IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	:	
v.	:	CRIMINAL NO.
ELI LILLY AND COMPANY	:	

GOVERNMENT'S MEMORANDUM FOR ENTRY OF PLEA AND SENTENCING

I. INTRODUCTION

The United States of America, by and through its counsel, the United States Attorney for the Eastern District of Pennsylvania, and the United States Department of Justice, Civil Division, Office of Consumer Litigation (collectively, the "Government"), hereby submits in the above-captioned matter the Government's Entry of Plea and Sentencing Memorandum. For the reasons set forth below, the Government respectfully submits that the Court should accept the guilty plea of Eli Lilly and Company ("Eli Lilly"), and sentence Eli Lilly in accordance with the parties' agreement.

The Government and Eli Lilly agree that the appropriate resolution of this matter consists of a guilty plea by Eli Lilly pursuant to a plea agreement. Eli Lilly has signed a plea agreement pursuant to Fed.R.Crim.P. 11(c)(1)(C) under which, with the Court's approval, it will plead guilty to a one-count misdemeanor information charging it with misbranding under the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq. ("FDCA"), and pay a stipulated penalty of $615,000,000 (which is comprised of a criminal fine of $515,000,000 and $100,000,000 in

criminal forfeiture). The plea agreement also proposes that the Court proceed to impose sentence immediately, without conducting a presentence investigation.

The plea agreement resolves a very significant criminal investigation into the promotional practices in the United States of Eli Lilly, a pharmaceutical manufacturer, for its drug Zyprexa. The essence of the charge is that Eli Lilly marketed Zyprexa for uses that had not been approved by the Food and Drug Administration ("FDA"), which resulted in the drug being misbranded. This guilty plea is part of a global resolution that includes a civil settlement agreement with the United States and relators (resolving four civil actions brought under the *qui tam* provisions of the False Claims Act.), and a Corporate Integrity Agreement with the Department of Health and Human Services, Office of Inspector General.

II. THE CRIMINAL CHARGE

The information filed in this case charges Eli Lilly with one count of misbranding its prescription drug Zyprexa (also known by its chemical name olanzapine) under the FDCA, 21 U.S.C. §§ 331(a), 333(a)(1), and 352(f)(1). A copy of this information is attached as Exhibit A.

As the information explains, the FDCA governs the interstate distribution of drugs for human use. The FDCA, and its implementing regulations, prohibit the sponsor of a new drug from distributing that drug in interstate commerce until the sponsor has obtained approval from the FDA, after an intensive application and review process. (Information, par. 2). To obtain that approval, the sponsor must file a New Drug Application ("NDA") with the FDA, which identifies all of the uses of the drug intended by the sponsor, and includes proposed labeling for those uses. The sponsor must also provide data, generated in randomized and well-controlled clinical trials, that demonstrates to the FDA's satisfaction that the drug would be safe and effective for those intended uses. 21 U.S.C. §§ 331(d) and 355(b). (Information, par. 3).

The sponsor can only distribute the drug once the FDA approves the NDA and the labeling for the drug. The approved labeling includes those uses of the drug, proposed by the sponsor, which the FDA has approved. Uses not approved by the FDA, and thus not included in the labeling for the drug, are unapproved or off-label uses. Once the FDA approves the drug, the sponsor can promote the drug, but only for those uses which the FDA approved. If the sponsor wants to promote the drug for a new use, the sponsor must apply to the FDA, support the new use with the proper data from well-controlled clinical studies, propose appropriate labeling, and obtain FDA approval. (Information, pars. 4-5).

Under the FDCA, a drug is misbranded if the labeling does not bear adequate directions for use. Adequate directions for use can only be written for uses for which the drug has been found by the FDA to be safe and effective. Drugs promoted for uses that have not been approved by the FDA are misbranded as a matter of law under 21 U.S.C. § 352(f)(1), and thus cannot be distributed in interstate commerce. (Information, pars. 6-7).

The information alleges that Eli Lilly misbranded Zyprexa by marketing it for off-label uses from September 1999 through at least November 2003. (Information, par. 19). During this time, Zyprexa was approved by the FDA for use in treating schizophrenia and certain aspects of Bipolar Disorder. (Information, pars. 9, 15). The FDA never approved Zyprexa for the treatment of dementia, Alzheimer's dementia or the cognitive deficits associated with dementia. (Information, par. 14). The information describes Eli Lilly's promotion of Zyprexa for the treatment of unapproved uses, including dementia, Alzheimer's dementia, agitation, aggression, hostility, depression, and generalized sleep disorder. Eli Lilly's management created marketing materials for these off-label uses, trained the sales force, and directed the off-label marketing. (Information, par. 20).

According to the information, Eli Lilly implemented this off-label promotion effort through its long-term care ("LTC") sales force and its primary care physician ("PCP") sales force. Starting in 1999, the LTC sales force targeted nursing homes and assisted living facilities, even though schizophrenia rarely occurs in the elderly. Eli Lilly sought to convince doctors to treat older patients for disorders which are prevalent in this population, including dementia, Alzheimer's dementia, depression, anxiety, sleep problems, and behavioral symptoms such as agitation, aggression, and hostility. Eli Lilly promoted Zyprexa for the treatment of psychotic and behavioral symptoms in patients with Alzheimer's dementia and for the treatment of behavioral and psychological symptoms of dementia, even though Eli Lilly knew that its studies of Zyprexa for the treatment of Alzheimer's psychosis had yielded "mixed clinical results," thus calling into question the effectiveness of Zyprexa for the treatment of this disease. (Information, pars. 19-29).

Building on its unlawful promotion and success in the long-term care market, Eli Lilly executives decided to market Zyprexa to primary care physicians, even though there was almost no on-label use for Zyprexa in this market. Eli Lilly began to target this market by creating patient profiles for the sales force to use to promote Zyprexa, including a fictitious patient called "Martha," who had behavior difficulty and dementia with agitation. Eli Lilly trained its primary care physician sales representatives to promote Zyprexa by focusing on symptoms, rather than Zyprexa's FDA approved indications. Eli Lilly trained its primary care physician sales representatives to lead with the "Martha" patient profile. The company's primary care physician sales representatives promoted Zyprexa using the "Martha" patient profile, including Zyprexa's ability to treat the symptoms of dementia, such as agitation. "Martha" was a very successful tool for selling Zyprexa. (Information, pars. 25-27).

The information also describes the harm caused by Eli Lilly's off-label marketing campaign by raising safety issues, affecting the treatment of patients, and undermining the FDA drug approval process. Eli Lilly knew that significant weight gain and obesity were adverse side effects of Zyprexa, and knew that significant weight gain and obesity were factors in causing hyperglycemia and diabetes. Despite the written caution from the FDA, Eli Lilly continued to promote adverse events as therapeutic benefits, particularly in elderly populations. For example, when promoting Zyprexa to health care providers for use in elderly populations, the company's sales representatives stated that weight gain was a therapeutic benefit, not an adverse event of Zyprexa. The LTC sales force told health care providers that 5 milligrams of Zyprexa at 5 P.M., referred to by the sales slogan "5 at 5," would help patients with night-time sleep problems, behavioral issues, and dementia. Eli Lilly undertook this illegal off-label promotion for its own financial gain, despite the potential risk to patients' health and lives. (Information, pars. 30-35).

The information specifically charges that Eli Lilly introduced and caused the introduction into interstate commerce of Zyprexa, a drug which was misbranded because it lacked adequate directions for its use in that Eli Lilly promoted it off-label, from September 1999 through March 31, 2001. (Information, par. 36). This is the charge to which Eli Lilly is pleading guilty.

III. THE GUILTY PLEA AGREEMENT

The essential terms of the plea agreement are set forth here. A complete copy is attached for the Court's reference as Exhibit B. In particular:

- Eli Lilly agrees to plead guilty to a one-count information charging misdemeanor misbranding of its drug Zyprexa between September 1999 and March 31, 2001, in violation of the FDCA, 21 U.S.C. §§ 331(a), 333(a)(1), and 352(f)(1). The charge arises from Eli Lilly's unlawful promotional practices, known as "off-label" marketing. Eli Lilly also agrees not to contest forfeiture as set forth in the agreement. (Plea Agreement, par. 1).

- The parties entered into this plea agreement under Fed.R.Crim.P. 11(c)(1)(C), with a stipulated sentence. (Plea Agreement, par. 2).

- The agreed-upon sentence is: payment of $615,000,000 ($515,000,000 as the criminal fine, plus $100,000,000 as the criminal forfeiture), all payable within 10 business days of sentencing; plus the special assessment of $125. In light of the anticipated Corporate Integrity Agreement (which has now been signed by Eli Lilly), the parties agree that Eli Lilly will not be placed on probation. (Plea Agreement, par. 2).

- The parties stipulate to the following facts and basis for the plea, criminal fine and forfeiture. (Plea Agreement, par. 6(A)):

  (1) Eli Lilly marketed Zyprexa, which was a drug within the meaning of 21 U.S.C. § 321(g)(1).

  (2) Shipments of a drug in interstate commerce must be accompanied by labeling bearing adequate directions for use for each of the drug's intended uses.

  (3) In September 1996, Zyprexa was approved by FDA for the short term management of the manifestations of psychotic disorders. In March 2000, FDA approved the addition of the subheading "schizophrenia" to the short term management of the manifestations of psychotic disorders. Also in March 2000, FDA approved Zyprexa for the short-term treatment of acute manic episodes associated with Bipolar I Disorder. In November 2000, FDA approved new labeling for Zyprexa for the short term treatment of schizophrenia in place of the management of the manifestations of psychotic disorders. Also in November 2000, FDA approved Zyprexa for maintaining treatment response in schizophrenic patients who had been stable for approximately eight weeks and were then followed for a period of up to eight months.

  (4) Between September 1999 and March 31, 2001, Eli Lilly promoted Zyprexa in elderly populations as treatment for dementia, including Alzheimer's dementia. Zyprexa is not approved by the FDA for treatment of dementia or Alzheimer's dementia. Eli Lilly's promotion of Zyprexa for these additional intended uses violated 21 U.S.C. § 352(f)(1), because Zyprexa's labeling did not bear adequate directions for each of the drug's intended uses.

- The United States contends that, as a matter of relevant conduct, the conduct at issue continued past March 31, 2001. Eli Lilly does not admit that this conduct extended past March 31, 2001. (Plea Agreement, par. 6(B)).

- The Plea Agreement includes a non-prosecution clause for conduct which (A) falls within the scope of the criminal investigation in the Eastern District of Pennsylvania relating to Eli Lilly's drug Zyprexa; or (B) was known to the United States Attorney's Office for the Eastern District of Pennsylvania or the Office of Consumer Litigation of the Department of Justice as of the date of the execution of this plea agreement, and which concerned the sale, promotion, or marketing of Zyprexa in the United States. The non-prosecution provisions of this paragraph are binding on the Office of the United States Attorney for the Eastern District of Pennsylvania, the Office of Consumer Litigation of the Department of Justice, and the United States Attorney's Offices for each of the other 93 judicial districts of the United States. The non-prosecution provisions are also binding on the Criminal Division of the United States Department of Justice, except that the investigation of Eli Lilly and its affiliates, divisions, and subsidiaries, being conducted by the Fraud Section of the Criminal Division regarding possible violations of the Foreign Corrupt Practices Act and related offenses in connection with the sales and marketing of Eli Lilly's products to foreign customers is specifically excluded from the non-prosecution provisions and release. (Plea Agreement, pars. 8-9).

- The Plea Agreement contains an appellate waiver. There can be no appeal if the Court enters the plea under Rule 11(c)(1)(C). (Plea Agreement, par. 12).

- If acceptable to the Court, the parties agree to waive the presentence investigation and report pursuant to Fed.R.Crim.P. 32(c)(1), and ask that Eli Lilly be sentenced at the time the guilty plea is entered. (Plea Agreement, par. 16).

IV. THE OTHER COMPONENTS OF THE GLOBAL RESOLUTION

The plea agreement is part of a global resolution reached between the United States and Eli Lilly following a criminal investigation by the United States. In a separate civil settlement among Eli Lilly, the United States and relators, Eli Lilly will pay up to $800,000,000, plus interest, to resolve False Claims Act claims by the United States Medicaid Trust Funds, and other federal programs and agencies, as well as claims by state Medicaid programs and the District of Columbia. This settlement also resolves four *qui tam* actions filed in this district.

Along with the civil settlement agreement, Eli Lilly has signed a five-year Corporate Integrity Agreement with the Department of Health and Human Services, Office of Inspector General. This agreement imposes a strict compliance program to ensure that the conduct does

not recur. Under the Corporate Integrity Agreement, Eli Lilly is subject to exclusion from Federal Health Care programs, including but not limited to Medicaid, for a material breach of the Agreement, and subject to stipulated monetary penalties for non-material breaches. The Corporate Integrity Agreement specifically defines "material breach," and outlines the violations that would subject Lilly to stipulated penalties.

V. THE ESSENTIAL ELEMENTS OF THE OFFENSE

A. Misbranding

The information charges one count of misbranding under the FDCA, in violation of 21 U.S.C. §§ 331(a), 333(a)(1), and 352(f)(1). Section 331 of Title 21 United States Code lists prohibited acts, including:

> (a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

Under 21 U.S.C. § 352 of the FDCA, a drug is "misbranded" under several circumstances, including (as relevant here):

> A drug or device shall be deemed to be misbranded –
>
> (f) Directions for use and warnings on label
> Unless its labeling bears (1) adequate directions for use . . . .

In order to prove the crime of misbranding, the Government must establish the following elements beyond a reasonable doubt:

- that Zyprexa is a drug
- that Zyprexa was misbranded in that it lacked adequate directions for the uses intended by Eli Lilly, and
- that Zyprexa was introduced into interstate commerce.

Under 21 U.S.C. § 333 of the FDCA, the penalties are set forth as follows:

(a) Violation of section 331 of this title; second violation; intent to defraud or mislead

> (1) Any person who violates a provision of section 331 of this title shall be imprisoned for not more than one year or fined not more than $1,000, or both.
>
> (2) Notwithstanding the provisions of paragraph (1) of this section, if any person commits such a violation after a 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.

The information in this case charges a misdemeanor under 21 U.S.C. § 333(a)(1). In 1985, Eli Lilly pleaded guilty to 25 counts of violating the FDCA for failing to make required reports to the FDA of serious adverse reactions to, and misbranding of, its arthritis drug Oraflex. In 2006, Eli Lilly pleaded guilty to violating the FDCA by misbranding its drug Evista. On the basis of either of these prior convictions, the Government could have charged the instant offense as a felony under 21 U.S.C. § 333(a)(2). As will be discussed below, in accordance with the Department of Justice's ("Department") Principles of Federal Prosecution of Business Organizations, the Government considered all factors in its decision regarding the overall disposition of this matter. Based on these factors, the Government charged Eli Lilly's conduct as a misdemeanor.

Lastly, the Government notes that it is not illegal for a doctor, using good medical judgment, to prescribe a drug for an off-label use. However, it constitutes criminal misbranding for a drug manufacturer to promote its drug for such off-label use.

B. Forfeiture

The forfeiture component of the information and plea agreement arises from the FDCA's provision for seizing misbranded drugs. 21 U.S.C. § 334 (allowing proceedings on libel of information, for condemnation, against drugs that are misbranded or adulterated so that the

Government can seize, destroy or sell them). These proceedings are by their nature classic civil forfeiture proceedings. Under federal forfeiture law, the Government can pursue criminal forfeiture in any case where the defendant is charged with a violation of an Act of Congress which contains a civil forfeiture remedy. See 28 U.S.C. § 2461(c) (allowing criminal forfeiture where the defendant is charged "in a criminal case with a violation of an Act of Congress for which the civil or criminal forfeiture of property is authorized . . . ."). Thus, if civil forfeiture is authorized in a statute such as the FDCA, then criminal forfeiture is as well.

As the misbranded drugs are no longer available for seizure or destruction, the Government can seek substitute assets. See 18 U.S.C. § 2461(c) (the procedures set forth in 21 U.S.C. § 853 apply to this criminal forfeiture); 21 U.S.C. § 853(p) (allowing the forfeiture of substitute assets if the items subject to forfeiture are no longer available).

VI. THE MAXIMUM PENALTIES

The maximum penalty for this offense is a fine of $200,000 (under 18 U.S.C. § 3571(c)(5)), or twice the gross gain or gross loss, whichever is greater (18 U.S.C. § 3571(d)); a special assessment of $125 (18 U.S.C. § 3013(a)(1)(B)(iii)); and a five-year term of Court supervision (18 U.S.C. § 3561(c)(2)); in addition, forfeiture may be ordered.

VII. THE FACTS AT TRIAL

In the plea agreement, the parties have stipulated to a factual basis sufficient to support the entry of this plea. (Plea Agreement, par. 6(A)). If the case were to proceed to trial, the Government would prove these facts beyond a reasonable doubt, as well as each of the other allegations set forth in the information.[1]

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[1] The case was investigated by agents from the Food and Drug Administration, Office of Criminal Investigations, the Defense Criminal Investigative Service, and the Department of

The Government would show a concerted plan to maximize revenue by the off-label marketing of Zyprexa. The proof would demonstrate that, for four years between 1999 and 2003, senior executives and managers of the company knew and approved of these efforts and engaged in a highly organized and deliberate effort to maximize revenue despite legal restrictions.

In September 1996, Zyprexa was approved by The FDA for the short-term management of the manifestations of psychotic disorders. Between September 1996 and 1999, Eli Lilly focused its proactive promotional marketing for Zyprexa to psychiatrists. Eli Lilly had a sales force that called on psychiatrists that might prescribe Zyprexa to patients with schizophrenia. In 1999, however, Eli Lilly changed its marketing strategy to increase revenue and profit.

A. **The Loss of Prozac Revenues and Profits**

In the late 1990s, Eli Lilly faced the loss of significant revenue with the expiration of its patent on Prozac. In anticipation of this event, but unsure exactly when it was going to occur (due to litigation), Eli Lilly prepared for "Year X" – the company's term for the year when it lost its patent on Prozac.

Around this time, Eli Lilly commissioned a report entitled "The Primary Care Opportunity" from a nationally-known consulting firm. This report found that "larger competitors [e.g., Merck, Pfizer, Bristol Myers] are migrating toward the primary care channel with drugs driven by profile improvements" as compared to Eli Lilly, which was headed in the direction of providing drugs in specialty markets. The consulting firm advised Eli Lilly that "Primary care is a large opportunity that is likely to remain important. . . . Lilly does not

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Health and Human Services, Office of Inspector General.

outperform its competitors in primary care and *is leaving money on the table with current and pipeline products*." (Emphasis added). The report identified Eli Lilly products, including Zyprexa, that if sold in the "primary care channel" could significantly increase Eli Lilly's worldwide sales. The evidence at trial would show that, given the loss of Prozac's patent, Eli Lilly could not afford "to leave money on the table."

Adding to the Zyprexa sales calls being made to psychiatrists, Eli Lilly launched the sale of Zyprexa in PCP offices in October 2000. On March 13, 2001, a Zyprexa Brand Team manager addressed the PCP sales force for Zyprexa:

> Don't get me wrong – unit share growth is good, and what we have accomplished in that area has not gone unnoticed. But dollars pay the bills and boost the stock price, so let's look at $ growth.
>
> Again, we are redefining the market. What had been a 3-point lead over Risperdal is now a 12-point lead. Look at how that Zyprexa sales line jumps. And if you ask Bill Robinson, our timing is impeccable. This is Year X for Eli Lilly, and the conventional wisdom is that companies just don't "bounce back" from losing patent protection from their biggest product. Well, this trend says we won't just hit our $60 million plan – it says we've got a great shot at exceeding our stretch goal of $100 million in incremental sales. $100 million incremental from this group isn't a nice-to-have; it's a must-have. We need to OWN this target, because the [U.S.] affiliate needs our help. Do I have your commitment on this? I personally challenge each of you [to] drive toward a goal that will help turn Year X into Year X-ceptional.

A short time later, at a meeting of the Zyprexa Product Team in July 2001, the high stakes were clearly laid out: "Straight Talk - What's at Stake. *The Company is betting the farm on Zyprexa* . . . the ability of Eli Lilly to remain independent and emerge as the fastest growing pharma company of the decade depends solely on our ability to achieve *world class commercialization of Zyprexa*. If we succeed, Zyprexa will be the most successful pharmaceutical product ever . . . we will have made history." (Emphasis and ellipse in original).

According to Eli Lilly's 2001 annual report: "the 'circle of life' in our innovation-driven business brought the role of Prozac in the company's growth to an end. . . . [W]e lost our exclusive rights to Prozac in the United States on August 2, 2001 – almost three years sooner than we had expected. . . . [T]he sales of this molecule dropped even faster than we had expected. Its sales declined 66 percent in the fourth quarter, bringing the total sales for the year down 23 percent, to $2.0 billion."

The evidence would show that in order to help compensate for the lost Prozac revenue and profits, Eli Lilly decided to broaden its efforts to promote and sell Zyprexa, including for off-label uses.

B. The Long-Term Care Market

The first step to promote Zyprexa in the long term care ("LTC") market was the creation of the Eli Lilly LTC sales force in the latter half of 1999. At its inception, the LTC sales force consisted of 15 sales representatives. This modest number, however, quickly grew. By August 1999, the LTC sales force had nearly quadrupled in size to 59. It took only six more months before Eli Lilly had deployed an army of 160 sales representatives across the country charged with promoting Zyprexa to nursing homes and similar LTC facilities.

At a January 2001 sales meeting, the sales representatives were told that the LTC market represented "A Golden Opportunity" for Eli Lilly, representing "one of the fastest growing segments of the U.S. population." In order to capitalize on this "Golden Opportunity," Eli Lilly directed its LTC sales force to focus their promotional efforts on a core message for Zyprexa, to deliver at every sales call: "Zyprexa safely stabilizes behaviors/symptoms and maintains response." Eli Lilly further elaborated on the "Zyprexa LTC Message." Among the "Key Message Points" for sales representatives to deliver to doctors were: "Zyprexa stabilizes

behavioral symptoms such as agitation, aggressive behavior, and paranoid delusions (AAP)" and "Zyprexa offers your patients the best chance of significant overall improvement." The focus of the LTC core messaging was on behavioral symptoms and not the FDA-approved indications.

In January 2002, the Zyprexa LTC message had evolved to differentiate the drug from a rival atypical antipsychotic drug, Risperdal. Eli Lilly touted Zyprexa in nursing homes as superior "in treating behavioral symptoms like agitation and aggression" and for a superior maintenance of response. Eli Lilly claimed that its data showed a 40% improvement in symptoms.

The evidence would show that, in addition to claiming that such symptom improvement helped the patient, Eli Lilly directed its LTC sales representatives to promote Zyprexa as an aid to the caregiver and the physician. The sales representatives were instructed that because Zyprexa purportedly worked to quell certain behaviors, the patient would demand less nursing time and the physician would in turn receive "fewer pages/phone calls from nursing staff." Focusing on these symptoms to the exclusion of the drug's approved indications was a thinly veiled effort to promote Zyprexa as a treatment for the behavioral and psychological symptoms of dementia, without explicitly saying so.

The use of dementia symptoms as the focus of promotional activities was the central pillar of the LTC sales force's mission. The message was carried by sales representatives in their discussions with health care professionals on detail visits, and was aided by the use of journal reprints in conjunction with a visual sales aid.

In October 2000, the Archives of General Psychiatry published a study submitted by Lilly Research Laboratories entitled Olanzapine Treatment of Psychotic and Behavioral Symptoms in Patients With Alzheimer Disease in Nursing Care Facilities (referred to as the

"Street study" or "Street Reprint").[2] In this study, Eli Lilly followed 206 elderly nursing home patients who had been diagnosed with Alzheimer's Disease, the most common form of dementia. In this randomized, double-blind, placebo-controlled six week study, low-dose Zyprexa was found to be effective in treating "agitation/aggression and psychosis in this population of patients with Alzheimer's Disease."

After the study's publication, Eli Lilly provided its LTC sales representatives with reprints of the article, and at January 2001 sales meetings directed them to integrate its use during their promotional calls. LTC sales representatives were directed to open the sales call with a discussion of the Street Reprint. The "Verbatim"[3] included the statement, "Data from this multicenter, double-blind, placebo-controlled trial of olanzapine [Zyprexa] indicates that low-dose olanzapine, 5 and 10mg/day, is effective in reducing behavioral disturbances and psychotic symptoms in patients with Alzheimer's Disease residing in nursing care facilities."

After opening the call with the discussion of Eli Lilly's latest research demonstrating Zyprexa's efficacy on nursing home patients with Alzheimer's Disease, the sales representatives were directed to "paint the patient picture" – the picture of a patient who was exhibiting aggression and agitation – the same symptoms identified in the Street Reprint. Then, the representative was directed to provide the "core message" – "Zyprexa stabilizes behavioral symptoms such as agitation, aggressive behavior, & paranoid delusions." In this way, the Street

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[2] The lead author of the study was Dr. Jamie Street. The study identified Dr. Street and other authors from Lilly Research Laboratories. The study also stated that Dr. Street and other authors were stockholders in Eli Lilly, a sponsor of the study.

[3] As the term "Verbatim" is used by Eli Lilly, it is a written script developed by the company for sales representatives to follow in communicating with health care providers.

Reprint set the stage for a sales visit that urged physicians to prescribe Zyprexa as a treatment for Alzheimer's Disease.

Eli Lilly's use of the Street study in promotion was misleading. Although the Street study suggested Zyprexa was effective in treating Alzheimer's Disease, other Eli Lilly studies had different results. Eli Lilly study HGOA (1995) demonstrated that Zyprexa worked no better than a placebo on Alzheimer's Disease. Likewise, study HGGU (2001) confirmed that Zyprexa was no better than a placebo or Risperdal. Because it could not substantiate Zyprexa's efficacy in Alzheimer's Disease, Eli Lilly abandoned efforts to secure regulatory approval for Alzheimer's psychosis in November 2001.

There is no evidence that Lilly's sales representatives provided physicians the studies that showed Zyprexa was not an effective treatment for Alzheimer's Disease, nor is there any evidence of sales representatives advising doctors that Eli Lilly had decided not to seek an Alzheimer's psychosis indication. The evidence would show that the Street study – whose findings stood alone – was widely used by the LTC sales force during its sales calls to promote Zyprexa. As a result, Eli Lilly's use of the Street study was not only unlawful off-label promotion, but misrepresented what Eli Lilly knew about Zyprexa's efficacy in this patient population.

The use of reprints to promote Zyprexa to nursing homes for the treatment of symptoms of dementia was not limited to the Street Reprint. In August 2001, the American Journal of Geriatric Psychiatry published another Eli Lilly-funded study: Antipsychotic Treatment of Behavioral and Psychological Symptoms of Dementia in Geropsychiatric Inpatients (referred to

here as the "Edell study" or "Edell Reprint").[4] As with the Street study, Eli Lilly armed its LTC sales force with reprints of the Edell study and instructed them on its use at the quarterly LTC sales force district meetings in September 2001. Describing it as "Hot off the press," LTC managers underscored how the study "Focuses on elderly patients with 'Behavioral Symptoms Associated with Dementia,'" concluding that "Zyprexa patients experienced significantly greater overall improvement in behavioral and psychological symptoms of dementia compared to Risperdal and Haldol." Thus, the Edell study suggested that Zyprexa is an effective treatment for dementia, despite the lack of FDA approval for such an indication.

The PowerPoint presentation that was provided to the LTC district managers for introducing the Edell Reprint included a slide that stated that the Edell Reprint is "non-promotional" and that sales representatives could only "answer unsolicited questions." However, district managers were instructed in the accompanying speaker notes to ask their representatives to share their best practices "for getting into a dialogue about the Edell Reprint." The PowerPoint suggested that a best practice was to ask the physician, "Do you have any questions about this study?" In this manner, Eli Lilly encouraged its sales representatives to induce a physician to ask an "unsolicited" question about the Edell study. Other "best practices" in discussing the Edell Reprint included asking the physician "What is your understanding of the data?" The evidence would show that the purpose of asking these questions was to induce the physician to prescribe Zyprexa to treat his or her dementia patients with Zyprexa.

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[4] The principal author of the study was William S. Edell, Ph.D., of Mental Health Outcomes, Inc., a subsidiary of Horizon Health Corporation. The other author of the study was Sandra L. Tunis of Eli Lilly.

Once the sales representative had accomplished moving from the Edell study to a description of the behaviors in that study, the LTC sales representatives were to transition to the Zyprexa sales aid, which featured a fictitious elderly patient named Rose Jackson: "Let's talk about a patient that you see everyday [sic] in your nursing home. A patient like Rose who is exhibiting these same behaviors." Another suggested transition between the Edell Reprint and the Rose detail aid was: "Dr., let's talk about a patient that requires that extra nursing time we talked about. It's a patient like Rose who is displaying aggressive behavior, she is thinking the nurses are trying to poison her, and she may be combative and refusing her meds."

Thus, the Edell study was seamlessly integrated as the new foundation of a Zyprexa sales call that had nothing to do with schizophrenia or acute bipolar mania. Rather, the sales call was focused entirely on symptoms of dementia and how Zyprexa was the solution to those behaviors.

The Zyprexa Brand Team developed several visual aids for sales representatives to use during their detail visits. Nowhere in the Zyprexa LTC selling aid, also know as a detail aid, were Zyprexa's approved indications identified. The implementation guide for sales representatives, accompanying the detail aid, stated that Eli Lilly wants "our long term care customers to believe 2 main points: ZYPREXA stabilizes symptoms and behaviors safely [and] ZYPREXA gets patients like Rose better and keeps them better." The focus of the detail aid was on Rose's symptoms, not any particular diagnosis such as schizophrenia.

A page in the detail aid described Rose's symptoms: "Increasingly agitated; Beginning to demonstrate aggressive behavior; Paranoid (thinks people are poisoning her food); Socially withdrawn." Although the implementation guide for this detail aid directed the sales representative to "Identify patient, Rose, and highlight her current symptomatology, clinical observations, and diagnosis" no diagnosis for Rose was found either in the detail piece or the

implementation guide. Eli Lilly suggested that sales representatives tell the physician, "Doctor, does it make sense to use ZYPREXA as a first choice for a patient like Rose, since ZYPREXA helps to safely stabilize symptoms and behaviors such as agitation, anxiety, hostility, delusions, and resistance to care?"

The sales aid highlighted that "Zyprexa helps repair the damage of behavioral symptoms; Stabilizes symptoms and behaviors; Reduces agitation and hostility; Reduces suspiciousness and delusions." Eli Lilly's focus on these symptoms, without reference to a specific diagnosis, was carefully crafted. These symptoms were the behavioral and psychological symptoms of dementia. With a prevalence of less than 1%, nursing home doctors were not likely to see a geriatric schizophrenic patient every day. However, with a prevalence of 60% to 80% among nursing home patients, these doctors did in fact see dementia patients daily.

The detail aid also touted Zyprexa as a treatment for depression and anxiety, claiming that in clinical trials, Zyprexa "significantly improved mood symptoms . . . including depressive symptoms, anxious symptoms, [and] somatic concerns." LTC sales representatives were instructed to tell doctors, "ZYPREXA has many additional benefits for your patients, including stabilizing depressive and negative symptoms as well as behaviors. . . . How does this data on the ability of ZYPREXA to improve mood and negative symptoms compare to your clinical experience?" Zyprexa was not approved for the treatment of depressive disorders (e.g., major depressive disorder, dysthymia), somatoform disorders (e.g., hypochondriasis) or anxiety disorders (e.g., generalized anxiety disorder, panic disorder, post-traumatic stress disorder).

The evidence would show that the nursing home patients these doctors treated did not have any of Zyprexa's approved indications. In order to sell Zyprexa to this population, Eli Lilly had another plan of attack – show the physician data suggesting that Zyprexa was effective in

treating dementia, and then sell to the behaviors of dementia that were commonly present in the nursing home.

Call notes would prove that Eli Lilly's sales representatives followed this direction and promoted Zyprexa off-label to physicians treating patients in LTC settings.[5] The call notes also contain evidence that Eli Lilly LTC sales representatives described the weight gain associated with Zyprexa as a benefit for elderly patients. In addition, there is evidence in the call notes that sales representatives used Zyprexa's purported ability to increase cognition as a reason for doctors to prescribe Zyprexa to their elderly patients. The FDA-approved label does not include any reference that Zyprexa is approved to improve or increase cognition in patients.

In addition, the evidence would show that Eli Lilly sales representatives were encouraged to utilize drug utilization reports ("DURs") containing private, individualized patient information as a marketing tool to increase prescriptions of Zyprexa. These DURs would enable Eli Lilly sales representatives to see whether the doctors they planned to detail were prescribing Zyprexa relative to other drugs. DURs typically include private patient information. The Winter 2003 issue of Eli Lilly's LTC Best Practices Newsletter included a section on why DURs were important and how to obtain them. As of April 14, 2003, health care providers, health care clearinghouses, and most health plans could disclose individually identifiable "protected health information" only as permitted under federal regulations promulgated by the Secretary of HHS.

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[5] Following their sales call, Eli Lilly's sales representatives were required to write a "call note" of their interaction with the health care customer. Eli Lilly sales representatives were instructed to document the calls immediately following interactions with their customers and document information that was considered essential for the sales representative and his/her territory partner to progressively sell their customers.

Despite this limitation, the evidence would show that sales representatives were encouraged to gain access to DURs in an effort to improve sales of Zyprexa.

C. **The Primary Care Market**

In addition to the LTC market, the evidence would demonstrate that off-label promotion was an important part of the Zyprexa marketing plan to promote and sell Zyprexa to PCPs. Building on its entry into the LTC market, Eli Lilly executives made a decision to start marketing Zyprexa to PCPs.

In the first part of 2000, a team within Eli Lilly recommended that Eli Lilly "Launch [Zyprexa] into broader PCP Market." Eli Lilly's document would disclose that the reasons for the recommendation included "ability to grow the market and increase corporate profits; opportunity to change lower decile PCPs prescribing habits and expand use as proven in PCP pilot." This presentation was covered with references to how low- and higher-prescribing PCPs prescribe for dementia. The Eli Lilly document noted that "[w]hile elderly data would be a plus, current schizophrenia data is appropriate (symptoms are the same). Current LTC message tested in PCP focus groups."

On September 9, 2000, three members of Eli Lilly's Zyprexa Brand Team created a presentation entitled: "Primary Care for Patients With Behavioral, Mood, and Thought Disturbances." The presentation stated that "Behavioral, mood, and thought disturbances frequently are the common clinical manifestations seen by Primary Care Physicians in patients with: Depression, Bipolar Disorder (manic); Thought Disorders (psychoses); Delirium; [and] Dementia." The presentation proceeded to describe three case studies, including "Martha" who had behavior difficulty and suffered from dementia with agitation.

The fictitious Martha patient profile was one of three first used by Eli Lilly to promote Zyprexa to PCPs. The detail aid featured Martha, David and Christine in that order, and described Martha as follows: "Martha is a widow who lives close to her family. She's been your patient for several years. She's becoming more complicated to manage with increasing agitation. Her family has shared their concerns with you . . . 'She thinks we're trying to take advantage of her.' 'At times she is confused.' . . . 'Recently, she's been getting angry with us.' Goals of treatment: Reduce behavioral disturbances. Decrease disorganized thinking." The detail aid pointed out that "ZYPREXA was approved for the short-term treatment of schizophrenia in 1996; ZYPREXA was approved for the short-term treatment of bipolar mania in 2000 . . . ." In response to questions posed in the detailing aid, under the heading "Know the efficacy of Zyprexa" the detail aid described the efficacy of Zyprexa: "Doctor: Will ZYPREXA calm the agitation of this patient? Zyprexa is proven effective in reducing positive symptoms including tension, agitation, hostility, anger, uncooperativeness and belligerence. Family: Will this product calm our mother without impairing her cognition? ZYPREXA is proven effective in reducing hostility, anger, uncooperativeness, and belligerence with no impairment in cognition."

The evidence would show that in October 2000, Eli Lilly began to detail Zyprexa to PCPs even though at least one internal Eli Lilly document acknowledged that there was virtually no on-label use for Zyprexa in the primary care market. The document, "ZYPREXA – Primary Care Strategy and Implementation Overview," provided that detailing PCPs was a major challenge because "Zyprexa's primary indications – schizophrenia and bipolar – are not viewed as PCP [primary care physician]-treated conditions, so there's not a specific indication for Lilly reps to promote in the PCP segment."

To get around the impediment that Zyprexa's indications – schizophrenia and bipolar mania – were not viewed as PCP-treated conditions, sales representatives were instructed to tout Zyprexa as a safe option for the treatment of a wide array of mood disorders commonly treated by PCPs. For example, the Zyprexa "Primary Care Strategy and Implementation Overview" detailed how to position Zyprexa:

> Zyprexa: The safe, proven solution in mood, thought, and behavioral disorders. We will emphasize safety to address barriers to adoption, and merchandise the brand's "Four years – Four million patients" base of experience. The word "solution" speaks to unmet medical need, and enables the PCP to take control of clinical situations that previously had led to referrals and/or poor outcomes. "Mental disorders" is intentionally broad and vague, providing latitude to frame the discussion around symptoms and behaviors rather than specific indications. We will position Zyprexa as the incremental next step in the PCP's expanding clinical orbit: e.g., SSRIs => 2nd generation antidepressants => safe, gentle psychotropics.

In October 2000, Eli Lilly had a meeting in Orlando, Florida for 510 PCP sales representatives to introduce them to the new message for promoting Zyprexa to primary care physicians. This meeting was called "Viva Zyprexa." According to the Zyprexa Brand Team, the Zyprexa Primary Care "Strategic Intent" was "Zyprexa can and will become an everyday agent in primary care. Ours is a growth strategy, not a niche strategy." The PCP sales representatives were trained to promote Zyprexa focusing on symptoms, not indications. The patient profiles were included in the first detail aid to be used by the sales force in promoting Zyprexa to PCPs. The "Zyprexa Implementation Guide" provided to sales representatives stated that:

> In order to succeed in the Primary Care market, we must focus on the symptoms and behaviors found in mood, thought, and behavioral disturbances. The sales aid has been organized in such a fashion that will allow you to identify specific symptoms for

> these disturbances. The message flow and the patient profiles (Martha, David, and Christine) will aid you in helping the physician to recognize these symptoms in patients he or she sees frequently. Use these tools to aim for early identification of relevant patient types, as well as pointing out the important role that family members play.

Around nine months after introducing Zyprexa into primary care, Eli Lilly introduced a new detail aid. According to the "Zyprexa Primary Care Implementation Guide," dated June 2001, "The primary difference in this piece is that we structure each major spread around a patient, not around data. In other words, when you paint a picture of a specific patient type, you need not jump around the piece to show supporting evidence. It's all right there, in one place, enabling you to create action on the spot. You'll see an old friend (Martha) and meet two new ones: Michael and Kelly. Michael exhibits clear signs and symptoms of bipolar disorder, without appearing to be as threatening as his predecessor (David). Kelly struggles with mild to moderate psychosis, with visible elements of a mood component. Again, the intent was to make Kelly more 'treatable' by a PCP (versus a defiant Christine)." The new detail aid avoided patients like David and Christine, whom PCPs were reluctant to treat, and made them less "threatening" or "defiant."

The two-page spread of the fictitious Martha patient profile in the detail aid highlighted the symptoms that Zyprexa purportedly treated, but did not reference the FDA-approved indications. In its effort to sell Zyprexa to PCPs, Eli Lilly instructed its sales representatives how to respond if a doctor objected to prescribing Zyprexa on the ground that he or she did not treat patients with schizophrenia or bipolar disorder. According to an Eli Lilly sales guide, if a doctor told a sales representative that he or she refers such patients to psychiatrists, the sales representative was instructed to reply, "Doctor, that makes sense. Patients with moderate to

severe symptoms of schizophrenia and bipolar disorder should be treated by a psychiatrist. However, in your own practice there are probably patients who may experience symptoms such as elevated mood, emotional withdrawal, and agitation who may benefit from ZYPREXA. Keep in mind that referrals can be expensive, time-consuming, or logistically difficult . . . ." In this manner, Eli Lilly sales representatives encouraged doctors to prescribe Zyprexa for patients who were not afflicted with the illnesses for which Zyprexa was approved.

The evidence would demonstrate that Eli Lilly promoted Zyprexa for other off-label uses, including treatment for agitation, dementia, depression and generalized sleep disorder. An internal Eli Lilly email dated February 2000, states "we have been driving the depression story with Zyprexa in our DTP [Direct to Physician] programs since Q3 1998. We were ahead to [sic] the curve in recognizing and communicating the importance of this attribute and how we can utilize it to differentiate ourselves in the marketplace." Zyprexa was not and never has been indicated for depression.

Eli Lilly's off-label promotion of Zyprexa did not go unnoticed by doctors. An internal Eli Lilly email to "Area Zyprexa Champions" dated November 2000, noted that some sales representatives were "getting a little grief from some of our docs [doctors] about promoting Zyprexa for dementia" because there is no FDA-approved drug for dementia. The email from an Eli Lilly PCP sales representative stated:

> Since the diagnosis of our 3 patients in the Zyprexa core message piece are: Martha - dementia, David - bipolar, Christine - schizo; can you enlighten us a little more about dementia. We know that we are to describe the symptoms and stay away from diagnoses, but for our own background, can you elaborate on dementia and how it is different from other things like Alzheimers, etc. We are getting a little grief from some of our docs [doctors] about promoting Zyprexa for dementia, but according to the slides in the audioconference set, there is no FDA-approved drug for dementia.

A member of the Zyprexa Brand Team in Indianapolis responded to several sales representatives asking them to disseminate the response to their colleagues:

> Dementia is a broad classification that basically indicates a disease which produces a decline in cognitive functioning. As we know, there are many other symptoms associated with this as well (behavioral disturbances, psychosis). Alzheimers disease is the most prevalent form of dementia, estimated at over 80% of dementia cases. Other forms may include vascular dementia, [lewy body] dementia, dementia NOS.

There is nothing in the email exchange which said sales representatives should not be promoting Zyprexa for dementia. This email was sent broadly throughout the Eli Lilly sales force and the Zyprexa Brand Team. Rather than instruct sales representatives not to promote Zyprexa for dementia, the message to the field was to continue the off-label promotion.

On Sunday, November 2 and Monday, November 3, 2003, the Knight Ridder newspaper chain ran a series of stories relating to injuries in patients prescribed drugs for unapproved uses. Based on its investigation, the authors of the series noted that nearly two-thirds of antipsychotic prescriptions were for off-label uses, including for insomnia and attention-deficit disorder. Following the publication of these articles, an Eli Lilly Regional Business Director sent a voicemail to a district sales manager, who passed it on to the sales representatives on his team:

> Message from [] going to the management team. I just wanted to share with you the importance of driving the business, being feared and respected by our competitors, but at the same time we need to make sure that we're doing it within the guidelines of the job. Sunday morning's Fort Worth newspaper, front page center, and on Monday morning's front page center, was two articles about companies and products that are being promoted off-label. And I just want to ensure that when we're in the field, that we are talking irritability + 4. We are not talking about just anxiety or just irritability, patients on antidepressants, and we're really asking for Zyprexa. ***We need to make sure that we are definitely talking about acute bipolar mania, we're not talking about the old Martha, which is totally off-label, especially when physicians say***

they're using it for dementia or Alzheimers; don't have an indication.

The evidence would show that shortly after the launch of Zyprexa into the primary care market, Eli Lilly conducted a survey of district managers and sales representatives to understand what worked and what needed to be changed. The market research showed sales representatives "having the most success when their message centers on identifying patient types and treating symptoms instead of focusing on patient diagnosis." A presentation by an Eli Lilly market research analyst identified "What's working in the message":

> Getting them to start in the office is the goal. "You are their last hope before the nursing home . . ."
>
> Transition from Prozac message: Prozac SSRI for elderly, some elderly pts [patients] transitioning to early dementia, they really need you, the last thing they need is to go to another doctor.

Under the heading "Cautions," the market research analyst stated: "Some PCPs focus on drug class, indication, and diagnosis and not appropriate patient types." The analyst then quoted a district manager that was interviewed during the survey and said: "The patient descriptors help, but it's hard not to have an indication they can sink their teeth into." One of the "lessons learned" according to the analyst's market research was the "PCPs uncomfortable with the fact that all detail data is about acute schizophrenia."

In March 2001, five months after the launch in primary care, Eli Lilly put together a message management team to provide feedback on the current message and direction on the refinement of the message. A summary of the "key take-aways" stated that "*What is working*: Martha - for patient identification. Symptom and Behavior management. Audioconferences. Simplicity of the 3x3 message. *What needs improvement*: Christine and David. Martha - a gap

exists in our comprehension of Martha and the MD's identification of Martha. Lack of diagnoses. Patient education."

According to an internal newsletter, Eli Lilly USA Online, published on July 25, 2001, the launch of Zyprexa into primary care was a huge success:

> Today, Zyprexa dominates segment share of voice, with more than 50 percent of all sales contacts and customer spend. Sales results have proven that speed can also be profitable. Through June, Zyprexa share of market of new prescriptions topped 27 percent – up more than six full share points in eight months. The team has cut the competition's lead from 12 points in October to just 3.5 percent in June. Based on this success, Sigma got approval last month to increase its targets from 22,000 primary care physicians (PCPs) to more than 50,000.

One year later, in June 2002, Eli Lilly's Vice President for U.S. sales announced a significant increase in the resources committed to the primary care market. "Due to the success of the launch," Eli Lilly decided to add three other sales divisions (each with 510 sales representatives) to promote Zyprexa in addition to the Sigma sales force of 510 sales representatives that had been promoting Zyprexa to PCPs for 18 months. The evidence would show that Eli Lilly employed more than 2,000 sales representatives who promoted Zyprexa in the primary care and long-term care marketplace.

The evidence would show that Eli Lilly considered seeking an indication for Zyprexa for the treatment of psychosis associated with Alzheimer's disease but did not follow through with a final supplemental New Drug Application. Later, following the "mixed" results from clinical trials, the most senior executive of the Zyprexa Product Team recommended to very senior executives within Eli Lilly not to pursue an indication for Zyprexa to treat Alzheimer's psychosis. That recommendation was accepted. Nevertheless, Eli Lilly continued to promote Zyprexa for treatment of the elderly with dementia even after they decided that given the mixed

results in the clinical trials, they could not meet the safety and efficacy standards of the FDA for approval for the treatment of Alzheimer's psychosis.

In 2000, when Eli Lilly started marketing Zyprexa to PCPs, the sales force was instructed to tout Zyprexa's safety, and to downplay negative side effects. Specifically, with respect to the issue of weight gain, sales representatives were instructed to tell doctors that, "[a]s with many agents in its class, ZYPREXA is sometimes associated with weight gain. For most patients, this is very manageable."

Indeed, despite specific warnings from the FDA not to do so, Eli Lilly continued to promote Zyprexa's adverse events as positive attributes to be touted. At the 2000 meeting to launch Zyprexa in the primary care market, Zyprexa's Product Team Leader told the Eli Lilly sales representatives: "our one clinical Achilles heel is weight gain. That's a plus in the elderly because of wasting of those individuals. . . . Weight gain is a side effect of Zyprexa. We knew it early on. It is a reality. In certain conditions, like the elderly, it's a plus. It's an advantage because of, because of [sic] the difficulty the elderly have in maintaining their weight." The Eli Lilly scientist told the sales representatives, even when weight gain occurred in younger patients, it was not a serious concern: "It occurs to a very extreme degree in only a very small number of patients, thankfully. . . . It's always important to position weight gain in it's proper perspective, in a constellation of efficacy and side effect, and to not solely focus on weight gain. . . So it's very important to always put weight gain in that context of efficacy, safety profile, et cetera." In promoting Zyprexa, Eli Lilly turned an adverse event of the drug into a therapeutic benefit.

VIII. THE SENTENCING CONSIDERATIONS

The agreed-upon sentence takes into account Eli Lilly's conduct under 18 U.S.C. §§ 3553 and 3572, and the United States Sentencing Guidelines. Eli Lilly's proposed sentence reflects

the breadth and length of the company's illegal conduct, including relevant conduct relating to the off-label promotion of Zyprexa.

The criminal fine is based on a number of factors, including an estimate of the amount of Zyprexa sold attributed to the company's illegal conduct. The Government then estimated the profit Eli Lilly derived from the sale of Zyprexa, and applied that profitability percentage to the amount of Zyprexa sold that could be attributed to the company's illegal conduct. The Government then multiplied the resulting dollar amount by an appropriate multiplier to reach a total penalty of $615,000,000. The $615,000,000 was then divided into two parts: a criminal fine of $515,000,000 and asset forfeiture of $100,000,000. The $515,000,000 is the largest criminal fine imposed against an individual defendant in the history of the United States. It is also the largest criminal fine in a health care criminal case in history. This agreed-upon sentence falls within the statutory maximum set forth in 18 U.S.C. § 3571(d) (twice the gross gain or loss).

The proposed criminal resolution accomplishes the goals of sentencing under 18 U.S.C. § 3553. The Government has considered the nature and circumstances of the offense and the history and characteristics of the defendant. The Government believes that this historic criminal fine reflects the seriousness of the offense and the defendant's earlier violations of the FDCA. The off-label marketing here was harmful in that it undermined the drug approval process mandated by statute, interfered with the doctor-patient relationship, was misleading to doctors, and posed potential risk to patients.

The Government also believes that the criminal fine promotes respect for the law. The Government believes that the proposed sentence will deter Eli Lilly from further unlawful promotion of its pharmaceutical products. A criminal fine of this magnitude, coupled with all of

the other aspects of the resolution of this matter, will also serve as general deterrence to others who might be tempted to go down the road of off-label marketing.

In accordance with the Department's Principles of Federal Prosecution of Business Organizations, the Government considered all the factors in its decision regarding the overall disposition. Those factors included, but were not limited to, any collateral consequences, including whether there would be disproportionate harm to shareholders, pension holders, employees, and other persons not proven personally culpable, and the impact on the public, arising from the prosecution. As a result, the Government decided to charge Eli Lilly with a misdemeanor violation of the FDCA and to agree to the criminal penalty set forth in the plea agreement.

All of the factors discussed in this section are difficult to quantify, but the Government believes the proposed criminal penalty is a just resolution of this matter. The stipulated criminal fine of $515,000,000 and asset forfeiture of $100,000,000 is the result of long and intensive negotiations between the parties. It represents a just resolution of the charge against Eli Lilly for its off-label marketing, particularly when coupled with the significant civil settlement and the obligations imposed by the significant Corporate Integrity Agreement.

IX. CONCLUSION

For the foregoing reasons, the Government respectfully recommends that the Court sentence Eli Lilly to a criminal fine in the amount of $515,000,000, impose asset forfeiture in the amount of $100,000,000, and require a special assessment of $125.

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CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing Memorandum was served upon defense counsel by hand-delivery and email, on this 15th day of January, 2009, as follows:

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EXHIBIT A

IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	:	CRIMINAL NO. _____
v.	:	DATE FILED: _____
ELI LILLY AND COMPANY	:	VIOLATION: 21 U.S.C. §§ 331(a), 333(a)(1) and
	:	352(f)(1) (distribution of misbranded drugs: inadequate directions for use - 1
	:	count) Notice of forfeiture

INFORMATION

COUNT ONE

THE UNITED STATES ATTORNEY CHARGES THAT:

At all times material to this information:

BACKGROUND

1. Defendant ELI LILLY AND COMPANY ("ELI LILLY") was a corporation operating and existing under the laws of the State of Indiana, with headquarters and manufacturing facilities located in Indianapolis, Indiana. ELI LILLY was engaged in the development, manufacture, promotion, and sale of pharmaceutical drugs intended for human use. ELI LILLY distributed its pharmaceutical drugs throughout the United States.

2. The Federal Food, Drug, and Cosmetic Act ("FDCA"), among other things, governed the interstate distribution of drugs for human use, as codified in 21 U.S.C. § 301, et seq. The FDCA and its implementing regulations prohibited the distribution of any new drug in interstate commerce until the sponsor or manufacturer of that new drug had received

approval from the United States Food and Drug Administration ("FDA"), based on an intensive application and review process. 21 U.S.C. § 355.

3. The FDCA required that the sponsor of a new drug submit a New Drug Application ("NDA") to the FDA, which identified all of the proposed uses of the drug intended by that sponsor, together with the proposed labeling for those uses, and data, generated in randomized and well-controlled clinical trials, that demonstrated to the FDA's satisfaction that the drug would be safe and effective for those intended uses. 21 U.S.C. §§ 331(d) and 355(b).

4. Until the FDA approved the NDA, including the proposed labeling, and found sufficient evidence of the drug's safety and efficacy for the uses proposed by the sponsor, the FDCA prohibited the sponsor from introducing the new drug into interstate commerce. 21 U.S.C. § 355(a). Only after the FDA approved the application was the sponsor permitted by law to promote and market the drug, and then only for the medical conditions of use specified in the approved labeling. Uses not approved by the FDA, and not included in the drug's approved label, were known as "unapproved uses" or "off-label uses."

5. Under the FDCA, if the sponsor of a drug wanted to market that drug for an unapproved or off-label use, the sponsor first was required to submit to the FDA each additional proposed use, together with evidence, in the form of randomized and well-controlled clinical studies, sufficient to demonstrate that the drug was safe and effective for each additional proposed therapeutic use. The sponsor could not label or promote the drug for any new intended use without the prior approval of the FDA.

6. The FDCA provided that a drug was misbranded if, among other things, the labeling did not bear adequate directions for its use. 21 U.S.C. § 352(f)(1). Adequate

directions for use could not be written for medical indications or uses for which the drug had not been found by the FDA to have been proven to be safe and effective through well-controlled clinical studies. Drugs that were promoted for uses that had not been approved by the FDA were thus deemed misbranded as a matter of law under Section 352(f)(1).

7. The FDCA prohibited the distribution in interstate commerce of a misbranded drug. 21 U.S.C. § 331(a) and (k).

FDA APPROVAL AND REGULATORY ACTION

8. On September 22, 1995, defendant ELI LILLY submitted an NDA seeking approval of a drug called Zyprexa (also known by the chemical name olanzapine) to treat schizophrenia and related disorders.

9. On September 30, 1996, the FDA approved Zyprexa for the short-term management of the manifestations of psychotic disorders.

10. On November 14, 1996, shortly after defendant ELI LILLY started to promote Zyprexa, the FDA sent ELI LILLY a letter informing the company that it found the company's promotional materials and activities "to be false or misleading, and in violation of the Federal Food, Drug, and Cosmetic Act." In particular, the FDA cautioned ELI LILLY about its marketing for elderly patients, advising the defendant that it was misleading to suggest that dosing of Zyprexa in the elderly was easy. In addition, the FDA cited false and misleading statements by an ELI LILLY officer, which characterized weight gain resulting from Zyprexa use as a therapeutic benefit, when in fact it was an adverse event noted in the approved labeling.

11. In October 1998, defendant ELI LILLY submitted a supplemental new drug application for the use of Zyprexa to treat psychosis associated with Alzheimer's disease.

In August 1999, defendant ELI LILLY withdrew its supplemental new drug application for the use of Zyprexa to treat psychosis associated with Alzheimer's disease.

12. Although defendant ELI LILLY submitted an application for use of an injectable form of Zyprexa to treat agitation associated with dementia, the FDA did not approve that use.

13. Defendant ELI LILLY never submitted a supplemental new drug application for the use of Zyprexa to treat dementia or Alzheimer's dementia.

14. The FDA never approved Zyprexa for the treatment of dementia, Alzheimer's dementia, psychosis associated with Alzheimer's disease, or the cognitive deficits associated with dementia.

15. In March 2000, the FDA approved the addition of the subheading "schizophrenia" in the Indications and Usage section of the Zyprexa label to modify "the short-term management of the manifestations of psychotic disorders." Also in March 2000, the FDA approved Zyprexa for the short-term treatment of acute manic episodes associated with Bipolar I Disorder. In November 2000, the FDA approved new labeling for Zyprexa for the short-term treatment of schizophrenia in place of the management of the manifestations of psychotic disorders, and for maintaining treatment response in schizophrenic patients who had been stable for approximately eight weeks and were then followed for a period of up to eight months.

16. On January 14, 2004, the FDA approved a label change for Zyprexa that added the following warning to the label, addressing the association of drugs such as Zyprexa (an atypical antipsychotic drug) with abnormalities in patients' glucose levels:

> Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

17. On February 16, 2006, the FDA approved a label change for Zyprexa that added a Black Box warning for increased mortality in elderly patients with dementia-related psychosis treated with atypical antipsychotics, including Zyprexa. The Black Box for Zyprexa stated:

> Increased Mortality in Elderly Patients with Dementia-Related Psychosis — elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. ZYPREXA (olanzapine) is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS).

A Black Box warning was the highest level of warning that the FDA could require on a drug's label.

18. On October 5, 2007, defendant ELI LILLY announced that it had updated the warnings section of the labeling for Zyprexa. The new changes included warnings for weight gain and hyperlipidemia (elevation of triglycerides and cholesterol), and updated information in the warning for hyperglycemia, including additional language on a greater association of increases in glucose levels with Zyprexa than with some other atypical antipsychotic medications. Specifically, the warning section of the label reads in part: "While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics."

ELI LILLY'S OFF-LABEL PROMOTION AND SALES PRACTICES

19. From approximately September 1999 through at least November 2003, defendant ELI LILLY unlawfully promoted Zyprexa for the treatment of agitation, aggression, hostility, dementia, Alzheimer's dementia, depression, and generalized sleep disorder. These intended uses were not approved by the FDA. In promoting Zyprexa for these off-label uses, ELI LILLY caused the drug to be misbranded under 21 U.S.C. § 352(f)(1).

20. Defendant ELI LILLY's management created marketing materials promoting Zyprexa for off-label uses, trained its sales force to disregard the law, and directed its sales personnel to promote Zyprexa for off-label uses.

21. Beginning in 1999, defendant ELI LILLY expended significant resources to promote Zyprexa in nursing homes and assisted living facilities, primarily through ELI LILLY's long-term care sales force. ELI LILLY focused its efforts on long-term care facilities

and the elderly, even though schizophrenia rarely occurs in elderly patients. ELI LILLY sought to convince doctors to prescribe Zyprexa to treat patients with disorders such as dementia, Alzheimer's dementia, depression, anxiety, and sleep problems, and behavioral symptoms such as agitation, aggression, and hostility, all of which are prevalent in the elderly population.

22. Defendant ELI LILLY's long-term care sales representatives executed this company plan, and promoted Zyprexa for the treatment of dementia, Alzheimer's dementia, depression, anxiety, and sleep problems, and behavioral symptoms such as agitation, aggression, and hostility.

23. Defendant ELI LILLY promoted Zyprexa for the treatment of psychotic and behavioral symptoms in patients with Alzheimer's dementia and for the treatment of behavioral and psychological symptoms of dementia using medical reprints that purportedly demonstrated Zyprexa's effectiveness in treating these diseases, even though ELI LILLY knew that its studies of Zyprexa for the treatment of Alzheimer's psychosis had yielded mixed clinical results, thus calling into question the effectiveness of Zyprexa for the treatment of this disease.

24. In late 2001, defendant ELI LILLY's most senior management decided to abandon ELI LILLY's efforts to obtain FDA approval for the use of Zyprexa for Alzheimer's psychosis. ELI LILLY's management made that decision in part because the drug's use in that disease produced mixed clinical results, a full clinical trial would be required, there were concerns about Zyprexa's safety risks, and the FDA threshold for approval was high. ELI LILLY never pursued FDA approval for Zyprexa for the treatment of dementia or Alzheimer's dementia.

25. Building on its unlawful promotion and success in the long-term care market, defendant ELI LILLY's executives decided to market Zyprexa to primary care

physicians. In October 2000, ELI LILLY began this off-label marketing campaign targeting primary care physicians, even though ELI LILLY knew that there was virtually no on-label use for Zyprexa in the primary care market.

26. Defendant ELI LILLY trained its primary care physician sales representatives to promote Zyprexa by focusing on symptoms, rather than Zyprexa's FDA approved indications. ELI LILLY created patient profiles for the sales force to use to promote Zyprexa in this market, including a fictitious patient called "Martha," who had behavior difficulty and dementia with agitation. ELI LILLY trained its primary care physician sales representatives to lead with the "Martha" patient profile.

27. Defendant ELI LILLY's primary care physician sales representatives promoted Zyprexa using the "Martha" patient profile, including Zyprexa's ability to treat the symptoms of dementia, such as agitation. "Martha" was a very successful tool for promoting and selling Zyprexa.

28. Anticipating the possibility of resistance from primary care physicians in prescribing Zyprexa, defendant ELI LILLY specifically trained its sales representatives on how to respond to doctors' concerns about off-label uses of Zyprexa, and how to continue to promote Zyprexa for off-label indications.

29. Defendant ELI LILLY retained medical professionals to speak to doctors during peer-to-peer sessions about off-label uses of Zyprexa, including depression, dementia and Alzheimer's dementia.

HARM CAUSED BY ELI LILLY'S OFF-LABEL PROMOTION

30. Defendant ELI LILLY's off-label promotion of Zyprexa raised safety issues, affected the treatment of patients, and undermined the FDA drug approval process. ELI LILLY undertook this illegal off-label promotion for its own financial gain, despite the potential risk to patients' health and lives.

31. Defendant ELI LILLY knew that significant weight gain and obesity were adverse side effects of Zyprexa. ELI LILLY knew that significant weight gain and obesity were factors in causing hyperglycemia and diabetes.

32. Despite the November 14, 1996 letter from the FDA, defendant ELI LILLY continued to promote adverse events as therapeutic benefits, particularly in elderly populations. For example, when promoting Zyprexa to health care providers for use in elderly populations, ELI LILLY's sales representatives stated that weight gain was a therapeutic benefit, not an adverse event of Zyprexa.

33. In addition, when promoting Zyprexa to health care providers for use in elderly populations, defendant ELI LILLY's sales representatives informed health care providers that somnolence was a therapeutic benefit, not an adverse event of Zyprexa. ELI LILLY's sales representatives informed health care providers that 5 milligrams of Zyprexa at 5 P.M., referred to by the sales slogan "5 at 5," would help patients at night with sleep problems, behavioral issues, and dementia.

34. More generally, the promotion of an off-label use for a prescription drug can interfere with the proper treatment of a patient. Off-label promotion can lull a physician into believing that the drug being promoted is safe and effective for the intended off-label use, and that the FDA has approved the drug for that use. Thus, off-label promotion can cause a doctor

and patient to forgo treatment with an FDA-approved drug that has been proven to be safe and effective, and instead to substitute a treatment urged by the sales representative that is not known to be safe and effective, and that may in fact be harmful.

PROFIT TO ELI LILLY

35. Defendant ELI LILLY profited by hundreds of millions of dollars by misbranding Zyprexa through off-label promotion, and distributing Zyprexa in interstate commerce.

36. From in or about September 1999 through on or about March 31, 2001, in the Eastern District of Pennsylvania and elsewhere, defendant

ELI LILLY AND COMPANY

introduced and caused the introduction into interstate commerce of quantities of Zyprexa, a drug within the meaning of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(g), which was intended for use in treating dementia, including Alzheimer's dementia, and which drug was misbranded within the meaning of Title 21 United States Code, Section 352(f)(1), in that Zyprexa's labeling lacked adequate directions for such uses.

In violation of Title 21, United States Code, Sections 331(a), 333(a)(1), and 352(f)(1).

NOTICE OF FORFEITURE

THE UNITED STATES ATTORNEY FURTHER CHARGES THAT:

1. As a result of the violation of Title 21, United States Code, Sections 331(a), 333(a)(1), and 352(f)(1) set forth in this information, defendant

ELI LILLY AND COMPANY

shall forfeit to the United States of America any quantities of Zyprexa, which between September 1999 and March 31, 2001 were misbranded when introduced into or while in interstate commerce, or while held for sale (whether or not the first sale) after shipment in interstate commerce, or which may not, under the provisions of Title 21, United States Code, Section 331, be introduced into interstate commerce.

2. If any of the property subject to forfeiture, as a result of any act or omission of the defendant:

(a) cannot be located upon the exercise of due diligence;

(b) has been transferred or sold to, or deposited with, a third party;

(c) has been placed beyond the jurisdiction of the Court;

(d) has been substantially diminished in value; or

(e) has been commingled with other property which cannot be divided without difficulty;

it is the intent of the United States, pursuant to Title 21, United States Code, Section 853(p), to seek forfeiture of any other property of the defendant up to the value of the property subject to forfeiture, that is $100,000,000.

All pursuant to Title 21, United States Code, Sections 334 and 853, and Title 28, United States Code, Section 2461(c).

LAURIE MAGID
ACTING UNITED STATES ATTORNEY

EUGENE THIROLF
DIRECTOR
OFFICE OF CONSUMER LITIGATION
CIVIL DIVISION
U.S. DEPARTMENT OF JUSTICE

EXHIBIT B

IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	:	
v.	:	CRIMINAL NO.
ELI LILLY AND COMPANY	:	

GUILTY PLEA AGREEMENT

Under Federal Rule of Criminal Procedure 11(c)(1)(C), the government, the defendant, Eli Lilly and Company (hereinafter "Eli Lilly"), and Eli Lilly's counsel enter into the following guilty plea agreement. Any reference to the United States or the government in this agreement shall mean the Office of the United States Attorney for the Eastern District of Pennsylvania and the Office of Consumer Litigation of the Department of Justice.

1. Eli Lilly agrees to plead guilty to Count One of an Information, waiving prosecution by indictment, charging it with the introduction into interstate commerce of drugs that were misbranded, a misdemeanor, in violation of 21 U.S.C. §§ 331(a), 333(a)(1) and 352(f)(1), and not to contest forfeiture as set forth in the notice of forfeiture seeking forfeiture of $100,000,000 in substitute assets, in lieu of the drugs which were promoted illegally and are no longer available, all arising from Eli Lilly's illegal promotion of its drug Zyprexa in the United States between September 1999 and March 31, 2001. Eli Lilly further acknowledges its waiver of rights, as set forth in Exhibit A to this agreement.

2. The parties agree that this plea agreement is made pursuant to Fed.R.Crim.P. 11(c)(1)(C) and that the following specific sentence is the appropriate disposition

of this case. Taking into consideration the factors set forth in 18 U.S.C. §§ 3553(a) and 3572, the agreed upon sentence is as follows:

A. Eli Lilly agrees to pay the special assessment in the amount of $125 on the date of sentencing.

B. Eli Lilly agrees to pay $615,000,000 to resolve this Information, of which $515,000,000 will be applied as a criminal fine, and $100,000,000 will be applied as substitute assets to satisfy the forfeiture obligation described in paragraph 2(C) below. Eli Lilly will pay these amounts within 10 business days of the date of sentencing. Eli Lilly and the government agree that this fine and forfeiture represent a fair and just resolution of all issues associated with loss, fine and forfeiture calculations.

C. Eli Lilly agrees that as a result of its acts or omissions, the forfeitable property, that is the drugs which were promoted off-label, are no longer available for forfeiture as the drugs cannot be located or have been transferred, sold or deposited with a third party, or otherwise disposed of, within the meaning of federal law. As a result, Eli Lilly agrees to the entry and satisfaction of a judgment and preliminary order of forfeiture on the date of the guilty plea, forfeiting to the United States the sum of $100,000,000 as substitute assets for the pertinent drugs. Eli Lilly agrees that, within 10 business days of the date of sentencing, Eli Lilly will make payment to the United States, by means of a wire transfer to the United States Marshal Service or check payable to same, in the amount of $100,000,000, this amount representing substitute assets of the offense for which it is pleading guilty, subject to forfeiture in full satisfaction of the judgment and preliminary order of forfeiture.

D. In light of the anticipated Corporate Integrity Agreement, Eli Lilly will not be placed on probation.

3. Eli Lilly and the United States intend to execute a separate civil settlement agreement. Eli Lilly waives any and all defenses and objections in this matter or in that civil proceeding which might be available under the Double Jeopardy and Excessive Fines clauses of the Eighth Amendment. The parties agree that, in light of the separate civil settlement agreement, and to avoid unduly complicating and prolonging the sentencing process, the appropriate disposition of this case does not include a restitution order.

4. Eli Lilly waives any claim under the Hyde Amendment, 18 U.S.C. § 3006A (Statutory Note), for attorney's fees and other litigation expenses arising out of the investigation or prosecution of this matter.

5. Eli Lilly understands, agrees and has had explained to it by counsel that the Court may impose the following statutory maximum sentence: a fine of $200,000, or twice the gross gain or gross loss, whichever is greater; a special assessment of $125; restitution as ordered by the Court; and a five-year term of Court supervision; in addition, forfeiture may be ordered. Eli Lilly further understands that the terms and conditions of any Court supervision may be changed, and extended, by the Court if Eli Lilly violates any of the terms and conditions of that supervision.

6. With respect to Eli Lilly's conduct:

A. The parties stipulate to the following facts and basis for the plea, criminal fine and forfeiture:

(1) Eli Lilly marketed Zyprexa, which was a drug within the meaning of 21 U.S.C. § 321(g)(1).

(2) Shipments of a drug in interstate commerce must be accompanied by labeling bearing adequate directions for use for each of the drug's intended uses.

(3) In September 1996, Zyprexa was approved by FDA for the short term management of the manifestations of psychotic disorders. In March 2000, FDA approved the addition of the subheading "schizophrenia" to the short term management of the manifestations of psychotic disorders. Also in March 2000, FDA approved Zyprexa for the short-term treatment of acute manic episodes associated with Bipolar I Disorder. In November 2000, FDA approved new labeling for Zyprexa for the short term treatment of schizophrenia in place of the management of the manifestations of psychotic disorders. Also in November 2000, FDA approved Zyprexa for maintaining treatment response in schizophrenic patients who had been stable for approximately eight weeks and were then followed for a period of up to eight months.

(4) Between September 1999 and March 31, 2001, Eli Lilly promoted Zyprexa in elderly populations as treatment for

dementia, including Alzheimer's dementia. Zyprexa is not approved by the FDA for treatment of dementia or Alzheimer's dementia. Eli Lilly's promotion of Zyprexa for these additional intended uses violated 21 U.S.C. § 352(f)(1), because Zyprexa's labeling did not bear adequate directions for each of the drug's intended uses.

B. The United States contends that, as a matter of relevant conduct, the conduct which forms the basis for this plea agreement, as set forth in subsection (A) above, continued past March 31, 2001. Eli Lilly does not admit that this conduct extended past March 31, 2001.

7. Eli Lilly and the United States retain the right to withdraw from this guilty plea agreement, and this plea agreement will be null and void, if the civil settlement agreement and Corporate Integrity Agreement are not executed prior to the filing of the Information.

8. Except as provided herein, the United States agrees that, other than the charges in the Information in this case, it will not bring any other criminal charges against Eli Lilly, its present and former parents, affiliates, divisions, and subsidiaries; their predecessors, successors and assigns for conduct which (A) falls within the scope of the criminal investigation in the Eastern District of Pennsylvania relating to Eli Lilly's drug Zyprexa; or (B) was known to the United States Attorney's Office for the Eastern District of Pennsylvania or the Office of Consumer Litigation of the Department of Justice as of the date of the execution of this plea agreement, and which concerned the sale, promotion, or marketing of Zyprexa in the United

States. The non-prosecution provisions of this paragraph are binding on the Office of the United States Attorney for the Eastern District of Pennsylvania, the Office of Consumer Litigation of the Department of Justice, and the United States Attorney's Offices for each of the other 93 judicial districts of the United States. The non-prosecution provisions are also binding on the Criminal Division of the United States Department of Justice, except that the investigation of Eli Lilly and its affiliates, divisions, and subsidiaries, being conducted by the Fraud Section of the Criminal Division regarding possible violations of the Foreign Corrupt Practices Act and related offenses in connection with the sales and marketing of Eli Lilly's products to foreign customers is specifically excluded from the non-prosecution provisions and release provided by this paragraph and agreement. Attached as Exhibit B is a copy of the letter to Acting United States Attorney Laurie Magid from the Assistant Attorney General, Criminal Division, Department of Justice, authorizing this agreement.

9. Eli Lilly understands that this guilty plea agreement does not bind any other government agency, or any component of the Department of Justice except as specified in paragraph 8 of this guilty plea agreement. Further, Eli Lilly understands that the United States takes no position as to the proper tax treatment of any of the payments made by Eli Lilly pursuant to this plea agreement, the civil settlement agreement, or the Corporate Integrity Agreement referenced in this plea agreement.

10. Eli Lilly agrees to waive the statute of limitations, and any other time-related defense, to the charge to which it is agreeing to plead guilty under this plea agreement, provided that the guilty plea is accepted by the Court.

11. Eli Lilly understands and agrees that, should it withdraw its plea or if Eli Lilly's guilty plea is not accepted by the Court for whatever reason, Eli Lilly may thereafter be prosecuted for any criminal violation of which the United States has knowledge arising out of this investigation, notwithstanding the expiration of any applicable statute of limitations between the time period when Eli Lilly signed this plea agreement and either Eli Lilly's withdrawal of its plea or the Court's rejection of its plea. In that event, Eli Lilly agrees that it will not raise the expiration of any statute of limitations as a defense to any such prosecution, except to the extent that the statute of limitations would have been a defense pursuant to the terms of a Tolling Agreement between the parties effective October 7, 2008, all subsequent extensions of the Tolling Agreement, and this paragraph.

12. In exchange for the undertakings made by the government in entering this plea agreement, Eli Lilly voluntarily and expressly waives all rights to appeal or collaterally attack the defendant's conviction, sentence, or any other matter relating to this prosecution, whether such a right to appeal or collateral attack arises under 18 U.S.C. § 3742, 28 U.S.C. § 1291, 28 U.S.C. § 2255, or any other provision of law. This waiver is not intended to bar the assertion of constitutional claims that the relevant case law holds cannot be waived.

13. Eli Lilly also waives all rights, whether asserted directly or by a representative, to request or receive from any department or agency of the United States any records pertaining to the investigation or prosecution of this case, including without limitation any records that may be sought under the Freedom of Information Act, 5 U.S.C. § 552, or the Privacy Act, 5 U.S.C. § 552a.

14. Eli Lilly is satisfied with the legal representation provided by its lawyers; Eli Lilly and its lawyers have fully discussed this guilty plea agreement; and Eli Lilly is agreeing to plead guilty because Eli Lilly admits that it is guilty of the misdemeanor described in paragraph 1.

15. Eli Lilly will acknowledge acceptance of this guilty plea agreement by the signature of its counsel and of an authorized corporate officer. Eli Lilly shall provide to the government for attachment as Exhibit C to this plea agreement a notarized resolution by Eli Lilly's Board of Directors authorizing the corporation to enter a plea of guilty, and authorizing a corporate officer to execute this agreement.

16. If acceptable to the Court, the parties agree to waive the presentence investigation and report pursuant to Rule 32(c)(1) of the Federal Rules of Criminal Procedure, and ask that Eli Lilly be sentenced at the time the guilty plea is entered.

17. It is agreed that the parties' guilty plea agreement contains no additional promises, agreements or understandings other than those set forth in this written guilty plea agreement, and that no additional promises, agreements or understandings will be entered into unless in writing and signed by all parties.

SIGNATURES FOR THE UNITED STATES

GREGORY G. KATSAS
Assistant Attorney General
Civil Division
United States Department of Justice

EUGENE M. THIROLF
Director, Office of Consumer Litigation
United States Department of Justice

JEFFREY T. STEGER
Trial Attorney
Office of Consumer Litigation
United States Department of Justice

ROSS S. GOLDSTEIN
Trial Attorney
Office of Consumer Litigation
United States Department of Justice

LAURIE MAGID
Acting United States Attorney

LINDA DALE HOFFA
Chief, Criminal Division
Assistant United States Attorney

CATHERINE VOTAW
Assistant United States Attorney

MARILYN S. MAY
Assistant United States Attorney

DATE: 1-14-09

DENISE S. WOLF
Assistant United States Attorney

SIGNATURE FOR ELI LILLY

DATE: 14 Jan. 2009

ROBERT A. ARMITAGE
Senior Vice President and General Counsel
Eli Lilly and Company

SIGNATURES OF ELI LILLY'S ATTORNEYS

DATE: 1/14/09

NINA M. GUSSACK
Pepper Hamilton LLP
Counsel for Defendant

DATE: 1/14/09

THOMAS M. GALLAGHER
Pepper Hamilton LLP
Counsel for Defendant

DATE: 1/14/09

PAUL E. KALB
Sidley Austin LLP
Counsel for Defendant

DATE: 1/14/09

BRADFORD A. BERENSON
Sidley Austin LLP
Counsel for Defendant

Exhibit A

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

UNITED STATES OF AMERICA :

v. : CRIMINAL NO.

ELI LILLY AND COMPANY :

ACKNOWLEDGMENT OF RIGHTS

Eli Lilly and Company ("Eli Lilly"), through its properly authorized officer, hereby acknowledges that it has certain rights that it will be giving up by pleading guilty.

1. Eli Lilly understands that it does not have to plead guilty.

2. Eli Lilly may plead not guilty and insist upon a trial.

3. At that trial, Eli Lilly understands:

   a. that Eli Lilly would have the right to be tried by a jury that would be selected from the Eastern District of Pennsylvania and that along with its attorney, Eli Lilly would have the right to participate in the selection of that jury;

   b. that the jury could only convict Eli Lilly if all twelve jurors agreed that they were convinced of Eli Lilly's guilt beyond a reasonable doubt;

   c. that the government would have the burden of proving Eli Lilly's guilt beyond a reasonable doubt and that Eli Lilly would not have to prove anything;

   d. that Eli Lilly would be presumed innocent unless and until such time as the jury was convinced beyond a reasonable doubt that the government had proven that Eli Lilly was guilty;

   e. that Eli Lilly would have the right to be represented by a lawyer at this trial and at any appeal following the trial, and that if Eli Lilly could not afford to hire a lawyer, the court would appoint one for Eli Lilly free of charge;

   f. that through Eli Lilly's lawyer Eli Lilly would have the right to confront and cross-examine the witnesses against Eli Lilly;

g. that Eli Lilly could call witnesses to testify in its defense if Eli Lilly wanted to, and Eli Lilly could subpoena witnesses for this purpose if Eli Lilly wanted to; and

h. that Eli Lilly would not have to call witnesses to testify or otherwise present any defense if Eli Lilly did not want to, and that if Eli Lilly did not present any evidence, the jury could not hold that against Eli Lilly.

4. Eli Lilly understands that if Eli Lilly pleaded guilty, there will be no trial and Eli Lilly would be giving up all of the rights listed above, as well as any other rights associated with the trial process arising under statute, common-law, or judicial precedent.

5. Eli Lilly understands that if Eli Lilly decides to enter a plea of guilty, the judge will ask Eli Lilly representatives questions under oath, and that if any of those representatives lie on behalf of Eli Lilly in answering those questions, those persons could be prosecuted for the crime of perjury, that is, for lying under oath.

6. Eli Lilly understands that if Eli Lilly pleads guilty, Eli Lilly has waived its right to appeal, except as set forth in appellate waiver provisions of the plea agreement.

7. Understanding that Eli Lilly has all these rights and that by pleading guilty Eli Lilly is giving them up, Eli Lilly still wishes to plead guilty.

ROBERT A. ARMITAGE
Senior Vice President and General Counsel
Eli Lilly and Company

PAUL E. KALB
Sidley Austin LLP
Counsel for Defendant

DCI 1305133v.1

Exhibit B

U.S. Department of Justice

Criminal Division

Acting Assistant Attorney General *Washington, D.C. 20530*

JAN 9 2009

The Honorable Laurie Magid
Acting United States Attorney
Eastern District of Pennsylvania
Philadelphia, Pennsylvania 19106

Attention: Catherine Votaw
Assistant United States Attorney

Re: Global Non-prosecution Agreement for Eli Lilly and Company

Dear Ms. Magid:

This is in response to your request for authorization to enter into a global case disposition agreement with the business entity known as Eli Lilly and Company.

I hereby approve the terms of the Plea Agreement, including Paragraph 8, in which the United States Attorney's Offices and the Criminal Division of the Department of Justice agree not to initiate further criminal prosecutions as set out therein.

You are authorized to make this approval a matter of record in this proceeding.

Sincerely,

Matthew W. Friedrich
Acting Assistant Attorney General

John C. Keeney
Deputy Assistant Attorney General
Criminal Division

Exhibit C

CERTIFICATE OF SECRETARY
ELI LILLY AND COMPANY

I, James B. Lootens, certify that I am Secretary of Eli Lilly and Company, an Indiana Corporation (the "Company"), and that I am authorized to give this Certificate on behalf of the Company.

I further certify that the resolutions set forth below were adopted by the Board of Directors of the Company at a meeting duly held on January 14, 2009, and that such resolutions remain in full force and effect as the date of this certificate.

WHEREAS, Eli Lilly and Company has found that it is in the best interest of the company to enter into proposed federal and related state settlements regarding Zyprexa, including entering into:

(1) a plea agreement with the United States Attorney's Office for the Eastern District of Pennsylvania and the Office of Consumer Litigation to plead guilty to a single misdemeanor count of violation of the Federal Food, Drug, & Cosmetic Act ("FDCA") substantially in the form presented to the meeting, initialed by the secretary, and ordered to be filed with the records of the meeting as Attachment 1;

(2) civil settlement agreements with the federal government and the coordinating states;

(3) a Corporate Integrity Agreement with the HHS Office of Inspector General substantially in the form presented to the meeting, initialed by the secretary, and ordered filed with the records of the meeting as Attachment 2; and

(4) all other documents necessary to effectuate the settlement;

it is

RESOLVED, That the company, having been counseled on the company's legal rights and the factual basis for the plea as set forth in Federal Rule of Criminal Procedure 11(b), does hereby authorize to cause its General Counsel, Mr. Robert A. Armitage, and such of its outside counsel as Mr. Armitage shall designate, to enter into and execute a plea agreement substantially in the form of Attachment 1 and the other settlement documents referenced above.

RESOLVED, FURTHER, That any and all agreements executed on behalf of the company in connection with the transactions contemplated, and all further actions necessary to complete and effectuate those transactions, including the personal appearance in court to enter a plea of guilty on behalf of the company by a corporate officer of at least the level of vice president as designated by Mr. Armitage, hereby are ratified and approved.

This certificate is executed on January 14, 2009.

James B. Lootens
Secretary

UNITED STATES OF AMERICA

STATE OF INDIANA)
) SS
COUNTY OF MARION)

Before me, a Notary Public for Marion County, State of Indiana, personally appeared James B. Lootens and acknowledged the execution of the foregoing instrument this 14th day of January, 2009.

Marie A. Thomas
NOTARY PUBLIC
Marie A. Thomas
My Commission Expires
February 10, 2009
Resident of Marion County

(SEAL)