3d 250 (1st Cir. 2010), precludes any finding of causation in this case. In Rule, plaintiffs in a proposed class action sought to recover for an undisclosed safety risk associated with a veterinary medicine. The plaintiff acknowledged that the drug was effective, i.e. that it prevented heartworms in dogs, but argued that she should recover under the Massachusetts consumer protection statute due to undisclosed safety risks. The court held that where a product had been consumed and provided the intended benefit, the plaintiff could not demonstrate a concrete injury. Id. at 253-54. The court also noted that "it was clear at the time of Rule's law suit that she neither now could show nor could suffer in the future any adverse economic impact." Id. at 253. The First Circuit's decision in Rule does not defeat the plaintiffs' claims here. The Court has found that plaintiffs proved Neurontin was totally ineffective in treating certain off-label conditions, and that plaintiffs relied on defendants' misrepresentations—in choosing to reduce restrictions on Neurontin prescribing in Kaiser's drug formulary and drafting drug monographs. Accordingly, the Neurontin purchased by Kaiser did not, in fact, provide its intended benefit. Moreover, even where the drug may have had effectiveness in some patients (for example, in some pain indications), Kaiser demonstrated that it suffered a significant adverse economic impact because it could

have paid for less expensive alternatives.

In Kaiser's case, there are three layers of causation that must be addressed. First, the Court must determine what misrepresentations and omissions Kaiser and DIS relied on and whether that reliance caused Kaiser to suffer injury. Second, I must determine whether or not PMG physicians would have nonetheless prescribed Neurontin to their patients if DIS had not published monographs recommending Neurontin or if the P&T Committees had added guidelines or restrictions to Neurontin's formulary status. Finally, the Court must also deal with how to quantify the number of prescriptions caused by fraudulent marketing. I deal with each thorny question in turn.

(i) Reliance by DIS and P&T Committees

Recent amendments to the UCL have imposed "an actual reliance requirement on plaintiffs prosecuting a private enforcement action under the UCL's fraud prong." In re Tobacco II Cases, 207 P.3d 20, 39, 46 Cal. 4th 298, 326 (2009). The California Supreme Court has provided a useful explanation of this reliance requirement:

> This conclusion [that a showing of reliance is required], however, is the beginning, not the end, of the analysis of what a plaintiff must plead and prove under the fraud prong of the UCL. Reliance is an essential element of fraud. Reliance is proved by showing that the defendant's misrepresentation or nondisclosure was an immediate cause of the plaintiff's injury-producing conduct. A plaintiff may establish that the defendant's misrepresentation is an immediate cause of the plaintiff's conduct by showing that in its absence the plaintiff in all reasonable probability

would not have engaged in the injury-producing conduct.

While a plaintiff must show that the misrepresentation was an immediate cause of the injury-producing conduct, the plaintiff need not demonstrate it was the only cause. It is not necessary that the plaintiff's reliance upon the truth of the fraudulent misrepresentation be the sole or even the predominant or decisive factor influencing his conduct. It is enough that the representation has played a substantial part, and so had been a substantial factor, in influencing his decision. Moreover, a presumption, or at least an inference, of reliance arises wherever there is a showing that a misrepresentation was material. A misrepresentation is judged to be material if a reasonable man would attach importance to its existence or nonexistence in determining his choice of action in the transaction in question, and as such materiality is generally a question of fact unless the fact misrepresented is so obviously unimportant that the jury could not reasonably find that a reasonable man would have been influenced by it.

Nor does a plaintiff need to demonstrate individualized reliance on specific misrepresentations to satisfy the reliance requirement. . . .

[W]hile a plaintiff must allege that the defendant's misrepresentations were an immediate cause of the injury-causing conduct, the plaintiff is not required to allege that those misrepresentations were the sole or even the decisive cause of the injury-producing conduct. Furthermore, where, as here, a plaintiff alleges exposure to a long-term advertising campaign, the plaintiff is not required to plead with an unrealistic degree of specificity that the plaintiff relied on particular advertisements or statements. Finally, an allegation of reliance is not defeated merely because there was alternative information available to the consumer-plaintiff, even regarding an issue as prominent as whether cigarette smoking causes cancer. Accordingly, we conclude that a plaintiff must plead and prove actual reliance to satisfy the standing requirement of section 17204 but, consistent with the principles set forth above, is not required to necessarily plead and prove individualized reliance on specific misrepresentations or false statements where, as here, those misrepresentations and false statements were part of an extensive and long-term advertising

campaign.

Id. at 39-41 (citations and internal quotations omitted).

Pfizer engaged in an "extensive and long-term advertising campaign," see id., to promote Neurontin for off-label indications for which the company was aware the drug had not been shown to be effective. Pfizer implemented this campaign through its publications strategies, the sponsorship of CMEs, direct contact by medical liaisons and drug representatives, and direct communication with third party payors like Kaiser.

Kaiser's DIS relied on Pfizer's direct misrepresentations to it, and on the positive information introduced into the published literature by studies funded by the defendants without the benefit of the negative trials sponsored and suppressed by defendant. This reliance was reflected in the drug monographs prepared by DIS, the direct communications between DIS's inquiry service and PMG physicians, and the communications to the P&T Committees.

Defendants also argue that Kaiser should not be found to have relied on any misrepresentations because "the evidence shows that the alleged misrepresentations were not a factor in their decision-making" (see Defs.' Proposed Conclusions of Law at 6 (citing Princess Cruise Lines, Ltd. v. Superior Court, 101 Cal. Rptr. 3d 323, 329 (Cal. Ct. App. 2009)) and because they knew "of an alleged falsity." (Id. (citing Laster v. T-Mobile USA, Inc.,

No. 05-cv-1167, 2009 WL 4842801, at *4 (S.D. Cal. Dec. 14, 2009); Buckland v. Threshold Enters., Ltd., 66 Cal. Rptr. 3d 543, 549-54 (Cal. Ct. App. 2007); Caro v. Procter & Gamble Co., 22 Cal. Rptr. 2d 419, 430 (Cal. Ct. App. 1993).) To support their argument, defendants point out that the Backonja study, as published in JAMA, expressly mentioned the potential issue of unblinding, which should have put Kaiser on notice of the potential problems with the study's results. However, when Dr. Backonja alluded to problems with unblinding in the JAMA article, he claimed that proper analysis had been done to verify the reliability of the positive results. (TX 1250 at 1835.) Backonja stated that "inclusion of patients who experienced three central nervous system adverse effects in the original analysis did not account for the overall efficacy seen in the trial." (Id.) As Dr. Jewell testified, when both the sleepy and the dizzy patients who were potentially unblinded were removed from the study, as opposed to only the sleepy patients or only the dizzy patients, the results were no longer positive. Accordingly, at the time it relied on the JAMA article in its 1999 monograph, Kaiser did not and could not have known the entire truth about the Backonja results without access to the study's raw data. Moreover, despite the fact that the Backonja study, as published in JAMA, discussed the potential issue of unblinding, Parke-Davis did not mention this key flaw that could undermine the study's

reliability in its public relations campaign that generated more than "85 million impressions." (TX 71 at 4.) The credible evidence is that Kaiser did not understand the true impact of the unblinding as explained by Jewell and did not give full weight to Gorson because it was placed in a letter to the editor as opposed to a peer-reviewed journal. (See, e.g., Trial Tr. vol. 9, 76-79, 86-88 (testimony of Dr. Millares that she did not have the complete data about the Backonja unblinding issue at the time of her recommendation); Trial Tr. vol. 12, 103-04 (testimony of Dr. Daniel explaining how a full understanding of the flaws in Backonja would have changed his opinion about Neurontin's efficacy).)

Pfizer also argues that Kaiser's true motive in its anti-Neurontin campaign was the drug's high cost rather than any lack of efficacy. As evidence, it points out that some regions put gabapentin back on the formulary after it went generic. (TX 810.) As such, it insists that any misrepresentations were not a substantial factor in Kaiser's decision-making. However, the fact that cost was a factor does not undermine the argument that lack of efficacy of a drug is also a substantial factor for consideration in determining which drugs to place on a formulary. If it had known the truth, Kaiser would likely not have removed restrictions on, or sanctioned widespread use of, an extremely expensive drug whose efficacy was not established, or even disproven (i.e., with respect to bipolar disorder).

(ii) Prescribing Behavior of PMG Physicians

The second causation analysis that the Court must perform is to determine whether or not PMG physicians would have nonetheless prescribed Neurontin to their patients if DIS had published monographs based on the true scientific evidence or if the P&T Committees had added guidelines or restrictions to Neurontin's formulary status.

No PMG physician testified during the trial that she would not have prescribed Neurontin had she known about defendants' misrepresentations as to efficacy or suppression of negative trials in the literature like Reckless and POPP in the area of neuropathic pain. To the contrary, defendants' presented the testimony of experts with impressive credentials like Dr. Shawn Bird, Dr. Gary Brenner, and Dr. Andrew Slaby who all stated that they had reviewed the data from the negative and positive Neurontin DBRCTs and still believe Neurontin might be an effective drug for certain patients suffering from bipolar disorder and neuropathic pain. Defendants correctly point out that proof of fraud on the market in the aggregate has not been embraced in the case law as a basis for proving causation in individual cases. See generally UFCW Local 1776 v. Eli Lilly & Co., __ F.3d __, 2010 WL 3516183 (2d Cir. Sept. 10, 2010). (reversing class certification in case alleging that the drug manufacturer had misrepresented the drug's efficacy and side

effects and alleging over-pricing.)

The fact that there is a 95% compliance rate among PMG physicians with the Kaiser formulary is proof that PMG physicians would likely have changed their Neurontin prescribing behavior had DIS issued negative monographs and had the P&T Committees made different decisions. This is likely true for the Southern California region, where Neurontin was placed on the formulary in 1994 but was restricted to prescribing by neurologists, the physicians who are often responsible for treating patients with epilepsy. The Court is persuaded that, had DIS and the Southern California P&T committee been aware of the truth about Neurontin, Kaiser would not have removed prescribing restrictions in 1999. Accordingly, PMG physicians in the Southern California region would more likely than not have reduced their off-label prescribing of Neurontin significantly.

Defendants point out that all other Kaiser regions placed Neurontin on their formularies during the 1990s without restrictions or guidelines. It is true that, even if Kaiser had known that Neurontin was not effective for the off-label conditions at issue, the other regions would not have removed Neurontin from the formulary because it was approved by the FDA for the adjunctive epilepsy treatment and, later, for the treatment of postherpetic neuralgia. Nonetheless, DIS probably would have issued monographs for Neurontin that were materially

different and would not have recommended the expanded prescribing of the drug for off-label indications. These monographs would have been shared with all Kaiser regions through the regular interregional P&T Committee meetings and the monthly teleconferences with formulary personnel from all regions that were chaired by Dr. Mirta Millares, the chairperson of DIS.

Based upon the fact that Kaiser did engage in the successful DRUG and DUAT campaigns starting in 2002 when it began to learn about Pfizer's fraudulent marketing, the Court finds that it is more likely true than not true that Kaiser would have taken action to reduce inappropriate Neurontin prescribing if it had known the truth earlier by distributing evidence of the suppressed trials (like POPP, Reckless, Pande, and Frye) through its monographs and responses to physician inquiries. The Court is persuaded that PMG physicians would have responded by reducing prescribing of Neurontin to Kaiser members. Even in the area of neuropathic pain, where there is some scientific evidence of efficacy for certain narrow indications, it is likely that a cheaper alternative like a tri-cyclic antidepressant would have replaced Neurontin. (See, e.g., Trial Tr. vol. 8, 57-58; Trial Tr. vol. 9, 13.) See Desiano v. Warner-Lambert Co., 326 F.3d 339, 349 (2d Cir. 2003) (acknowledging as valid the plaintiff TPPs' argument that the defendant pharmaceutical company's "fraud directly caused economic loss to them as purchasers, since they

would not have bought Defendants' product, rather than available cheaper alternatives, had they not been misled by Defendants' misrepresentations") (emphasis added).

(iii) Quantifying the Fraud

As discussed in the Findings of Fact, the Court accepts Dr. Rosenthal's analysis of the percentage of Neurontin prescriptions caused by defendants' off-label promotion. By indication, those percentages are as follows: (1) bipolar disorder: 99.4%; (2) neuropathic pain: 70%; (3) migraine: 27.9%; (4) doses over 1800 mg/day: 37.5%. (TX 405-K.) These percentages were translated into dollar amounts by plaintiffs' expert, Dr. Hartman, and the Court accepts his calculations as limited by the Court's findings with respect to the time periods during which defendants violated the UCL.

Defendants claim the Second Circuit's decision in Eli Lilly makes it impermissible for the Court to award damages in this case. Eli Lilly found that a proposed class should not have been certified because plaintiffs could not prove their theory of injury using generalized proof. 2010 WL 3516183, at *9-*14. Pfizer's position is that by admitting Dr. Rosenthal's and Dr. Hartman's testimony the Court is permitting plaintiffs to establish their injury through "generalized proof." However, Pfizer is gilding the Lilly. The instant case is not a class action and is therefore distinguishable from Eli Lilly. Moreover, while the testimony of Dr. Rosenthal and Dr. Hartman

was allowed in for the purpose of quantifying the defendants' fraud, the Court has found, that plaintiffs established individualized reliance by Kaiser's DIS on Pfizer's misrepresentations, thereby eliminating the concerns expressed by the Second Circuit about the many variables that affect an individual physician's prescriptions. Id. at *10. Indeed, the Second Circuit allowed the so-called "quantity effect theory" to go forward for consideration with respect to individual TPPs.

C. Restitution

The California UCL empowers courts to "restore to any person in interest any money or property, real or personal, which may have been acquired by means of such unfair competition." Cal. Bus. & Prof. Code § 17203. Under the UCL, Kaiser can recover amounts it paid for Neurontin as a result of defendants' unlawful, unfair, or fraudulent conduct even if Kaiser purchased the drug through a wholesaler or other intermediary rather than directly from the defendants. See Shersher v. Superior Court, 65 Cal. Rptr. 3d 634, 638-41 (Cal. Ct. App. 2007) (citing Hirsch v. Bank of America, 132 Cal. Rptr. 220 (Cal. Ct. App. 2003)). A federal district court has written that "the goal of restitution is to restore the status quo ante as nearly as possible." Tomlinson v. Indymac Bank, F.S.B., 359 F. Supp. 2d 891, 893-94 (N.D. Cal. 2005) (citations omitted).

Under the California UCL, the "court's discretion is very

broad" as to the remedy it awards, Cortez v. Purolator Air Filtration Prods. Co., 999 P.2d 706, 717, 23 Cal. 4th 163, 180 (2000), and the standard of proof for a damages determination is "patently less stringent" than the requirements for standing under the UCL. McAdams v. Monier, Inc., 105 Cal. Rptr. 3d 704, 715 (Cal. Ct. App. 2010). However, an award of restitution must not be "arbitrary and capricious," see People v. Fortune, 28 Cal. Rtpr. 3d 872, 874 (Cal. Ct. App. 2005), and there must be some support in the record for a restitution award. See Colgan v. Leatherman Tool Group, Inc., 38 Cal. Rptr. 3d 36, 63 (Cal. App. Ct. 2006).

Because PMG physicians would likely have prescribed alternative medication to their patients had they not prescribed Neurontin, I conclude that the appropriate measure of plaintiffs' damages is the difference between the cost of Neurontin and the cost of the cheaper and more optimal drug that would have been prescribed. I rely on the list of medications that Kaiser considered cheaper and more optimal than Neurontin as the alternative medications that would have been prescribed the Health Plan members but for the defendants' fraud. Defendants argue that efficacy is a patient-specific issue. For example, they point out that while tri-cyclic anti-depressants are generally effective for the treatment of pain, they fail for certain patients and can have unpleasant side effects. (See Trial Tr. vol. 17, 28, 37, 47, 55-57; Trial Tr. vol. 18, 21-22.)

They argue that Neurontin will be better tolerated by some patients because it is not metabolized by the liver, is not protein-bound in the blood, and does not interact with other drugs. Even if true, Kaiser has proven that other drugs are equally or more effective and much cheaper, and would likely have been the first line of treatment if the truth about Neurontin's efficacy had been known. Moreover, Neurontin has its own drawbacks; that is, depression with or without suicidal ideation in some patients.

Based on Dr. Hartman's calculations, the Court will award the following restitution to the plaintiffs: (1) bipolar disorder: $18,541,526; (2) neuropathic pain: $41,579,607; (3) migraine: $1,288,141; (4) doses greater than 1800 mg/day: $4,009,145. This totals $65,418,419.

In California, "[e]very person who is entitled to recover damages certain, or capable of being made certain by calculation, and the right to recover which is vested in him upon a particular day, is entitled to recover interest thereon from that day." Cal. Civil Code § 3287(a). Prejudgment interest, as provided by California law, is a recoverable component of restitution in a UCL action. See Ballard v. Equifax Check Servs., 158 F. Supp. 2d 1163, 1176-77 (E.D. Cal. 2001); Irwin v. Mascott, 112 F. Supp. 2d 937, 956 (N.D. Cal. 2000). On a UCL claim, the applicable rate of interest is 7% per annum. See Cal. Const., Art. XV § 1 ("In the absence of the setting of such rate by the legislature, the

rate of interest on any judgment rendered in any court of the state shall be 7 percent per annum."); see also Pro Value Props., Inc. v. Quality Loan Serv. Corp., 88 Cal. Rptr. 3d 381, 384 (Cal. Ct. App. 2009). After adding prejudgment interest to the award at the statutorily determined rate of 7% per annum, the restitution totals are as follows: (1) bipolar disorder - $26,150,953; (2) neuropathic pain - $61,596,338; (3) migraine - $1,949,431; (4) doses greater than 1800 mg/day - $5,589,796. This totals $95,286,518.

III. ORDER

The Court finds the defendants liable under the California Unfair Competition Law for conduct related to the following off-label conditions: (1) bipolar disorder; (2) neuropathic pain; (3) migraine; and (4) doses greater than 1800 mg/day.

The Court orders defendants to pay restitution to the Kaiser Foundation Health Plan in the amount of $95,286,518.[25]

/s/ PATTI B. SARIS
PATTI B. SARIS
United States District Judge

[25] Because this figure reflects the same damage claims encompassed by the jury claim, it will not be added to the jury verdict.