UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA	)	CRIMINAL NO. 04-10150 RGS
v.	)	
WARNER-LAMBERT COMPANY LLC	)	
Defendant	)	

SENTENCING MEMORANDUM OF THE UNITED STATES

I. INTRODUCTION

The United States submits this sentencing memorandum in support of the Rule 11(c)(1)(C) plea agreement and sentence, and the attendant global settlement agreement entered into between the United States Attorney in this District, the United States Department of Justice, the negotiating team for prosecutors in fifty states and the District of Columbia, and the Office of General Counsel for the Department of Health and Human Services, on the one hand, and the defendant Warner-Lambert Company LLC ("Warner-Lambert"), on the other hand.

Warner-Lambert and the Government have reached a global criminal and civil settlement agreement resolving Warner-Lambert's criminal and civil liability regarding the marketing of the drug Neurontin for uses not approved by the United States Food and Drug Administration ("FDA"). Such marketing is often referred to as "off-label promotion." The broad terms of the agreement are set forth in the second section of this memorandum.

Warner-Lambert has been charged with and has agreed to plead guilty to a two-count information for its introduction into interstate commerce of a misbranded drug by reason of the drug being inadequately labeled for Warner-Lambert's intended uses and for its introduction of

an unapproved new drug into interstate commerce in violation of Title 21, United States Code, Sections 331(a), 331(d), 352(f)(1) and 355(a).

Before this Court for review is the proposed plea agreement pursuant to Rule 11(c)(1)(C) and whether that agreement as part of the global settlement fairly and adequately addresses Warner-Lambert's criminal conduct and provides appropriate restitution to victims of that conduct. The third section of this memorandum details the law applying to this criminal conduct. The fourth section is a description of the conduct itself. In addition to introducing an inadequately labeled drug and an unapproved new drug into interstate commerce, Warner-Lambert also introduced a misbranded drug into interstate commerce in that the label was false or misleading because Warner-Lambert had developed intended uses for Neurontin that were not described on the label. While the parties disagree regarding the nature of Warner-Lambert's liability in connection with this last type of conduct, as relevant conduct it is also described in the fourth section of this memorandum.

The fifth section describes the appropriate punishment for the criminal conduct. In evaluating the harm to the United States, and in reaching this global resolution, the Government was cognizant of, and took into account, a number of factors including related conduct and possible additional losses caused thereby to insure that the global criminal and civil settlement fully and fairly reflects the magnitude of Warner-Lambert's criminal conduct, and fully and fairly compensates the affected health care programs for their losses.

The final section of this memorandum describes why this global resolution is sufficient to comply with the purposes of sentencing under 18 U.S.C. § 3553. As part of this resolution, the agreement contemplates Warner-Lambert's continued participation as a provider of prescription

drugs to various federal and state health care programs. As further described below, an integral aspect of the proposed resolution is an amendment to and expansion of the existing Corporate Integrity Agreement of Warner-Lambert's parent company, Pfizer Inc. The Corporate Integrity Agreement includes auditing of marketing conduct and the dissemination of information by Pfizer's Medical Information Department, and the agreement contains numerous other provisions relating to Pfizer's marketing activities. The inclusion of Pfizer in the Corporate Integrity Agreement is not intended by the parties to suggest wrongdoing by Pfizer separate from Warner-Lambert, but is a reflection of Pfizer's ownership of Warner-Lambert and the integration of former Warner-Lambert units and personnel into Pfizer.

II. THE PROPOSED GLOBAL CRIMINAL AND CIVIL RESOLUTION

The proposed civil and criminal resolution in this matter is the product of more than six years of investigation and approximately two years of negotiations between the Government and Warner-Lambert. The overall resolution includes: the plea agreement in this case setting forth Warner-Lambert's acknowledgment of and punishment for its criminal conduct; a civil settlement agreement between Warner-Lambert and the United States, resolving Warner-Lambert's civil fraud exposure to the Medicaid program; a Corporate Integrity Agreement with the Office of Inspector General, Department of Health and Human Services, governing Warner-Lambert's (and Pfizer's) future conduct as a provider of pharmaceutical products to beneficiaries of the various federal and state health care programs; and agreements between fifty states and the District of Columbia concerning Warner-Lambert's responsibilities to the state Medicaid programs and to the state Consumer Protection divisions.

In summary:

(A) Warner-Lambert agreed to plead guilty to inadequately labeling Neurontin and to introducing Neurontin into interstate commerce for unapproved purposes, which, by virtue of its prior violation of the Food, Drug & Cosmetic Act, constitute felony violations of the Food, Drug & Cosmetic Act, and to pay a $240,000,000 criminal fine;

(B) Warner-Lambert agreed to settle its federal False Claims Act and other civil liabilities and to pay the United States Government $83,600,000, plus applicable interest, in civil damages for losses suffered by the federally funded portion of the Medicaid program as a result of Warner-Lambert's off-label promotion of Neurontin;

(C) Warner-Lambert agreed to settle its civil liabilities to the fifty states and the District of Columbia in an amount of $68,400,000, plus applicable interest, in civil damages for losses suffered by the state-funded portion of the Medicaid program as a result of Warner-Lambert's off-label promotion of Neurontin;

(D) Warner-Lambert agreed to settle its civil liabilities to the Consumer Protection divisions of fifty states and the District of Columbia state attorney general's offices in an amount of $38,000,000, plus applicable interest, in civil damages for losses suffered by consumers of those states and to fund a remediation program designed to offset the impact of the improper marketing of Neurontin; and

(E) Warner-Lambert agreed to comply with the terms of an amendment to the corporate compliance program of its parent, Pfizer Inc, which, among other things, proscribes off-label marketing and requires training of employees and audits of its marketing practices.

This global resolution will not take effect until Warner-Lambert is sentenced by this Court. Warner-Lambert seeks to be sentenced at the time it enters its plea of guilty. The United States does not object, provided that the Court is satisfied that it has been fully apprised of the basis for the proposed resolution and has had an opportunity to inquire as it sees fit.

III. THE LAW

A. Misbranding Violations Generally

The Food, Drug & Cosmetic Act (FD&C Act), 21 U.S.C. § 301 et seq., regulates the development, manufacturing and distribution of drug products in the United States. Any person

who commits one of the prohibited acts set forth in 21 U.S.C. § 331 has violated the FD&C Act. Any person who commits such an act after having been previously convicted under the Act is guilty of a felony and is subject to up to three years' imprisonment and a $500,000 fine per count, 21 U.S.C. §§ 333(a)(2), or an alternative fine of up to twice the gross pecuniary gain from the offense, 8 U.S.C. §3571(d).

In particular, the statute prohibits the introduction into interstate commerce of any drug which is either misbranded or adulterated. 21 U.S.C. § 331(a); see, e.g., United States v. Hiland, et al., 909 F.2d 1114, 1124 (8th Cir. 1990). The statute defines misbranded drugs as those drugs for which the labeling is false or misleading, or which contain inadequate directions for use, in addition to several other alternative criteria. 21 U.S.C. § 352(a) & (f).

B. Inadequate Directions for Use

The first charge to which Warner-Lambert has agreed to plead guilty is introducing a misbranded drug into interstate commerce which did not have adequate directions on the label for the intended uses of the drug. The use, or uses, which must be addressed by the label is to be determined from the manufacturer's conduct. It is not limited to the use or uses approved by the FDA.

1. Directions for use: 21 C.F.R. § 201.5 provides as follows:

> *Adequate directions for use* means directions under which the layman can use a drug safely and for the purposes for which it is intended. Directions for use may be inadequate because, among other reasons, of omission, in whole or in part, or incorrect specification of:
>
> (a) Statements of all conditions, purposes, or uses for which such drug is intended, including conditions, purposes, or uses for which it is prescribed, recommended, or suggested in its oral, written, printed, or graphic advertising, and conditions, purposes, or uses

> for which the drug is commonly used....
>
> (b) Quantity of dose, including usual quantities for each of the uses for which it is intended and usual quantities for persons of different ages and different physical conditions.

2. Intended uses: In addition, "use" or "purposes for which it is intended" are defined in 21 C.F.R. § 201.128 (emphasis supplied):

> The words *intended uses* or words of similar import... refer to the objective intent of the persons legally responsible for the labeling of drugs. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. The intended uses of an article may change after it has been introduced into interstate commerce by its manufacturer.

Under this definition, the off-label uses promoted by Parke-Davis, as described below, were "intended," and thus required proper labeling. Since labeling, which must be approved by the FDA, does not provide directions for an unapproved use, it is presumptively inadequate if the manufacturer intended, as Parke-Davis did, that the drug be used off-label. See generally Hiland, 909 F.2d at 1129 (8th Cir. 1990)(whether the substance at issue was a drug "depended on the purposes for which the defendants intended it to be used, as evidenced by the product's labeling and marketing"). "The FDA may consider the manufacturer's subjective intent... based upon objective evidence in this determination," Nutrilab, Inc. v. Schweiker, 547 F. Supp. 880, 883 (N.D. Ill. 1982)(starch blockers intended by the manufacturer to be used as a drug, for which no approval was obtained). As stated in United States v. 3 Cartons, Etc., 132 F. Supp. 569

(S.D. Cal. 1952):

> Where a person has set in motion forces that result in creating an impression that an article has value in the treatment of disease, he cannot avoid the legal consequences of such action by a disclaimer in the labeling asserting there is no scientific evidence that the article has therapeutic value.

Id., at 574.

Moreover, the intended uses can be derived from the oral statements of persons speaking on behalf of the company about its product; United States v. Articles of Drug, 239 F. Supp. 465, 473-74 (D.N.J. 1965)(commentator's radio broadcasts that had been adopted by distributor held to be statements of the vitamin manufacturer demonstrating its intended use); United States v. Kasz Enter., 855 F. Supp. 534, 543 (D.R.I. 1994).

C. Introduction of an Unapproved New Drug: 21 U.S.C. §§ 331(d), 355 (a)

The second charge to which Warner-Lambert has agreed to plead guilty under the Food, Drug and Cosmetic Act is the introduction of an unapproved new drug into interstate commerce. The FD&C Act, 21 U.S.C. § 331(d), prohibits the introduction into commerce of any drug which is not in compliance with section 355; this latter section requires, inter alia, approval by the FDA prior to such introduction into commerce of any new drug. The manufacturer must demonstrate both safety and effectiveness for the intended uses before it may be marketed for those uses. No marketing may occur unless a New Drug Application (NDA) has been approved; any subsequent marketing must be confined to the use that was approved. Additional uses, considered off-label or unapproved uses, must be approved prior to marketing even for drugs which have already been approved for a separate use. Since under the statute and FDA regulations a drug may be new if a particular use, dosage or method of administration is new, Warner-Lambert's Neurontin

was new for the off-label uses and higher dosages promoted by the company even though it had been approved for a certain use. 21 C.F.R. § 310.3(h)(4) & (5). By marketing Neurontin for therapeutic uses which the FDA had not approved, Warner-Lambert violated this statutory provision as well.

D. Misbranding/False or Misleading Labeling or Advertising

1. Labeling and advertising: The term "labeling" encompasses all written, printed or graphic material "(1) upon any [drug or device] or any of its containers or wrappers, or (2) accompanying such [drug or device]." 21 U.S.C. § 321(k),(m). Material need not physically accompany the product in order to be deemed labeling, as long as it supplements or explains it. United States v. Diapulse Mfg. Corp. of Amer., 389 F.2d 612, 616 (2nd Cir. 1968). The term has been construed to include a variety of drug company promotional materials, including booklets, pamphlets, and literature that is textually related to the product. See Kordel v. United States, 335 U.S. 345, 349 (1948); V.E. Irons, Inc. v. United States, 244 F.2d 34, 39 (1st Cir. 1957). Advertising has been construed broadly to include content that is disseminated without the presence of the drug. Id.

2. Legal requirements for labeling and advertising: Labeling must provide adequate directions for the intended use, while both labeling and advertising must be fair and balanced. Labeling or advertising which is false or misleading constitutes a misbranding offense under 21 U.S.C. §§ 331(a) and 352(a). Actually false or misleading information, such as recommending a dosage that is not demonstrated to be safe for an intended use, even if shown to be safe for a separate approved use, constitutes improper labeling or misleading advertising. It is not required that the label or advertising contain an intentional lie; it is sufficient that a statement

made by the manufacturer, or on behalf of the manufacturer, suggests that the drug is safe and effective for uses which have not been approved by the FDA. Labeling or advertising which give directions of use for an unapproved use, selectively or inaccurately report data, or make unfounded claims of superiority are improper also. 21 U.S.C. §§ 352(a) & (f), 321(n); 21 C.F.R. §§ 201.1(e)(5), (6) & (7) & 201.5.

Warner-Lambert also misbranded Neurontin by distributing it with false or misleading labeling and advertising. Because labeling and advertising are broad concepts under the statute and regulations, this conduct involves promotional statements made by Warner-Lambert or its agents which are deemed to be part of the labeling or advertising and which were inaccurate because they overstated the safety and efficacy of Neurontin for the off-label uses. This conduct, while not charged, is relevant for evaluating the appropriateness of the proposed criminal fine and sentence.

E. Second Offense Felony

Title 21, Section 333(a)(2) provides that "if any person commits such a violation [of the statute] after conviction of him under this section has become final, or commits such a violation with the intent to defraud or mislead, such person shall be imprisoned for not more than three years or fined not more than $10,000, or both." In November 1995, Warner-Lambert was convicted of a felony offense under the FD&C Act for fraudulently failing to report to the FDA drug stability failures concerning Dilantin and other drugs. Therefore, the current charges constitute "second offenses" for purposes of 21 U.S.C. § 333(a)(2) and are punishable as felonies without regard to proof of intent to defraud or mislead See, e.g., United States v. Bradshaw, 840 F.2d 871 (11th Cir. 1988).

F. Off-label Prescribing

Generally, once Neurontin was approved by the FDA for adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy, physicians could, using their independent and untainted medical judgment, prescribe the drug for any medical condition as to which the doctor believed the drug was beneficial for the patient without violating the FD & C Act. This is so even if the FDA had not determined that it was safe and effective for treating that condition. This practice, known as "off-label" use, includes treating a condition not indicated on the label, or treating the indicated condition but with a different dosing regimen or in a different patient population (i.e., treating children with a drug approved for use in adults). Although a physician may prescribe most, but not all, drugs for an off-label use without violating the FD & C Act, a manufacturer may not market or promote it for such unapproved uses. If a manufacturer wishes to market or promote a drug for a new use, it must demonstrate, with adequate studies, to the FDA's satisfaction that the drug is safe and effective for that new use. See 21 C.F.R. § 314.54. It must also receive FDA approval for the revised labeling that includes the new use. See 21 C.F.R. § 314.70(b)(3).

IV. RELEVANT FACTS

A. Overview of Unlawful Scheme

Although approved only as an epilepsy drug for specific indications, Parke-Davis nonetheless promoted Neurontin for a multitude of pain uses, psychiatric conditions such as bipolar disorder and anxiety, and for certain unapproved uses within epilepsy, among other unapproved uses. Parke-Davis employees engaged in this conduct from at least June of 1995 through at least April of 2000, across the United States. The breadth of the unlawful off-label

promotion is exemplified by a taped telephone message, sent to all medical liaisons in the northeast by their manager:

> Medical Liaisons, this is [the northeast Associate Medical Director]. I am calling in regard to the-- you know, there's a Neurontin push that's supposed to be on. ...So, what we need to do is focus on Neurontin. When we get out there, we want to kick some ass on Neurontin, we want to sell Neurontin on pain. All right? 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 about where we are with Neurontin. We've got to take it into our own hands and really kick some ass on it, all right? Let's do it up.

The misuse of the liaisons, who were supposed to be neutral, scientific experts on the company's products, was just one tactic among many used by the company in a coordinated, multi-faceted effort to boost off-label Neurontin sales. Parke-Davis mobilized hundreds of teleconferences, meetings, sales representative visits to doctors and other promotional efforts in this successful national campaign. Since 1995, the amount spent on Neurontin for off-label uses substantially increased. The specific planning of this campaign and the techniques used to implement it are set out following a background section.

B. Background

Warner-Lambert, through its Parke-Davis division, is a manufacturer of drugs subject to the Food, Drug and Cosmetic Act's approval process. Among other drug products, it manufactured, processed, distributed and sold the anti-seizure drug Neurontin, a prescription drug within the meaning of 21 U.S.C. § 353(b)(1). In June of 2000, after the events to which Warner-Lambert has agreed to plead guilty and the events alleged herein, Warner-Lambert was purchased by Pfizer Inc.

In preparation for its commercialization of Neurontin, and prior to seeking approval of

the drug from the FDA, Warner-Lambert's Parke-Davis division filed a patent application on November 23, 1990, in which the company sought protection for use of the drug as a method of treating neuro-degenerative diseases. This patent, the most important of several relating to Neurontin, was granted on January 28, 1992. The company expected that the patent would expire in 1998.

Thereafter, Warner-Lambert submitted a new drug application ("NDA") to the FDA for approval of Neurontin under the chemical name "gabapentin." In order for a manufacturer to introduce a new drug into interstate commerce, the manufacturer must first demonstrate to the FDA through pre-clinical and clinical trials that the drug is both safe and effective for each of its intended uses. 21 U.S.C. § 355(a) & (b). The NDA submitted to the FDA sought approval on a much narrower basis than was presented in the patent application. The double-blinded, well-controlled studies of gabapentin submitted to the FDA addressed only the safety and efficacy of gabapentin as an adjunctive anti-seizure medication for adult epileptics (i.e., as a second-line defense for patients who were already taking another anti-seizure medication). Gabapentin was approved by the FDA as adjunctive anti-seizure therapy on December 30, 1993 and officially launched into the market by Warner-Lambert on February 18, 1994 under the trade name "Neurontin." As part of the approval process, the FDA reviewed the labeling for the drug, which included the proposed claims about the drug's risks and benefits, as well as the directions for use.

As an anti-seizure medication, Neurontin was launched into a field which already had a large number of drugs. After an initial period of sales growth for its approved use, Neurontin's epilepsy sales began to plateau. The company, meanwhile, was facing substantial financial pressure because it had two large "blockbuster" drugs that it had heavily invested in, and which

it was preparing to launch with considerable attendant expense, but which had not yet generated any revenue. Warner-Lambert expected that these two products would contribute heavily to its income once launched, but in the meantime the company needed to generate more revenue from its existing products such as Neurontin.

C. The Company Embraced the Off-label Market

Warner-Lambert saw the slow growth of Neurontin's epilepsy sales as a potential problem, but found opportunity in the recent literature references to non-epilepsy uses of Neurontin and the continued growth of those uses. Warner-Lambert obtained detailed information on a monthly basis regarding the number of prescriptions and the general usage (i.e., pain, psychiatric, epilepsy, etc.) for which those prescriptions were written for its own product, Neurontin, and also for its competitors' anti-seizure drugs. The Company noted in October of 1995 that two of Neurontin's competitors in the epilepsy market, Tegretol and Depakote, were being prescribed for bipolar and pain diagnoses; 18-27% of total sales of those drugs were for bipolar and up to 9% were for pain. In contrast, Neurontin had only 1-2% of its sales for bipolar and pain at that time. These off-label uses were identified by Parke-Davis as an opportunity for growing Neurontin sales.

In 1995, the Company began considering whether it should seek FDA approval for several of these specific off-label uses or whether it should market Neurontin for the uses without approval. Warner-Lambert chose to market without approval; thereafter, off-label uses grew from approximately 15% of all uses in 1994, the first year Neurontin was marketed, to 94% in 2002.

The off-label marketing scheme had both national and regional components. In 1994,

Warner-Lambert had five regional sales units called "Customer Business Units," or "CBUs." The five units were the Northeast Customer Business Unit ("NECBU"), the Southeast Customer Business Unit ("SECBU"), the South Central Customer Business Unit ("SCCBU"), the North Central Customer Business Unit ("NCCBU"), and the West Customer Business Unit ("WCBU").

Each CBU was headed by its own Vice President, who reported directly to the President of Parke-Davis. The CBUs had their own sales and marketing personnel and budgets as well. There was also a Medical and Scientific Affairs staff operating out of each unit, ostensibly to coordinate with physicians regarding technical questions on Warner-Lambert products or studies. Because the CBUs were marketing directly to physicians, they were aware of the limited prescription of Neurontin by epileptologists for its approved use. By late 1994, the CBUs were also aware that some doctors were experimenting with Neurontin for off-label use.

Corporate headquarters was also aware of the growth in off-label sales. Parke-Davis had three important units that all played a role in the development and implementation of the off-label promotion. The three departments were Portfolio Management, Sales, and Medical and Scientific Affairs. Portfolio Management, which was the marketing department, did the market evaluation and marketing planning for each of the drug products, including Neurontin.

Portfolio Management, in consultation with other components of the company, set annual and quarterly plans for the marketing strategy for each of the company's drugs. Thus, for Neurontin, sales targets were set and four or five principal goals were established, along with a series of tactics to implement the goals, in a document called the "strategic plan." A parallel budget was set, with funding allocated to each of the specific goals and tactics. From 1995 on, substantial evidence demonstrates that Parke-Davis formally set a marketing goal of "expanding

the emerging uses," which meant increasing off-label sales. Each significant planning and budget document refers to this goal explicitly, and sets out the tactics that would be used to achieve this unlawful purpose.

For example, the 1997 Neurontin Strategic Plan references "increase in emerging uses" as both an issue and an opportunity. This document states: "Primary marketing objectives for Neurontin in 1997 will be to grow the use of the brand for epilepsy indications and to maximize Neurontin opportunities in emerging applications" (emphasis supplied).

In another planning document, the following list of Neurontin strategies is presented:

1. USE AREA EXPANSION
   expand Neurontin uses by educating medical profession on emerging use areas such as pain, bipolar.

2. AUDIENCE EXPANSION
   expand user base beyond neuros with epilepsy specialty, leverage their experience w/Neurontin for pain.

3. COMMUNICATION
   use of personal and non-personal communication to increase Neurontin monotherapy use. Identification of patient types in attempt to show Neurontin appropriate for all partial seizure patients.

4. PUBLICATION
   support expanded use of Neurontin and comparative efficacy with "other first line AEDs" by supporting and publishing "legitimate" studies.

5. THOUGHT LEADERS
   groom emerging thought leaders for peer to peer selling, ad board members and spearheading expanding use areas investigation

This and other substantial evidence demonstrates that Parke-Davis was routinely and carefully planning how to maximize its Neurontin revenue through off-label sales.

These national marketing plans were implemented by the business or sales department, which was primarily decentralized into the CBUs. Annual sales goals were set for each product

at headquarters in Morris Plains, New Jersey, as was the advertising and promotion budget, including amounts for each CBU, allocated by strategic goal and tactic. The CBUs then developed their own plans and budgets to implement the national off-label marketing plan. Thus, the goal of increasing off-label uses was advanced with specific tactics and funding. The CBU plans were then reconciled to the national budget in a process that ultimately went up to the highest levels in Warner-Lambert, the parent of Parke-Davis.

As an example of the Company's aggressive approach to off-label promotion, the SECBU listed marketing of Neurontin for pain and bipolar as one of its key strategies for 1996. The SECBU also boasted to upper management in Warner-Lambert that the SECBU was "exploiting the new frontiers of pain management and bipolar depression...." The SECBU created a plan for the marketing of pain, outlined in a slide show, which included a slide entitled "SECBU RIGHT ON THE MARK WITH NEURONTIN AND PAIN" over a picture of a target. The slide listed "Neurontin for Pain Strategies" and included conference calls and consultant meetings on pain. A psychiatric series of meetings was also planned.

An NCCBU document labeled "Neurontin Can Do/Can't Do" extols marketing Neurontin to psychiatrists and pain specialists. It states, "don't need indication to sell!" with reference to Neurontin for pain and bipolar. Pediatric use of Neurontin is also one of the strategies set out in the document, with the same notation that an indication (FDA approval) was not needed.

In addition to the Portfolio Management and the Business, or Sales, departments, there was the Medical and Scientific Affairs department which was responsible for overseeing the medical research that was sponsored by Parke-Davis but done by doctors who were not Parke-Davis employees. This department was also responsible for responding to inquiries about

company products from the medical community. The medical liaisons, although located in the CBUs, were part of the Medical and Scientific Affairs department and their bosses, the Associate Medical Directors, purportedly reported to the head of that department. In reality, the Associate Medical Directors and medical liaisons worked closely with the CBU Business Directors and sales representatives with little supervision from headquarters. Further, the medical liaisons were rarely involved in studies. The promise of a study grant was held out by the medical liaisons as an enticement to key doctors, however.

D. Parke-Davis Decided Not to Seek FDA Approval to Preserve Sales of Its Next Drug

At various times, both before and after Neurontin was commercially launched, Parke-Davis' management considered whether it should seek FDA approval of additional uses for Neurontin beyond adjunctive anti-seizure treatment. These uses included such areas as pain, pediatric use, psychological disorders, ALS (amyotrophic lateral sclerosis or Lou Gehrig's disease) and, especially, monotherapy for epilepsy. Among the factors considered were the potential market value of the use both with and without FDA approval, the likelihood of obtaining FDA approval, the short patent life of Neurontin and the impact of broader Neurontin indications on a new drug being developed.

1. Anticipated end of the Neurontin patent: Parke-Davis was concerned about the time line for getting new indications such as pain and psychiatry approved in view of the limited patent protection available for Neurontin. Early on, Parke-Davis thought the patent would expire in mid-1998 and generic competition would follow within several months.[1] The

[1]For reasons not relevant here, Parke-Davis was able to extend its patent protection until 2000. The labeled indications for a generic drug must be the same as for the innovator drug.

Neurontin Development Team meeting minutes address patent exclusivity concerns with specific reference to other potential uses for Neurontin at least as early as August 31, 1994.

2. Decisions to forego FDA approval: In late 1994 and early 1995, Parke-Davis was still considering whether it should seek FDA approval prior to marketing Neurontin for the new, unapproved uses. By mid-year in 1995, however, the dominant strategy of promoting off-label uses of Neurontin without seeking approval had emerged. In April of 1995, for example, the Neurontin Development Team minutes report that the New Product Committee reviewed the proposed psychiatric indications and concluded that "clinical studies should be designed for publication rather than regulatory purposes." It was planned that the Neurontin data would be presented to a group of psychiatrists at the next American Psychiatric Association meeting in May of 1995. A May 19, 1995 Parke-Davis Marketing Assessment on bipolar disorder called the disease "an attractive commercial opportunity that warrants clinical development" notwithstanding the acknowledged lack of scientific evidence of Neurontin's effectiveness in this area. It recommended that FDA approval of Neurontin for psychiatric indications **not** be pursued given the limited patent protection and market prospects.

As part of the May 19, 1995 Marketing Assessment, Parke-Davis forecast potential revenue from Neurontin for bipolar and anxiety treatment under two scenarios: with and without FDA approval. Without FDA approval, Parke-Davis still projected Neurontin annual revenues relating to bipolar disorder of $6 million in 1997 to $36 million dollars in 1999, before tapering

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Thus, by not seeking broader approvals for Neurontin, Parke-Davis limited the scope of generic competition. This also meant that the "son of Neurontin" drug, pregabalin, if approved for broader uses, would be protected from generic competition for those broader uses.

downwards after 1998 based on an assumption that generic competition would begin in 1999. With FDA approval, the numbers range from almost $12 million (1997) to over $80 million (2002), based on an assumption of expanded patent protection from generic competition. Despite the higher revenue projected if FDA approval was obtained, the Company decided not to seek regulatory approval.

Similar analyses were made of the market potential for other new uses, as well, including various types of pain, through 1995, 1996 and into 1997 at least. The outcome from these discussions was the same, however: after detailing the potential revenue to be derived from a particular use, both with and without FDA approval, Parke-Davis made the decision not to seek FDA approval and instead to promote the off-label uses without approval. Indeed, in May of 1997, Parke-Davis' senior management vetoed the recommendation of the upper level marketing executives that the company seek FDA approval for certain pain indications for Neurontin.

3. Expectations for pregabalin: A major factor affecting Parke-Davis' decision-making with regard to Neurontin was the potential effect that obtaining FDA approval for additional Neurontin uses would have on the sales of a new drug in the company's pipeline. This drug, pregabalin, is chemically similar to Neurontin, but the company anticipated obtaining approval for a broader range of uses than just adjunctive epilepsy therapy. The problem for Parke-Davis was that if FDA approved Neurontin for use in one or more of the areas for which pregabalin would be marketed (assuming pregabalin was also approved for these uses), the Neurontin approval would allow generic competitors of Neurontin to compete not only with

Neurontin but also, in practical terms, with pregabalin because of the chemical similarity.[2]

The idea was to maximize sales of Neurontin while it remained on patent but not to undermine future sales of pregabalin, which would have a much longer patent life remaining after approval. This decision, in and of itself, was within the manufacturer's legitimate prerogative. However, Parke-Davis' parallel decision to continue its off-label promotion of Neurontin was not. It is this combination of choices, exploiting the off-label market while deliberately not seeking FDA approval, that is at the core of the criminal conduct.

E. Off-label Uses Promoted

Neurontin was marketed for four broad categories of unapproved use: pain, psychiatric use, monotherapy and dosage.[3]

1. Use of Neurontin to treat pain: Pain is a broad category with numerous sub-categories. This is significant because a drug that works for one type of pain may have no effect in a different type. At least as early as October of 1995, and probably much earlier, the senior management of Parke-Davis was focused on exploiting the market for Neurontin in the treatment of pain. Parke-Davis promoted Neurontin for a variety of pain types, including painful diabetic neuropathy, post-herpetic neuropathy, reflex sympathetic dystrophy and migraine headaches, among others. Use of Neurontin for pain has grown tremendously since the drug's introduction in 1994 and now exceeds epilepsy use by a large margin.

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[2]Mere chemical similarity is not generally a sufficient basis for generic substitution, unless a physician makes a medical judgment that the generic is an adequate substitute.

[3] Parke-Davis promoted Neurontin for so many unapproved uses, often with, at most, scant anecdotal evidence of its effectiveness, that some employees referred to the list of these uses as the "snake oil" list.

One of the primary means of marketing Neurontin for pain was physician detailing by the sales representatives. One former sales representative indicated that the sales representatives were instructed in September or October of 1995 to begin recruiting doctors to use Neurontin for pain. The representatives were given targets for an increase in Neurontin prescriptions in their territory and were placed on a three month work improvement plan if they failed. If they continued to fail, probation and, ultimately, termination would follow. This management of the sales force was in fact successful in causing the sales force to promote Neurontin for unapproved uses. For example, in July 1996, a sales representative conveyed to one doctor in Louisiana he should use Neurontin for pain. Similarly, in March 1997, another sales representative visited another doctor in Louisiana and told the doctor that in addition to seizure use, the "force is with pain use" for Neurontin. In August 1998, another sales representative visited a doctor in New Jersey and told that doctor that there was "research and FDA approval for chronic pain" [use of Neurontin]. This was a false statement, as no approval for use of Neurontin in treating chronic pain existed. This doctor practiced anesthesiology and pain management and thus had no use for Neurontin on-label. Pain specialists, who had no reason to prescribe Neurontin for an approved use, were one of the groups targeted in the company's marketing.

The marketing went on notwithstanding the fact that there was little evidence at that time, other than anecdotal reports, to support the use of Neurontin for pain or what a safe and effective dosing regimen would be for this use. Nor had any studies been conducted of possible interactions between Neurontin and other drugs prescribed for pain. In a March, 1996 letter from a doctor employed by Parke-Davis to a practitioner in North Carolina, the Company admitted to a lack of data in support of treating pain with Neurontin:

> We are aware that Neurontin is sometimes prescribed for conditions unrelated to its labeled indications, and that it has been used in the treatment of neuropathic pain. However, Parke-Davis has not investigated the use of Neurontin for this purpose, and I am not aware of any clinically controlled data describing the efficacy of Neurontin for this treatment parameter.

It was not until mid-1997 that two double-blinded, well-controlled studies were completed in any pain area, one on treating post-diabetic neuropathy with Neurontin and the other on post-herpetic neuralgia (shingles) use. Only this latter use has been approved by the FDA, and the approval was sought after the United States' investigation was known to the company and after it had been acquired by its current owner, Pfizer Inc.

2. Psychiatric use: Parke-Davis also promoted Neurontin for a variety of psychiatric conditions, including bipolar disorder, anxiety, social phobia and general mood stabilization, among others, commencing, the Government believes, as early as October 1994, when additional indications for Neurontin in psychiatry were discussed by Parke Davis managers as part of a "development strategy."

While that psychiatric market was evaluated by the company in 1994 and 1995, the marketing effort for psychiatric uses did not gain significant momentum until 1996 and 1997. For example, in 1997, Parke-Davis sent out a large direct mailing, budgeted at $120,000, to psychiatrists to encourage their participation in a medical education program it was sponsoring. In addition, sales representatives actively recruited psychiatrists for the program, which was intended to cover, and did cover, off-label use of Neurontin.

One of the psychiatric uses for which Neurontin was promoted by Parke-Davis, bipolar disorder, was particularly troubling because the Company had very weak evidence of Neurontin's efficacy in treating this condition. Indeed, in one study sponsored by Parke-Davis,

the placebo was as effective or more effective than was Neurontin.

3. Monotherapy: The use of Neurontin by itself to control epileptic seizures, rather than in combination with another drug, is called monotherapy. Since Neurontin was approved only as adjunctive epilepsy treatment, monotherapy is an off-label use of the drug. Parke-Davis put a lot of effort into obtaining FDA approval for a monotherapy indication; this was a major goal from the beginning. Not only would a monotherapy indication have allowed expansion of Neurontin sales by encouraging doctors to prescribe Neurontin on a first-line basis for seizures, it would also have modified the perception of the drug so it was seen as more powerful and reliable, according to the company's market research.

Parke-Davis pursued the monotherapy approval over the course of four years, first through studies and then with a formal application to the FDA. While the company built up to a major marketing effort keyed to the anticipated FDA approval, actual marketing by some sales employees commenced prior to FDA approval. The company was aware of, and encouraged, this improper, premature physician detailing. Monotherapy was, for example, discussed at dinner meetings by Medical Liaisons and physician speakers, and in various other symposia sponsored and shaped by Parke-Davis long before Parke-Davis thought it might obtain regulatory approval.

Dr. David Franklin, the Relator in the civil qui tam suit which is being resolved as part of the proposed global resolution, was a medical liaison for Parke-Davis. He was instructed to push physicians into prescribing Neurontin as monotherapy for the treatment of epilepsy. One of the misleading methods he was given was to present himself as a neurology specialist who was conducting research into the control of epilepsy and the mode of action of anti-epileptic drugs.

This was untrue. Franklin holds a doctorate in biochemistry and had no medical specialization or clinical experience. Franklin also told physicians exaggerated claims regarding a large body of data to support the use of Neurontin as monotherapy. Dr. Franklin understood that Warner-Lambert, through his supervisor in the NECBU, was aware of and encouraged these and other off-label promotional claims that Dr. Franklin made to doctors.

Parke-Davis sought supplemental approval from the FDA for a monotherapy indication on September 16, 1996. However, one of two clinical trials conducted by Parke-Davis showed no demonstrable monotherapy efficacy. On August 26, 1997, the FDA rejected Parke-Davis' application for monotherapy.[4] Nonetheless, Parke-Davis actively promoted Neurontin for monotherapy before it applied for FDA approval, before it received the FDA's response, and, most amazingly, after the FDA had rejected its application for monotherapy. In meetings held immediately after the FDA's rejection in the fall of 1997, and continuing right through at least 2000, the slides, lecture summaries and audiotapes obtained by the Government during the investigation demonstrate that Parke-Davis continued to promote Neurontin for monotherapy by saying that it was effective for it, without ever mentioning the material fact that the FDA had rejected its application for monotherapy based on its finding that the clinical trials performed did not establish effectiveness.[5]

Documented examples of statements made by Parke-Davis about monotherapy after FDA

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[4] As part of its monotherapy application, Parke-Davis sought approval for higher doses of Neurontin. This was denied as well.

[5] The company attempted to obscure its promotion of Neurontin for monotherapy after the FDA's non-approval by removing the word "monotherapy" from titles of talks and official company-approved slides and agendas, but the subject of the meetings was the same.

non-approval include: (1) in a 1998 event, Parke-Davis falsely stated that Neurontin "is effective as monotherapy;" (2) in June 1998, a Parke-Davis sales representative stated that Neurontin was "moving toward monotherapy indication in seizures;" and (3) in a Parke-Davis marketing event later in 1998, Parke-Davis went so far as to state that Neurontin was "now approved as monotherapy for seizures." These are selected from numerous such examples.

4. Dosage: When a new drug is approved by the FDA, the agency approval is typically for a particular starting and maximum dose. The labeling will refer to an effective dose, or dose range, and may also separately refer to the tolerability of a range of doses. In the case of Neurontin, the label was approved with an effective dose range of 900 to 1800 mg. per day, with doses tolerated as high as 2400 mg./day long-term and 3600 mg./day short-term.

All claims by Parke-Davis as to the *effectiveness* of Neurontin at doses above 1800 mg./day were off-label and constituted misbranding under the FD&C Act. The evidence shows that Parke-Davis made such claims as part of a concerted effort to get doctors to increase the level of Neurontin prescribed, even as the company unsuccessfully sought approval for a higher dose. This was done to combat the perception that Neurontin was ineffective at existing doses. A March 24, 1995 document summarizing a committee meeting shows concern that the approved dosing was too low and suggested that higher dosing be pursued along with monotherapy approval:

> It was agreed that the currently recommended dose range for efficacy of 900-1800mg seems too low with the result that some physicians are perceiving the drug as a weak one and abandoning it. It was confirmed that ample safety data exists for us to be comfortable with the use of the drug at 3600mg/day. Experts have recognized this and are quickly going to higher doses in many of their [patients] but the average dose for all neurologists remains low at about 1140 mg/day. Current open label studies in refractory

> [patients] are going to 2400 or 3600 (STEPS) but will not result in a labeling change. The group agreed that no new pivotal studies should be initiated in refractory [patients] to extend the dosage range, but rather we should rely on data from the monotherapy pivotal studies.

Parke-Davis lacked solid data upon which to seek approval from the FDA of a higher dose. For example, the February 21, 1995 Neurontin Development Team minutes indicated that there was insufficient data to justify a planned application for a dose increase to 3600 mg. In May of 1995, it was admitted by the Neurontin Development Team that there was no data indicating whether higher blood levels of Neurontin were more effective. A little over one year later, a September 2, 1996 Core Marketing Team meeting slide stated that approval of "2400 mg [was] unlikely," in connection with the monotherapy and dosage labeling application status. These doubts were not shared with the medical community to whom Parke-Davis was marketing higher doses of Neurontin, however. Former employees stated that they were told that Neurontin doses above 3600 mg./day were just excreted in the urine without any additional therapeutic benefit to the patient; nonetheless, dosing to 4800 mg/day represented a significant sales increase and therefore the liaisons were told not to reveal this information.

G. Six Tactics Were Used to Implement the Illegal Scheme

Among the key tactics Parke-Davis set out in its planning documents and which it used to achieve its goal of increasing off-label use of Neurontin were the following:

(1) Encouraging sales representatives to provide one-on-one sales pitches ("details") to physicians about off-label uses of Neurontin;

(2) Utilizing medical liaisons, who represented themselves, often falsely, as neutral scientific experts in the area of a particular drug, to promote off-label uses for Neurontin, working in tandem with the sales representatives to directly sell Neurontin to physicians for off-label uses;

(3) Paying physicians to allow a sales representative to see patients with the doctor and to participate in discussing the treatment plan;

(4) Paying physicians, through both direct payments, and the provision of trips, hotel rooms, dinners and other benefits, to attend a variety of meetings termed "consultant" or "advisory" meetings or "speaker bureau trainings" in which doctors received presentations about off-label uses of Neurontin;

(5) Implementing frequent teleconferences in which doctors were paid by Parke-Davis to speak about Neurontin on off-label topics to other doctors; and

(6) Sponsoring ostensibly independent "medical education" events on off-label Neurontin uses where there was actually extensive input from Parke-Davis regarding topics, speakers, content, and participants.

1. Detailing by sales representatives: Parke-Davis management and sales representatives knew that the sales representatives were not supposed to actively promote off-label uses with the doctors to whom they were selling Neurontin. Nonetheless, Parke-Davis sales representatives were instructed to initiate the topic of off-label uses with doctors in their sales calls. One technique was called "probing," which involved questions of a general nature designed to elicit a physician inquiry. An example might be, "Doctor, are you aware that over half the patients on Neurontin do not have epilepsy?" Virtually any response to such a question would provide a lead-in for the representative to discuss off-label uses from the company's perspective. Management was aware of, and encouraged, off-label promotion. For example, the Business Director for the Northeast CBU stated that both the sales representatives and the medical liaisons were used as marketing tools without any restriction as to whether the targeted doctor had first inquired about the off-label uses discussed.

Reports from one independent data vendor show that in 30-50% of sales representative details with doctors, the primary message was one or more off-label uses of Neurontin. The prevalence of off-label messages in the sales calls was noted in a memorandum circulated by the

Associate Product Director for Neurontin for the entire country, on October 24, 1995, to the Vice President of Marketing and other supervisors. However, there is no evidence that management did anything to stop the off-label promotion. Indeed, the percentage of physician details that involved an off-label use of Neurontin remained high until at least 2000. Despite corporate awareness of the frequent promotion of Neurontin for unapproved uses, there is no evidence that at any time prior to the Government's investigation any employee was disciplined for off-label promotion. Nor were any memoranda sent out to the field personnel to curtail the illegal promotion.

2. Use of Medical Liaisons to Market Off-Label: A related development was the institution of the medical liaisons in late 1995. Parke-Davis took the position that medical liaisons could address off-label issues with medical professionals, so long as the professional asked about the subject first, but that sales representatives could not. In actuality, medical liaisons did not simply respond to medical professionals' inquiries, but initiated off-label promotions by raising off-label subjects. On occasion, medical liaisons and sales representatives "cold-called" doctors together without a prior appointment or any inquiry regarding off-label uses by the doctor. Mostly, the medical liaisons pitched off-label uses with a prior appointment or at a luncheon or dinner event set up with multiple doctors. Because the medical liaisons were understood by the medical community as persons with a scientific background and who were not employed to sell the company's drugs, they were often able to gain access to doctors that the sales representatives could not. The medical liaisons were seen by Parke-Davis as a very useful sales tool, particularly in the off-label area. For example, a January 31, 1996 SECBU memorandum states as one of its annual goals: "utilize the medical liaison group to target the

Neurontin, Pain & Psychiatric market. Objective to conduct twice weekly Pain Teleconferences moderated by key Neuro Consultants. Goals 250 Physician participants quarterly."

The best way to work together and to maximize the number of new prescriptions resulting from the medical liaison physician calls was discussed in a conference call, and in a follow-up audio-message from the NECBU business director:

> To entire Northeast CBU: introducing a message from [X] [a medical liaison] on how we can better coordinate our liaison calls and keep them quote legal, as well as [X] gives us some nice specific language that we can use on our calls. Keep in mind that the number one priority for the liaisons right now is Neurontin with the decile 8 to 10 neurologists. We've got to focus on their questions that they've given to us on monotherapy, primarily pain and bipolar depression, that sort of thing and other psychiatric uses. That's the number one priority. We have to keep that in mind as we schedule them. ... And there's just a heck of a lot more profit potential right now with the liaisons in Neurontin than there is with Accupril, that's why we're doing it. And considering how we can [expand] the market with monotherapy, pain and bipolar, it makes sense to do so.

The liaison, answering a question as to what makes a call on a physician with a medical liaison successful, says on the broadcast message:

> **I think really the first point to remember is that this is a team effort between the rep and the liaison.** The rep's role is just so crucial in this situation for success as far as setting the stage for the liaison visits with the doctor, **closing the sale** and completion of the call. And really, then, following up with the doctor on the next call.
>
> * * *
>
> Setting the stage for the liaison is really done after the physician asks the question about off-label uses of our product **or after the representative steers the doctor towards needing more information on, for example, Neurontin in treatment of pain....** We can really use this and build the doctor's ego by letting him know that they're important to them and their business, and they say then that they would like to personally bring a researcher in

> from medical affairs to give them the latest information on, for example, Neurontin use in pain.... Once the call's complete, it's then extremely important for the rep to generally summarize what data was presented and to use this to **close the doctor and ask for the business**, 'cause this is something we can't do. But it's for them to close the doctor right then. ... If the physician requested any information from medical affairs, or even if they haven't, for the rep to be back in there within a week or two, to really close the doctor again, go over any other information sent from medical affairs, and so forth.

(emphasis supplied)

From the broadcast messages sent out to the medical liaisons and the area business managers, as well as from witness testimony and documents, there is substantial evidence that Parke Davis' management was aware that the sales conduct was unlawful. Were this case to be tried, the Government believes it could prove that management viewed the medical liaisons, first and foremost, as a highly useful marketing tool. Education and scientific discourse were way down the list of priorities; profit was at the top. Not only were the medical liaisons used to reach doctors who were difficult for the sales representatives to see, they were part of a team that was going to steer the doctor towards off-label uses, if need be, and close the sale.

One example that demonstrates the use of medical liaisons to promote off-label marketing concerns a medical society meeting in June of 1996, in Pennsylvania. The event was organized by a sales representative with a medical liaison as speaker. It was described in a voice mail sent to Northeast medical liaisons and the Business Director of the NECBU as "another great example of use of the medical liaisons:"

> This sounds like one heck of a program, and I tell you, these medical liaisons definitely move some products. So, it's in our best interest to use them wherever we can, whenever we can, because they definitely do a heck of a job of selling... Neurontin or whatever it is they're talking about.

There is no doubt from the voice mails and testimony that the medical liaison spoke off-label at this meeting:

> [The medical liaison] was nice enough to come down on a Saturday and speak to the group. Needless to say, [his] presentation was outstanding. ... and delivered a real strong message about Neurontin. And he dealt, of course, in the beginning with Neurontin's use in seizures, and then he delved into some of the usage of Neurontin that's been going on in terms of pain management, tremors, migraines, et cetera. And the reason I think this was so successful was that, you know, this group of Filipino physicians is actually a mixed breed in terms of specialties. There are GP's, internal medicine specialists, there's some anesthesiologists, some rehab folks. Also some psychiatrists, as well. So, a real mixed bag, and that's where we, you know, from talking among ourselves, decided that Neurontin would be the best way to go. So a tremendous amount of interest was sparked. ... I definitely think we will see increased business as a result of this program. ... So, just a tip of the hat to [the medical liaison]. He did an excellent job. You know, he — the target was there and [he] hit a bull's eye....

Since the description of the off-label discussion was forwarded to all the medical liaisons as well as to the CBU Business Manager, with only praise for the excellent job done, the Government believes that knowledge of the use of the medical liaisons to promote off-label was both widespread and well-accepted within the company. Other evidence developed during the investigation establishes that this event was by no means unique and was a part of a strategy to encourage the use of medical liaisons in settings like these to promote off-label uses of Neurontin.[6]

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[6] Parke-Davis also helped to develop slide kits used at various programs by both medical liaisons and paid physician speakers to make off-label presentations. The Medical Liaisons were given copies of slides so that they could also use them in marketing one-on-one to doctors. Copies of the slides were given to doctors on occasion as well. Many of these slide kits addressed off-label uses and were shared with doctors who spoke on Parke-Davis' behalf.

3. Preceptorships: Another method of promoting face-to-face was the preceptorship, or "shadowing." This involved paying a doctor a fee to allow the sales representative to follow the doctor through the course of a day or half-day, seeing patients with the doctor. In one example, a sales representative did a preceptorship with a New York neurologist that he frequently called on. During the preceptorship, after they saw the patient together, the doctor and the sales representative discussed treatment options. The sales representative encouraged the doctor to increase the Neurontin dose being given to a young teenager and, at the same time, taper the patient off other epilepsy medication to reduce side effects, thus resulting in Neurontin being used for monotherapy, an off-label use. According to the sales representative, as recorded in a voice mail sent out to the NECBU, "I really felt I made a difference. I saw the actual prescription generated in front of me... and I certainly felt that me being there, I had some influence on that medical decision."

Another patient seen in this preceptorship was a 65 year old veteran who suffered neuralgia, or pain, in his limbs. The patient developed blurred vision while on Neurontin for his pain; the Parke-Davis sales representative told the doctor that such side effects are mild and transient. As a consequence, the doctor kept the patient on Neurontin. Again, in the sales representative's own words: "I felt like I influenced that particular situation. So again, another prescription was generated for us. Overall, the day went, you know, very well. And we had the immediate impact of two prescriptions written." This sale representative's voice mail message describing the preceptorship was forwarded by the Business Director for the NECBU to the entire Northeast CBU with the approving and exhorting message: "check this one out. It's on shadowing. You'll learn what you need to learn and you'll drive the business." Clearly, both

Parke-Davis management and the sales representatives saw preceptorships as a means of getting doctors to write more off-label prescriptions for Parke-Davis' drugs.

4. Consultant meetings, speakers bureaus and advisory boards:

a. *Physician meetings generally:* Parke-Davis held hundreds of meetings relating to Neurontin in which the physician attendees were given a promotional message. The doctors were paid to attend, paid even more to speak, and given a variety of other benefits such as airfare, fully-paid trips to expensive resorts in such places as Florida, California and Hawaii, as well as expensive tickets to sporting or cultural events, and yacht cruises. At the core of the conduct was an attempt to gain the doctors' attention, advocacy and prescribing, all in furtherance of Neurontin off-label sales. Parke-Davis was especially interested in cultivating two types of physicians. One type was known as high-decile prescribers, or, occasionally, "whales," i.e., doctors who prescribed large amounts of anti-convulsants drugs, of which Neurontin was one. The second type was doctors who had a prominent reputation. These people were often referred to as the "movers and shakers" or "thought leaders" because of their influence, and were developed as spokespersons on behalf of Neurontin.

Parke-Davis paid substantial sums to its key "thought leaders," the doctors who could be counted on to deliver a strongly favorable message on Neurontin off-label use. At least twenty of these doctors received over $50,000 (in total) for speaking on the company's behalf. Some received in excess of $250,000. The most common forums for the use of the thought leaders were consultant and advisory board meetings, where doctors were gathered to listen to a presentation by the influential doctor. Such meetings were a central tactic for the company in its off-label campaign. Parke-Davis justified holding these meetings, even though the content was

off-label, because it entered into pro forma consultant agreements with the physician attendees. Ostensibly, physicians were paid anywhere from $250-$2,500 to serve as consultants or advisers, providing expertise to the company. The consultant meetings often involved a larger number of physician attendees, whereas the advisory boards tended to be smaller and involve a higher percentage of leading specialists. The two terms were not always used in this manner and many employees confused them.

While some physician meetings had legitimate purposes, the investigation showed that Parke Davis held hundreds of meetings where the intent of the company was to promote off-label uses. In one six-month period alone, Parke-Davis held over fifty such meetings; the frequency and close proximity (both geographic and temporal) of the meetings demonstrates that the true purpose of the meetings was not to gather information from the attendees. Despite their being called "consultant" meetings, the actual objective was to provide off-label information to the attendees rather than for the company to receive information from the consultants. In fact, the number of written reports on the outcome of these consultant meetings was remarkably low in relation to the number of meetings held. It appears that management rarely received any consultant meeting reports and paid them little, if any, attention.

A discussion in detail of several meetings illustrates the manner and means used to promote Neurontin off-label:

b. *Atlanta Olympics:* One purported advisory board was linked to a Parke-Davis extravaganza in connection with the 1996 summer Olympics in Atlanta, Georgia. Parke-Davis was an Olympic sponsor with a limited number of tickets to give away to its most favored "customers," i.e., the doctors who had been strong supporters of the company's products.

Along with free Olympics tickets (and tickets to the Closing Ceremonies, valued at $650 each), Parke-Davis staged an Epilepsy Advisory Meeting, at the Chateau Elan Winery and Resort, in Atlanta, Georgia from August 1-5, 1996.[7] Parke-Davis paid all the expenses for eighteen "advisers" and their spouses to attend the Olympics and, to give it a gloss of propriety, held a minimal number of business meetings, including some on explicitly off-label topics. In addition to payment of all expenses, each adviser also received $750. By this conduct, Parke Davis was unlawfully rewarding its strongest advocates, or thought leaders, for their past promotion of Neurontin as well as encouraging their future support. There is very little evidence to suggest that Parke Davis obtained any advice in connection with this event from these attendees, many of whom had been faculty at other advisory board meetings in 1996, any advice. Parke-Davis, in planning the Olympics advisory board meeting, referred to the cost as a "$3 million investment." Parke Davis did not receive from this event medical advice worth three million dollars.

c. Jupiter Beach Resort and Aspen Consultants Meetings - April 1996:

Parke-Davis staged two "consultants" meetings on the same weekend in April, 1996, one at the Jupiter Beach Resort in Palm Beach, Florida, and the other at the Ritz-Carlton in Aspen, Colorado. Both were three day, two night affairs, with $250 payments to the attendees, plus

[7] The brochure for the event describes the facility thus: "[s]ince opening in 1981, Chateau Elan has made a name for itself as a fine winery. It is now earning a reputation as a one-of-a-kind resort... the Inn at Chateau Elan. Here, you'll enjoy all the comforts and amenities you'd expect of a fine resort, mellowed by the warm ambiance of a French country inn. During your meeting breaks, you will have the opportunity to play a round at one of three accessible golf courses, swim, play tennis, explore the Georgia hill country by foot or by horseback, or escape to Chateau's European style spa for a pampering body treatment...."

airfare, and all expenses at the resort for the weekend (including, at Jupiter Beach, a yacht cruise). Doctors who acted as faculty were paid between $1,500 and $2,000. The total cost for Jupiter Beach was approximately $361,000. There were approximately 100 doctor attendees. Thus, the cost per doctor was approximately $3,000. The Aspen costs were similar.

Both the Jupiter Beach and Aspen meetings included explicitly off-label topics in the presentations to the consultants (such as "Neurontin (gabapentin): Use as Monotherapy" and "Reduction of Pain Symptoms During Treatment with Gabapentin") and were designed primarily to present information to the attendees, rather than to receive information from them. The company also circulated internal agendas listing the off-label topics for speeches at these events while using a more generic agenda at the actual meeting, even though the talks were not changed. For example, the Aspen internal agenda listed talks on "Other uses of Neurontin" and "Clinical and Scientific Reports on other Uses for Neurontin: Migraine." These titles were not listed in the official program distributed at the event. One of the speeches was by a physician specializing in pain, who was known to regularly speak about the use of Neurontin in treating pain. His speech was listed as "Anticonvulsant Advances" in the brochure, but introduced and recorded at the meeting as "Reduction of Pain Symptoms During Treatment with Gabapentin." In this manner, Parke-Davis concealed the off-label purpose of the meeting from the attendees in advance and from those not attending the meeting. Another speech at this conference was recorded as being entitled "Anticonvulsant Advances: Nonepileptic Uses of Anti- Epileptic Drugs." It explicitly included off-label claims for Neurontin such as: "Gabapentin has been reported to be effective for essential tremor and episodic dyscontrol, to be analgesic for a variety of pain disorders . . . ."

Moreover, in the planning documents for the Jupiter Beach meeting, the Parke-Davis planners, including the Northeast CBU Neurontin Project Manager, explicitly targeted high decile doctors to be attendees. According to the Project Manager, "[t]he meeting was a great success and the participants were delivered a hard-hitting message about Neurontin."

On or about May 8, 1996, after the Jupiter Beach conference was over, the NECBU Neurontin Project Manager circulated copies of the actual agenda (with off-label topics listed), faculty list, attendee list and presentation abstracts (which confirmed the off-label content) to her supervisors and the field sales representatives for the Northeast CBU, along with a "Jupiter Beach Trending Worksheet." The Project Manager stated that "the attendees from your district are listed. This tool is very valuable in tracking the value of participating in this program," i.e., whether the attendees prescribed more Neurontin after the conference than they did before.

d. *Advisory Board in Maui, Hawaii, April 2000:* Another example of the many lavish meetings for off-label promotion held by Parke-Davis is the Western Advisory Board Meeting at the Grand Wailea Resort, Hotel & Spa in Maui, Hawaii in April 2000. Only one of the attendees resided in Hawaii. Parke-Davis paid for all of the others to fly to Hawaii and for a two night stay at the highly luxurious resort for only three hours of business meetings -- on off-label uses of Neurontin. In planning this meeting, Parke-Davis targeted anesthesiologists, and deliberately did not invite epileptologists – thus targeting those doctors whose potential uses for Neurontin were only off-label. Like many such events arranged by the Company, evidence shows this event was promotional, not an independent, scientific meeting.

e. *Speakers bureau meetings:* The "movers and shakers" doctors were offered as much as $2,500 per event to speak on Neurontin. To encourage their cooperation, and to shape

the content of their subsequent talks, Parke-Davis held regular Speakers Bureau training events. According to the vendor for speakers bureau meetings, Physician's World, there were 6,961 speakers bureau meetings relating to Neurontin in the years 1996-2000, broken down as follows:

Year:	1996	1997	1998	1999	2000
# of Meetings:	1,846	1,256	1,521	1,256	1,082

While not all of these meetings focused on off-label topics, the evidence suggests that at almost all of them there was some discussion of unapproved uses. At many of the meetings, which Parke-Davis itself called promotional events, Parke-Davis paid doctors to make, or had its own employees make, off-label presentations.

For example, in one training session held in January, 1996 at the Ritz-Carlton in Palm Beach, Florida, Parke-Davis requested that a doctor give an entire talk on the off-label uses of Neurontin. Monotherapy was also the topic of at least two presentations at that meeting, including one by a Parke-Davis employee. Parke-Davis knew before the meeting that this event would include off-label promotional speeches. In a facsimile from the doctor to a Parke-Davis employee on December 12, 1995, the doctor wrote "I will be calling you for help in preparing my talk for the P-D speaker's bureau meeting in Palm Beach January 5 on off-label uses of gabapentin." Afterwards, the Neurontin Project Manager for the NECBU drafted a summary of the event in a memorandum dated January 9, 1996, noting that monotherapy was discussed and that the doctor "gave a very comprehensive talk on other uses of Neurontin (pain, etc.) ...even though there is not much supportive data". This event tied into the 1996 supplemental budget in which speaker training programs were a significant portion of the promotional budget.

While this is just one example, the evidence collected during the investigation demonstrates that the programs for many of the meetings were virtually identical in the promotion of Neurontin for off-label use. Parke-Davis planned these meetings, including the agenda and speakers, its employees attended the meetings, and it paid for the meetings out of its advertising and promotion budget, all with the intent and expectation that the meetings would promote off-label usage of Neurontin.

5. Series of teleconferences were held to disseminate off-label uses: Parke-Davis held hundreds of teleconferences relating to Neurontin. Immediately after the launch of Neurontin, the teleconferences were on-label. By 1995, the focus shifted increasingly, the Government would prove, to off-label topics.

Parke-Davis used the teleconferences to spread the word on the potential new uses for Neurontin. Doctors were recruited by the sales representatives to call into a special number where the doctors would listen to an introduction by a Parke-Davis employee and then a twenty minute lecture from a physician recruited by the company to speak during the call. The speaker's remarks were frequently scripted by the Company. The participants then had a chance to ask the speaker or the Parke-Davis moderator questions or offer their own experiences and opinions. The speaker was paid a fee; for at least some of the teleconferences, the participants also received some type of fee. For some of the teleconferences, there was no outside speaker; instead, only a Parke-Davis medical liaison or a medical director spoke.

It is the Government's position that the frequency of the teleconferences, their sheer number, the repetition of the content and the organizing documentation and invitations demonstrate that the Company was actively recruiting doctors to prescribe Neurontin for off-

label indications, rather than merely responding to existing interest.

6. Control of Purportedly Independent Medical Education

Parke-Davis also used its control over continuing medical educational programs that were ostensibly, but not in fact, independent, as part of its strategy to promote off-label uses of Neurontin. Use of medical education programs for this purpose was a separately labeled and funded tactic in its annual marketing plans. For example, a March, 1996 SCCBU Situation Analysis says: "A premise used in developing the 1996 SCCBU Operating Plan is that Neurontin is more responsive to certain types of promotional media. The most effective promotional media utilized in 1995 were Medical Education programs." (i.e., consultants meetings, regional CME and local speaker events). Similarly, a draft NCCBU Situational Analysis states:

> The medical education strategy has been and will continue to be the main tool used to promote Neurontin.... 134 speaking events were held in the 1st quarter... The most significant adjustment made to the implementation of the 1996 plan has been the increased emphasis placed on the Life Cycle Management strategy or the non-epilepsy uses of Neurontin. Physicians have a very high level of interest in the use of Neurontin for pain and the Medical Liaisons along with the CME programs are being used to address these areas that are off limits to TM promotion.

The evidence demonstrates that Parke-Davis influenced the content of purportedly independent medical education, while the programs explicitly disclaimed any such influence, and concealed and made false statements about the payments that it had made to doctors who acted as speakers and faculty for such education. For example, Parke-Davis entered into an undisclosed partnership with a company known as Physicians World. The agreement called for the two parties to participate in a "Partnering Program," in which Physicians World offered a reduction in fees in return for a commitment from Parke-Davis for a minimum level of projects

and Physicians World's access to Parke-Davis's office space and networks. As part of the arrangement, Parke-Davis employees were transferred to Physicians World to run Parke-Davis' speakers' bureau.

A division of Physician's World, known as Professional Post-Graduate Services, held itself out as an independent medical education provider without revealing Parke-Davis's influence, and created a major program entitled "Use of Antiepileptic Drugs in the Treatment of Chronic Pain Syndromes" at the Company's request. In fact, the program was designed to promote Neurontin for pain, and Parke-Davis' staff planned, and participated in, each stage of its development including curriculum planning meetings, creation of "home study groups" and dinner meetings carrying out the program, and the recruitment of doctors to participate and to be speakers for each segment of the program.

This program was provided to thousands of doctors around the country. In each instance, the materials distributed to the participants falsely stated that they were created in compliance with ACCME guidelines, which prohibited such content control by Parke-Davis as a condition of program accreditation, and required disclosure of all financial affiliations. The materials did not, however, disclose the relationship between Physicians World and Parke-Davis, nor did they disclose the known financial and other affiliations between Parke-Davis and each of the faculty members, all of whom were paid consultants to Parke-Davis -- and several of whom had received many thousands of dollars in speaker payments and /or grants from Parke-Davis. One physician in particular was a regular Neurontin speaker who had received payments from Parke-Davis of more than $10,000. To the contrary, by the listing of each of these faculty, there was an asterisk indicating "no significant financial or other affiliation reported" – even while

affiliations with other drug companies were listed and despite the knowledge of the financial relationships by both Physicians World and Parke-Davis. This evidence demonstrates that Parke-Davis knew that these events were unlawful promotional activities.

Similarly, in 1996, Parke-Davis sponsored a mailing to 10,000 neurologists in the United States. The mailing was ostensibly prepared by the Medical Education Network with a grant from Parke-Davis. However, the only drugs mentioned in the mailing (called a "Medi-Fax Express Report") were Neurontin and Cerebyx, another Parke-Davis product.[8] In the Medi-Fax mailing, all of the Neurontin topics concerned off-label uses of the drug and several discussion were misleading as well.

IV. DETERMINING THE APPROPRIATE SENTENCE

A. Overview

There are five principal areas of harm that resulted from Parke-Davis' illegal off-label promotion, or which were made more likely by that conduct. The first harm is to health care reimbursement programs such as Medicaid which paid more in prescription reimbursement as a result of the unlawful marketing. The second and third types of harm are to consumers, who may have paid money for ineffective, experimental use of Neurontin and who may have been improperly medicated. Improper medication could have resulted from prescribing Neurontin for an unapproved use for which it was not effective or not as effective as another medication which was approved for that use. A fourth harm is the unnecessary exposure of patients to adverse side

[8] This mailing is referenced in a December 12, 1995 memorandum to a senior executive from the Portfolio Manager in headquarters.

effects of Neurontin.[9] The Government notes that in a May 18, 2004 letter to the Court, an attorney, who stated that he represents thousands of former Neurontin users, objected to the proposed criminal resolution on, apparently, the ground that it does not go far enough. The United States believes that evaluation of thousands of claims by individual Neurontin users, each of whose experience is unique, would unduly complicate and prolong sentencing. See U.S.S.G. § 5E1.1(b)(2). Moreover, the proposed global settlement does not foreclose the rights of non-governmental victims to seek redress.[10]

A fifth form of harm is to the regulatory scheme itself; by foregoing FDA approval while nonetheless marketing Neurontin for off-label uses, Parke-Davis circumvented the safeguards inherent in the drug approval regulatory scheme and undermined the fairness, reliability and integrity of that program.

Both Title 18 and the sentencing guidelines look to the financial loss or gain caused by illegal conduct as a principal, but not a sole, basis for determining the appropriate punishment for a corporation. The cumulative financial (and non-financial) impact of the illegal promotion of Neurontin by Parke-Davis is very difficult to calculate with precision. The Company engaged in both on-label and off-label promotion of Neurontin. There is no direct way to measure exactly the fiscal impact of the off-label promotion.

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[9] One doctor told the Government that he believed much use of Neurontin was for the placebo effect, i.e., a patient gets some positive results because he or she believes the medication will work, even if it does not. But Neurontin is an expensive placebo, and it has more significant potential side effects than a sugar pill.

[10] The Government notes that the proposed resolution does include a significant state consumer protection component, which has not routinely been part of prior health care fraud settlements arising out of federal Department of Justice investigations.

B. Violations of the Food, Drug & Cosmetic Act

The maximum fine provided by statute for a violation of the Food, Drug & Cosmetic Act, 21 U.S.C. §§ 331(a) and 333(a)(2) (introducing and delivering for introduction into interstate commerce a misbranded drug) by an organization is the greatest of: (1) the amount specified in the law setting forth the offense (in this case, $10,000, pursuant to 21 U.S.C. § 333(a)(2)); (2) $500,000; (3) twice the gross pecuniary gain derived by the organization from the offense; or (4) twice the pecuniary loss suffered by another person because of the offense. See 18 U.S.C. §§ 3571(c) and (d). In addition, or in the alternative, an organization may also be sentenced to a term of organizational probation of up to five years. See 18 U.S.C. §§ 3561(a) and (c). The court may also order restitution. See 18 U.S.C. § 3663.

Clearly, twice the gross pecuniary gain is the largest of the statutory alternatives in this case. Because this calculation is common to either a statutory or a guidelines-based calculation, the method of calculating pecuniary gains is set out below within the guidelines discussion.

C. Calculation of the Appropriate Fine under the Guidelines

1. Determining the applicable guidelines: Warner-Lambert has agreed to plead guilty to two violations of 21 U.S.C. § 331, which are felonies by virtue of its prior FD&C Act conviction. See 21 U.S.C. § 333(a)(2). Therefore, U.S.S.G. Chapter 8 applies.

Although Chapter 8 applies generally, the fine guidelines in Chapter 8, U.S.S.G. §§ 8C2.2 through 8C2.9, apply only to specified types of offenses. See U.S.S.G. §§ 8A1.1, app. n. 2; 8C2.1. To determine whether the fine guidelines apply to these FD&C Act violations, the court must look at U.S.S.G. § 8C2.1 (Applicability of Fine Guidelines). This section states that the fine guidelines apply to "each count for which the applicable guideline offense level is

determined under" one of those listed in subsections (a) and (b).

The applicable guideline offense level for Warner-Lambert's violation of 21 U.S.C. §333(a)(2) (which is based upon a prior FD & C Act violation and not an intent to defraud or mislead) is determined under U.S.S.G. § 2N2.1. See U.S.S.G. Appendix A. Section 2N2.1 is not listed under § 8C2.1(a) or (b). Accordingly, the fine guidelines of Chapter 8 do not directly apply to these FD&C Act violations.

In the absence of an applicable fine guideline, U.S.S.G. § 8C2.1 instructs the court to apply U.S.S.G. § 8C2.10 (Determining the Fine for Other Counts). Section 8C2.10 states: "For any count or counts not covered under § 8C2.1 ("Applicability of Fine Guidelines"), the court should determine an appropriate fine by applying the provisions of 18 U.S.C. §§ 3553 and 3572."

Determining an appropriate fine for Warner-Lambert's FD&C Act offenses, therefore, requires evaluating the general factors to be considered in imposing a sentence under 18 U.S.C. § 3553(a) and to the factors specific to fines set forth in 18 U.S.C. § 3572, including, "the need to deprive the defendant of illegally obtained gains from the offense."[11] Many of the same considerations before the court in a statutory analysis are considerations under a guidelines analysis. Title 18 U.S.C. § 3553 (a)(4) also references the sentencing guidelines, providing a

[11] 18 U.S.C. § 3572(a)(5). Section 3572 of Title 18 also directs the sentencing court to consider: (1) defendant's resources; (3) any pecuniary loss to others; (5) the need to deprive the defendant of illegally obtained gains from the offense....; and (8) the size of the organization. See, e.g., United States v. Bertoli, 854 F. Supp. 975, 1154 (D.N.J. 1994). Among the factors set out in section 3553 of Title 18 are: (1) the nature and circumstances of the offense and the history and characteristics of the defendant; (2) the need for the sentence imposed (A) to reflect the seriousness of the offense, to promote respect for the law, and to provide just punishment for the offense; and (B) to afford adequate deterrence to criminal conduct. Id.

basis for using the guidelines to calculate the appropriate sentence for a violation which is a second-offense felony. Moreover, where there is no applicable sentencing guideline the court must "have due regard for the relationship of the sentence imposed to sentences prescribed by guidelines applicable to similar offenses and offenders." 18 U.S.C. § 3553(b).

2. Pecuniary Gain Generally: Whether the court operates under the sentencing guidelines or the statutory fine provisions to determine the appropriate fine amount, the court must first estimate the pecuniary gain to the company as a result of its illegal conduct. Under the fine guidelines, in this case, the pecuniary gain would determine the "base fine" amount.[12] The background commentary to U.S.S.G. §8C2.4 offers a useful interpretation of this guideline:

> As a general rule, the base fine measures the seriousness of the offense. The determinants of the base fine are selected so that, in conjunction with the multipliers derived from the culpability score in §8C2.5 (Culpability Score), they will result in guideline fine ranges appropriate to deter organizational criminal conduct and to provide incentives for organizations to maintain internal mechanisms for preventing, detecting, and reporting criminal conduct. In order to deter organizations from seeking to obtain financial reward through criminal conduct, this section provides that, when greatest, pecuniary gain to the organization is used to determine the base fine.

If the Court applies the sentencing guidelines, Guideline 2B1.1 is the analogous guideline for these offenses. The sentencing guidelines expressly take the position that sentencing under § 2B1.1 is based on losses, or gains, which the defendant *intended* to result from its conduct, whether or not such losses or gains did, in fact, result. See U.S.S.G. § 2B1.1 App. Note 3(A) (the "loss is the greater of actual loss or intended loss." Application Note 3(A)(i) states that "actual loss means the reasonably foreseeable pecuniary harm that resulted from the offense."

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[12] See U.S.S.G. §8C2.4; 18 U.S.C. §§ 3571(c),(d); U.S.S.G. § 8A1.2, app. n. 3(h)("pecuniary gain" is derived from 18 U.S.C. § 3571(d) and is defined as "the additional before-tax profit to the defendant resulting from the relevant conduct of the offense.") .

Note 3(A)(ii) defines "intended loss," and includes within the definition those losses which were intended but which were impossible or unlikely to occur. See United States v. Johnson, 16 F.3d 166, 170-71 (7th Cir. 1994); United States v. Johnson, 908 F.2d 396, 398 (8th Cir. 1990). Application Note 3(b) states that gain may be used if there is a loss but it reasonably cannot be determined. Accord United States v. Andersen, 45 F.3d 217 (7th Cir. 1995); United States v. Galbraith, 20 F.3d 1054 (10th Cir. 1994). [13]

Furthermore, the Court is not required to identify each and every fraudulently obtained prescription. Thus, for example, the Court need not specifically identify particular victims when sentencing a defendant convicted of transporting forged bank instruments; so long as there likely are such victims, or that defendant intended them to exist, it is sufficient to show actual or intended loss. See United States v. Resurreccion, 978 F.2d 759 (1st Cir. 1992); United States v. Berndt, 86 F.3d 803 (8th Cir. 1996).

3. Pecuniary Gain to Warner-Lambert: Because the Government's proof of Warner-Lambert's intent to increase its off-label sales is so overwhelming, the Court should have no difficulty in finding that it intended to cause all of the off-label sales.[14] The fact that

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[13] The Government has the burden of establishing only that defendant attempted to inflict the loss. United States v. McCormac, 309 F.3d 623, 627 (9th Cir. 2002)("2001 amendments adopt a broad definition of intended loss. Intended loss includes the "pecuniary harm that was intended to result from the offense, whether or not that pecuniary harm would have been impossible or unlikely to occur"); United States v. Joetzki, 952 F.2d 1090 (9th Cir. 1991); United States v. Holloman, 981 F.2d 690 (3rd Cir. 1992). In this case, there was loss to the federal Medicaid program.

[14] In numerous marketing assessments, Parke-Davis projected revenue from off-label uses pursuant to a non-approval strategy in which it would promote via publication and medical education (e.g., the company's Core Marketing Team noted expected revenue of $100 million from five principle off-label uses).

some portion of those sales might have been caused by other factors for which Warner-Lambert is not, at least directly, responsible, is of no legal consequence given its intent to cause off-label sales. The Court need not engage in analysis of whether Warner-Lambert's intent was to cause less than all off-label sales because it is irrelevant whether the Company's unlawful promotion was more successful than it anticipated. Section 2B1.1, Application Note 3(C) provides that "the court need only make a reasonable estimate of the loss [or gain]."

The Government sets forth below what it believes is a reasonable method of calculating the pecuniary gain to Parke-Davis, looking at (1) when the unlawful promotion began for each unapproved use, when the promotion developed momentum and when it tapered off, and (2) what independent reasons (i.e., not the result of unlawful sales promotional activities by Parke-Davis) could have caused an increase in the prescription of Neurontin for off-label uses. The Government's goal was to craft a reasoned estimate of the proportion of total off-label sales which was caused by the criminal conduct.[15]

The evidence demonstrates that the illegal off-label promotion began to have an impact midway through 1995. The evidence also demonstrates that the conduct diminished somewhat after September of 1997 and thereafter tailed off after the first quarter of 1999. Although it is impossible to determine the precise beginning and ending points, these dates were used in calculating the pecuniary gain. The end point for the impact of the off-label marketing was particularly difficult to establish; however, in light of other independent factors that would have

[15] The Company is liable for all off-label sales it intended to cause through its unlawful marketing, and there is no clearly defined limit to that intent. Nonetheless, it is reasonable to take into account factors which may have increased off-label prescribing of Neurontin which Parke-Davis neither created nor controlled.

resulted in an increase in off-label prescriptions, the end point selected appears reasonable.[16] In this time period, the total number of new Neurontin prescriptions was 5,540,000. The quarter-by-quarter figures are shown in a spreadsheet attached hereto as Exhibit A.

The percentage of Neurontin prescriptions that were for off-label uses was next calculated, using contemporaneous documents from the company, testimony, and third-party commercial sources of sales data that are routinely relied upon by the pharmaceutical industry. The information showed that the percentage of total sales that were off-label ranged from 40% in the third quarter of 1995 to 84% in the first quarter of 1999. See Exhibit A for the quarterly breakdown.

The Government also sought to determine how many of the off-label prescriptions, within the four year time period described above, were attributable to the company's illegal conduct. By examining contemporaneous documents showing how much Neurontin was sold for off-label uses before the scheme began, and by looking at levels of experimentation with other anti-seizure medications, the evidence demonstrates by a preponderance that approximately 26% of Neurontin sales would have been for off-label uses even if there had been no improper promotion. This reflects the degree to which neurologists and pain specialists experimented with anti-epileptic drugs in general, as well as the fact that Neurontin's safety profile made it an

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[16] For example, two major positive studies of Neurontin for use in certain types of pain were published in 1997. In addition, in 1998, one of the drug use compendia (listed in the Medicaid statute, 42 U.S.C. §1396r-8 (g)(1)(B)(i)) included references to off-label uses for Neurontin. It is possible to conclude that these events would have resulted in an increase in off-label prescriptions by physicians wholly independent of any conduct by Parke-Davis. The United States does not concede that, in the facts of this case, any compendia references during the time period investigated constituted adequate support of the referenced uses, beyond the FDA approved use, for purposes of Medicaid reimbursement.

attractive choice for this type of experimentation.[17] Further, because such experimentation may have led to additional experimentation, particularly if the drug showed some promise, as Neurontin did for certain types of pain, the Government calculated a modest growth factor of 4.345% per year for this "credit" of untainted off-label sales. The percentage of total sales that was not attributable to the criminal conduct is set out in Exhibit A as well.

This credit was then deducted from the total off-label sales for each quarter. The Government thereafter multiplied the remaining off-label prescriptions by an average per-prescription profit figure of $80.00 obtained from Parke-Davis but verified from documentation and public records.[18] In sum, the pecuniary gain to Parke-Davis from its off-label promotion of Neurontin can be calculated using the following equation: (Neurontin new prescriptions) x (percentage of off-label Neurontin sales attributable to the Company's illegal conduct) x (per prescription profit) = pecuniary gain. As is shown in Exhibit A, this calculation leads to a pecuniary gain figure of approximately $150,000,000. The parties have agreed that this figure represents the pecuniary gain Warner-Lambert derived from its illegal scheme.

4. Culpability score and multiplier: Once the court determines the base fine (in this case, the pecuniary gain) the next step is to determine the organization's culpability score. See U.S.S.G. § 8C2.5. The culpability score is the sum of numeric points which are assigned for

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[17] If the level of experimentation found for the anti-epileptic class of drugs was influenced by illegal off-label marketing, either by Warner-Lambert or other manufacturers, the appropriate adjustment for this factor would have to be re-considered. Evaluation of such influence would unduly complicate and delay sentencing, however.

[18] A sound argument can be made that the calculation should be based on total revenues, rather than profit; however, in this case it makes relatively little practical difference since the profit margin on Neurontin was so high.

certain organizational behavior, such as the organizational involvement in or tolerance of the criminal activity, U.S.S.G. § 8C2.5(b)(1), the prior history of the organization, U.S.S.G. § 8C2.5(c)(2), and the organization's cooperation and acceptance of responsibility U.S.S.G. § 8C2.5(g)(2), among other things. The result of this tally yields a number from 1 to 10 (the "culpability score") which corresponds to a maximum and minimum multiplier, ranging from 0.05 to 4.0. The guidelines start with **5** points, then add **5** more if the organization had 5,000 or more employees and:

> (i) an individual within high-level personnel of the organization participated in, condoned, or was willfully ignorant of the offense; or
>
> (ii) tolerance of the offense by substantial authority personnel was pervasive throughout the organization.

Warner-Lambert had more than 5,000 employees; in addition, for the reasons stated above regarding the knowledge and approval of the off-label marketing scheme among senior management, the conditions of either subsection (i) or (ii) are met and the additional 5 points apply.

Warner-Lambert is entitled to a **2** point reduction under § 8C2.5(g) for cooperating with the investigation and accepting its responsibility. This leads to a total of **8** points, and a multiplier range of 1.6 to 3.6. However, because the statutory maximum penalty is two times the amount of gain or loss, the effective range is **1.6 to 2.0**. The parties have agreed upon a multiplier of **1.6** as leading to a fair fine and one that comports with the factors that the Court is required to consider under 18 U.S.C. §§ 3553(a) and 3572(a). See U.S.S.G. § 8C2.8. By multiplying the pecuniary gain of $150,000,000 by 1.6, the criminal fine is $240 million.

If the court were proceeding under a statutory fine analysis, the court could consider the

factors set forth in 18 U.S.C. §§ 3553(a) and 3572(a) to derive similar "multipliers" of up to two times[19] the pecuniary gain to arrive at an appropriate fine.

V. THE RECOMMENDED GLOBAL RESOLUTION

The Government recommends that the Court approve the proposed criminal sentence as part of the global resolution of Warner-Lambert's criminal and civil liabilities under the factors set forth in 18 U.S.C. § 3553(a)(2). The criminal fine of $240,000,000 and the total civil payment of $190,000,000, plus interest, for total payments of $430,000,000, plus interest, will provide just punishment of Warner-Lambert, and full and fair restitution to the Medicaid program. The amendment to the Corporate Integrity Agreement between Warner-Lambert, its parent Pfizer Inc and the Office of Inspector General of the Department of Health and Human Services, attached as Exhibit C to the Plea Agreement, will insure that going forward, the public will be better protected because, among other things, Warner-Lambert (and Pfizer) will engage in comprehensive training and certification of its employees regarding appropriate marketing practices, reviews of its marketing practices by an independent review organization, and reports and certification of the information to the Department of Health and Human Services.[20]

VI. CONCLUSION

For the foregoing reasons, the Government urges that the Court approve the sentence of a

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[19] Since the maximum statutory fine is twice the gross pecuniary gain, see 18 U.S.C. 3571(d), any "multiplier" could not exceed two.

[20] Pfizer Inc instituted policies, or applied its existing policies, when it took over Warner-Lambert, by which the parent company says it intended to curtail improper marketing. The United States does not vouch for the company's intent or the effectiveness of those policies, however. In addition, the United States notes that Pfizer has cooperated with the United States' investigation.

criminal fine in the amount of $240,000,000 as set forth in the Plea Agreement dated May 11, 2004, together with a special assessment of $400.

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Department of Justice

June 2, 2004

Certificate of Service

I hereby certify I served a copy of the foregoing on counsel for Warner-Lambert by overnight courier on this date.

_____
Thomas E. Kanwit