[redacted]

([redacted]) Lilly hid the risks and massaged the label to minimize safety concerns. But they were legally and ethically obliged to do just the opposite.

4. In February 2000, European Regulators Asked for a Full Review of Prior Adverse Event Reports

213. Although Lilly had been in possession of adverse event data and internal studies demonstrating the risk of diabetes associated with Zyprexa for years, not until regulatory agencies in Europe and the United States pressured Lilly to provide clinical data, review prior studies, and assess the safety of olanzapine did Lilly do so. Lilly begrudgingly obeyed, but only under compulsion.

214. On February 21, 2000, the European Agency for the Evaluation of Medicinal Products ("EAEMP") sent a telefax to Mr. J.C. Saunder of Eli Lilly Ltd. UK. Specifically, Dr. Juhana Idanpaan-Heikkila of the EAEMP ordered Lilly to step up its review of risk factors and provide that information to the EAEMP: "[redacted]." ([redacted])

215. Further, the EAEMP requested full review of all known cases of diabetic ketoacidosis: "[redacted]."

([redacted]) Lilly was aware of numerous instances of diabetic ketoacidosis. In an NDA Periodic Report, Lilly had previously reported three incidents of ketoacidosis from April 1 to June 30, 1998. ([redacted]) In another Periodic Adverse Drug Event Report, Lilly had previously reported five instances of diabetic acidosis and two instances of diabetic coma between September 30 and December 30, 1997. ([redacted]) Lilly had failed to clearly disclose those instances to the European regulatory authorities.

216. Rather than provide critical information as it arrived, Lilly waited for regulatory authorities in both Europe and the United States to demand a thorough accounting of the risks of olanzapine.

5. In May 2000, the FDA Asked Lilly to Look at Larger Patient Pools and Conduct a Thorough Assessment of Previous Studies But Lilly Spun the Science According to Its Marketing Strategy

217. The FDA evidently did not trust the research done by Lilly on diabetes and hyperglycemia, in part, because of the small numbers of patients treated in each study. Consequently, on May 1, 2000, the FDA sent Lilly "[redacted]." ([redacted]) The FDA basically told Lilly that it needed credible data on diabetes and hyperglycemia.

218. Specifically, the FDA asked for the following information, apparently not trusting that Lilly had previously and fully disclosed these harms:

[redacted]

[redacted]

([redacted]) In addition, the FDA had required a "[redacted]." *Id.* The FDA also wanted "[redacted]." *Id.*

219. Nearly three months later, Lilly partially responded to the FDA's request of May 1, 2000. Gregory T. Brophy, Director of Lilly's US Regulatory Affairs, sent a letter to the FDA on July 31, 2000. Dr. Brophy attached a "Note to Reviewer" to his letter. The Note to Reviewer stated: "[redacted]." ([redacted])

220. As part of its July 31, 2000 response to the FDA, Lilly submitted an analysis of 78 controlled trials. In addition, Lilly provided "[redacted]." ([redacted]) However, most of the information was misleading, especially as it pertained to full disclosure of the risks of prolactin, weight gain, and hyperglycemia.

221. Lilly misled the FDA on prolactin. In "[redacted]" of the "[redacted]", Lilly suggested that Zyprexa did not elevate prolactin levels, writing [redacted]

[redacted]." ([redacted]) Lilly implied that olanzapine did not produce heightened prolactin levels. But Lilly's own proposed label of October 2000 admitted the risk of heightened prolactin: "[redacted]." In July 2000, however, Lilly said that risperidone was "[redacted]."

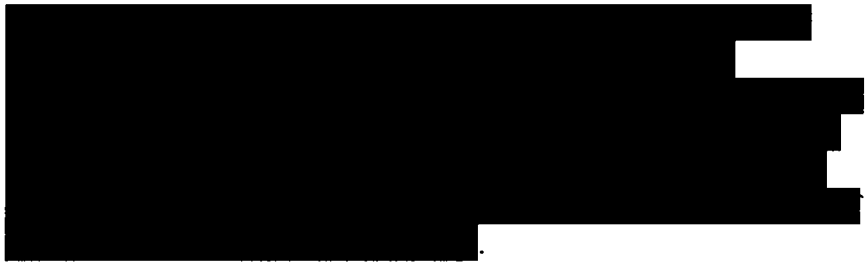
222. Lilly also misled the FDA on weight gain. In "[redacted]" of the "[redacted]" submitted on July 31, 2000, Lilly admitted that [redacted]." Sticking to formula, Lilly deflected responsibility from its own drug and dispersed blame among the class as a whole. Lilly spent nearly an entire page discussing study after study on—of all things—clozapine's association with weight gain. In a subsequent short paragraph, Lilly mentioned that "[redacted]" and "[redacted]." These bare references to olanzapine masked the fact that olanzapine was among the top one or two atypical antipsychotics for weight gain. Lilly's discussion of clozapine only clouded the picture.

223. In "[redacted]" of its July 31, 2000 attachment, Lilly told the FDA that "[redacted]." ([redacted]) But Lilly downplayed the

results:

Lilly absurdly suggested that all patients enrolled in studies gain weight and, therefore, it was not olanzapine's fault if those patients gained weight too. Lilly did not mention that its own 1993 study had shown "[redacted]" and consistent weight gain among olanzapine patients. ([redacted]) Nor did Lilly mention the possibility that olanzapine caused weight gain. Instead, Lilly practiced its blame-the-victim marketing strategy on the FDA.

224. Lilly tried to hide the likelihood of hyperglycemia, blaming it on pre-disposed factors among schizophrenic patients. In the "[redacted]" attached to its July 31, 2000 letter, Lilly told the FDA:



225. Lilly effectively blamed the victims. To Lilly, it was the pre-disposed factors that made hyperglycemia more likely – not olanzapine. What this explanation intentionally overlooked was that increased incidence of diabetes in Zyprexa users appeared in studies in which *all* subjects were diagnosed schizophrenics. Since Zyprexa increased the incidence of diabetes over placebo when both the Zyprexa group and the placebo group were schizophrenics, Lilly's assertion that schizophrenics are pre-disposed to diabetes did nothing to exonerate Zyprexa. Lilly was aware of this fact but continued to push the pre-disposition explanation rather than admit to the dangers associated with its blockbuster drug.

226. In "[redacted]," Lilly claimed that hyperglycemia simply occurred in the population at large and that olanzapine produced no risk of hyperglycemia:

[redacted]

([redacted]) Lilly claimed that olanzapine led to no more hyperglycemia than a placebo, and it said that 78 trials supported this conclusion. In actuality, Lilly knew that hyperglycemia occurred more often under olanzapine than in placebo.

227. Almost one year later, on May 21, 2001, Lilly sent a second letter to the FDA to complete its response to the original FDA letter of May 1, 2000 requesting further information on the risks of diabetes and hyperglycemia. ([redacted]) Gregory T. Brophy, the director of Lilly's U.S. Regulatory Affairs, sent the FDA a "[redacted]." He attached a "[redacted]" ("[redacted]") to his letter. ([redacted])

228. The Note summarized Lilly's additional research. Lilly had analyzed data from an "[redacted]" database with thousands of patients on antipsychotics. Lilly concluded from this database that hazard ratios for diabetes were 3.5 for conventional antipsychotics, 3.1 for atypical antipsychotics, and 3.0 for olanzapine. In addition, Lilly analyzed a British database called the "[redacted]" with 8 million patients from the United Kingdom. Lilly found that [redacted]." The hazard ratio for atypical antipsychotics was 3.3.

229. On top of analyzing these larger pools, Lilly summarized its own clinical trials. That showed "[redacted]." In essence, this was an admission that patients on olanzapine had higher levels of glucose. Lilly finally concluded that "[redacted]." This was another admission. But, as usual, Lilly deflected responsibility by pointing its finger at competitors and older antipsychotics with similar problems.

230. Lilly's response to the FDA's inquiries was of a piece with its overall strategy for dealing with concerns that Zyprexa was associated with diabetes. Whether responding to the FDA or prescribing doctors, Lilly consistently employed the two dodges of pre-disposition and class effect to deflect inquiries about what its own studies had demonstrated that Zyprexa increases the incidence of diabetes in patients who take it. An internal Lilly memorandum confirms this fact, stating "[redacted]." ([redacted])

6. In October 2000, the FDA Required Lilly to Add the Risks of Diabetic Coma and Neuroleptic Malignant Syndrome to the Label and to Delete Language That Suggested Olanzapine Did Not Increase Glucose Levels

231. On May 9, 2000, Lilly submitted a "[redacted]" to the FDA. ([redacted], reporting that "[redacted]".) Lilly claimed that this label change was based on [redacted]." ([redacted]) According to Lilly, this label

change was not connected to the FDA's letter of May 1, 2000 because Lilly had received that letter one day *after* proposing the May 9, 2000 label change.

232. Specifically, Lilly sought two changes to the Zyprexa label in its proposal of May 9, 2000:

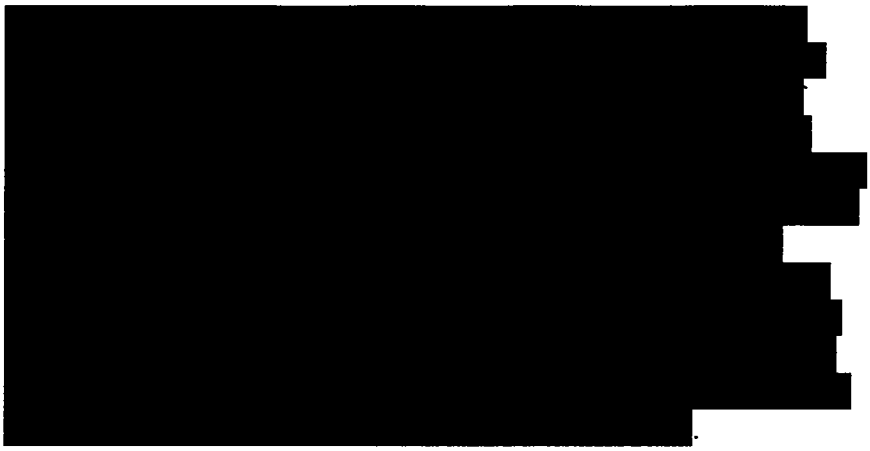
[redacted]

Id. On July 31 2000, Gregory Brophy, Director of US Regulatory Affairs at Lilly, repeated this same offer to change the label in a letter to the FDA. ([redacted])

233. The phrase "diabetic coma" was inserted into the label after the FDA approved it via a letter to Lilly dated October 11, 2000. However, the FDA rejected Lilly's proposed "[redacted]." As a result, there were no changes in the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section from 1996 until at least January 2004. That section remained precisely the same from 1996 through 2003.

234. The reason why the FDA rejected Lilly's proposed change to that section in 2000 was because Lilly's proposed revision was misleading. In essence, Lilly tried to say that olanzapine caused no increase in glucose levels. This is the text that Lilly proposed:

[redacted]



This summary suggested that random glucose levels were the same in olanzapine patients as a placebo. If Lilly had its way, this misleading statement would have been inserted into the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section. But the FDA said, "no."

235. On October 11, 2000, Dr. Russell Katz, Director of the Division of Neuropharmacological Drug Products, Office of Drug Evaluation I, FDA Center for Drug Evaluation and Research, wrote to Gregory T. Brophy, Director of US Regulatory Affairs, regarding the October 2000 proposed label change. Dr. Katz felt that the paragraph on glucose levels would be misleading:

The FDA characterized Lilly's proposed statement as "[redacted]" for the label. To Dr. Katz and the FDA, Olanzapine was not as safe as Lilly made it out to be. There was simply not enough data and analysis to support Lilly's proposed revision to the label. And the FDA would not permit Lilly to use the label as a marketing device to infer "[redacted]"

that was not proven to exist.

236. As a result of the FDA's refusal in 2000, the ADVERSE REACTIONS, Additional Findings Observed in Clinical Trials, Laboratory Changes section was not revised until years later when the FDA approved language that told the truth—i.e., olanzapine increased the level of glucose. The olanzapine label that was ultimately revised on September 20, 2005 warned:

[redacted]

This is what the FDA was looking for all along. But Lilly did not provide it in October 2000 when it denied that olanzapine led to glucose increases.

237. In his letter of October 11, 2000, Dr. Russell Katz of the FDA approved a new warning for Neuroleptic Malignant Syndrome (NMS). Dr. Katz said the following addition to the "[redacted]" section was "[redacted]," pending Lilly's submission of 20 paper copies of the "[redacted]":

[redacted]

In other words, from October 2000 onwards, Lilly would have to warn about NMS on the label. This was a first.

238. Dr. Katz approved the addition of "[redacted]" to the label warnings in his letter dated October 11, 2000. This addition to the "[redacted]" section was "[redacted]" pending submission of "[redacted]." Lilly was obligated to insert the term "[redacted]" into the "[redacted]" subsection of the "ADVERSE

REACTIONS" section. As a result, the label subsequently warned:

> Adverse events reported since market introduction which were temporally (but not necessarily causally) related to ZYPREXA therapy include the following: allergic reaction (e.g., anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, pancreatitis, and priapism.

(Zyprexa Zydis Label (revised 2003) ("action date" of Jan. 14, 2004)) The term "diabetic coma" had not previously appeared in this section until the FDA's requirement of October 11, 2000.

I. 2001-2002: Ongoing Operations of the Unlawful Marketing Enterprises

239. Despite the mounting evidence known to Lilly regarding the adverse weight gain, hyperglycemia, diabetes, cardiovascular, and other risks of Zyprexa, the lack of superior comparative efficacy of Zyprexa to other antipsychotics and the recklessness of their off-label promotions, in the early 2000's Lilly continued its ongoing operation of the Zyprexa Unlawful Marketing Enterprises and planned to further market Zyprexa for use in patients for whom the drug's approval was never intended. According to an internal document, Lilly decided that "[redacted]" These new indications included "[redacted]." ([redacted])

240. In order to reach those goals, Lilly undertook a massive strategy change in late 2000 and began to target primary care physicians with the aim of increasing their utilization of Zyprexa. ([redacted]) The strategy encouraged physicians to focus on symptoms and behaviors rather than diagnoses, emphasizing how Zyprexa is "[redacted]." ([redacted]) Suppression of side effects and metabolic risks continued to be part and parcel of the plan.

1. Continued and Growing Knowledge of Adverse Side Effects

241. As Lilly continued to downplay the risks of Zyprexa to consumers, doctors, and the FDA, more and more of its own studies and clinical trials conclusively demonstrated the life-threatening risks associated with the use of its drug.

242. In a study entitled "[redacted]" with an amended protocol dated March 9, 2001, Lilly noted "[redacted]" and that "[redacted]." ([redacted])

243. While most of the attention to date had been on the glucose and metabolic side effects of Zyprexa, they were not the only risks of which Lilly was aware. In March 2001, Ernie Anand of Lilly brought to the attention of some of his colleagues an article on atypical antipsychotic cardiovascular risk. He noted that it was "[redacted]" and that the "[redacted]." In response, Dr. Charles Beasley stated that [redacted]." In the same breath, however, Dr. Beasley pointed out:

[redacted]

[redacted]

([redacted].)

244. An April 6, 2001 Lilly internal analysis of its UK General Practice Research database (GPRD) found that patients treated with either conventional or atypical antipsychotics had a higher risk of developing diabetes during exposure to the drug. The risk was found to be higher for those taking atypicals such as olanzapine and risperidone than for those taking conventional antipsychotics. As the study states, "[redacted]." ([redacted]) The study also notes that

[redacted]

([redacted]) This study was forwarded for discussion in an e-mail sent by John Holcombe on April 9, 2001, where he calls it "the most recent version of the epidemiological data from the GPRD regarding antipsychotic drug use and dia[redacted]." ([redacted] 219615[redacted]6)

245. The companion study entitled "[redacted]" analyzed a prescription claim database and concluded [redacted]." ([redacted]) The study abstract, dated

April 18, 2001, also noted [redacted] Further, the authors stated, [redacted]

246. On April 12, 2002, Lilly conducted a Policy Committee Meeting on the Zyprexa safety overview, addressing clinical data on weight gain and diabetes in connection with Zyprexa use. In summarizing the clinical data on diabetes, Lilly draws attention to a "[redacted]" Continuing on metabolic issues, Lilly states that "[redacted]" and that "[redacted]." Instead of working to protect patients from these effects, Lilly focused on continuing sales, concluding "[redacted]."

2. Suppression of Side Effects and Risks

247. In early 2001, Lilly was well aware that Zyprexa was among the worst of the antipsychotics in terms of weight gain. In a "[redacted]" slide set presentation dated February 2001, Lilly stated that the main "[redacted]" of olanzapine, as compared to its competitors, were weight gain, sedation, value for money, and reduction of depressive episodes.

In fact, Zyprexa ranked at the very bottom of its competition on weight gain and ability to avoid sedation. ([redacted])

248. Despite this knowledge, Lilly attempted to avoid or minimize the issue, misleading physicians as to the degree, manageability, and incidence of weight gain in olanzapine patients. Further, Lilly adopted a campaign summed up by the words "[redacted]," instructing its sales force to tell psychiatrists and physicians that "[redacted]." ([redacted])

249. In a February 8, 2001 presentation for the "[redacted]," Lilly instructed sales representatives on how to address mounting concerns among prescribing physicians about Zyprexa use and weight gain, hyperglycemia, and diabetes. Market research indicated "[redacted]." ([redacted]) Accordingly, Lilly directed the force to "[redacted]." [redacted]. ([redacted]) Sales representatives were thus instructed to "[redacted]" with them to handle the objections of the two types of physicians. ([redacted])

250. The "[redacted]" [redacted]:

[redacted]

251. Overall, the strategy appeared to work for Lilly. Initial market research showed a "[redacted]" ([redacted])

252. In March 2001, Lilly further revised its "[redacted]

[redacted]e" to help its sales force when "[redacted]." ([redacted]) The strategy guide notes "[redacted]." ([redacted]) Despite the stated differences in blood glucose for patients on Zyprexa and the known connection between increased blood glucose and diabetes, Lilly continued to tell physicians that "[redacted]." ([redacted])

253. Concurrently, Lilly developed other materials "[redacted]" based on the company's belief that "[redacted]." ([redacted]) These materials, including slide sets, studies, physician management tools, and trainings, were designed to "[redacted]," provide data to "[redacted]" for use in presentations on Zyprexa and weight gain or hyperglycemia/diabetes, and provide "[redacted]." ([redacted])

254. In a June 20, 2001 "[redacted]." ([redacted].) Part of McKinsey's

recommended strategy entailed Lilly acknowledging weight gain, diabetes, and hyperglycemia as "[redacted]" rather than avoiding the issue. However, a second part involved a new "[redacted]" aimed at emphasizing Zyprexa's efficacy "[redacted]" while showing diabetes risk was a class effect rather than one limited to olanzapine. This strategy was to be used in the United States, Canada, France, and the UK. ([redacted]) Lilly followed the second part to the letter, but continued to omit a warning about the "[redacted]" of diabetes and hyperglycemia for years to come.

255. Lilly instead continued to sidestep questions about the risk of treatment-emergent diabetes while on olanzapine. In two marketing presentations from 2001, Lilly informed its sales force "[redacted]!" Regarding diabetes, Lilly states

[redacted]:

1) [redacted]
2) [redacted]
3) [redacted]
4) [redacted]
5) [redacted]!

([redacted].) Not addressing the "[redacted]" unless raised by a physician is both a violation of the mandate of fair and balanced information and a willful omission of material fact, especially given Lilly knew that many PCPs were not aware of the issue.

256. Concurrently, and in line with its avoidance of the "[redacted]," Lilly continued to emphasize that treatment with Zyprexa was "[redacted]" and "[redacted]," promoting the claim in marketing brochures in October 2001. ([redacted])

257. In April 2002, the Japanese government forced Lilly to revise its label in Japan and warn of the risk of treatment-emergent diabetes. Even after the Japanese government mandated that Lilly include warnings of the risk of diabetes (after only nine adverse event reports), Lilly continued to omit any warning of diabetes from its Zyprexa label in the United States.

258. Notably, Lilly knew long before April 2002 that the Japanese government had serious concerns about Zyprexa's safety. In an email dated September 25, 2001 (only about 3 months after Zyprexa was launched in Japan), Takashi Taniguchi, a representative of Eli Lilly's Japanese affiliate, directed an email to Lilly's Timothy F. Parshall and several other Lilly insiders concerning "[redacted]". Due to its' significance, Mr. Parshall subsequently forwarded the email to Lilly's Jared G. Kerr. In the email, Mr. Taniguchi stated:

[redacted]

[redacted]

([redacted])

259. Despite this substantial evidence linking Zyprexa use with diabetes and/or hyperglycemia, Lilly continued to down-play these problems. In mid-2002, a Lilly market research analyst wrote:

[redacted]

([redacted])

260. Lilly's suppression or manipulation of side effects and risks of olanzapine did not go unnoticed. On June 15, 2002, Eli Lilly's Dennis G. West sent an email to Dr. John Newcomer, a one-time Lilly consultant, concerning a mailing Lilly sent to physicians focusing on positive statements about Zyprexa made by John Buse, M.D, another consultant for Lilly. The email also related to previous discussions between Mr. West and Dr. Newcomer relating to Zyprexa use and its relationship to glucose/insulin irregularities. Mr. West stated:

[redacted]

[redacted]

([redacted]) Lilly did not make a change in their warnings to this effect until September of '03.

261. Dr. Newcomer immediately took exception to Mr. West's comments and accused Lilly of engaging in a "[redacted]." Specifically, Dr. Newcomer stated,

[redacted]

([redacted])

262. The sales force raised a similar concern shortly thereafter. In internal email correspondence dated September 13, 2002 with the subject line "[redacted]" sales representative Jerry D. Clewell asked

[redacted]

[redacted]

([redacted]) Despite Dr. Newcomer's concern that Lilly was playing fast and loose with study results and the connection between olanzapine use and diabetes and questions from the sales force about such connections, Lilly stuck to the party line. Robert Browne, Senior Outcomes Research Advisor for Lilly, responded that he had not heard of any such plans to send "[redacted]" to physicians. ([redacted])

3. Off-Label Promotion to Primary Care Physicians

263. Lilly began promoting Zyprexa to primary care physicians in September 2000. ([redacted]) The strategy, building on the 1996-2000 off-label campaign to target various forms of depression, sought to position Zyprexa as a "[redacted]" and "[redacted]" References to this positioning abound in Lilly's internal documents, testifying to the strength of the effort directed at the PCP market.

264. In an undated overhead training presentation entitled "[redacted]", Lilly identified the "[redacted]" for opening the door to the elderly market for Zyprexa: "[redacted]" ([redacted]) Lilly instructed the sales force that patient profiles "[redacted]" and that the focus should be on "[redacted]" such as "[redacted]" rather than

diagnoses. ([redacted]) Incredibly, Lilly went so far as to direct its sales representatives to misrepresent the uses for which Zyprexa had received FDA approval, stating it was "[redacted]" ([redacted]) Zyprexa has never been approved for use in the treatment of dementia.

265. In 2001, Lilly's Michael Bandick (Brand Manager of Zyprexa) met with sales representatives to detail the positive aspects of the Pierre Tran study on Zyprexa, published in the Journal of Clinical Psychopharmacology in 1997, and encourage them to promote the drug to "[redacted]" ([redacted]) Bandick directed the sales representatives to rely upon the Tran study, which favored Zyprexa over Risperdal, but not to give it to customers. In a mock discussion with a physician following Bandick's intro, sales representatives were encouraged to market to physicians who don't prescribe antispsychotics by telling the physician that "[redacted]" ([redacted])

266. Likewise, a February 20, 2001 presentation authored by Bandick reemphasized Lilly's plan to "[redacted] The strategy entailed an "[redacted]", "[redacted]" and "[redacted]" ([redacted])

267. Lilly reinforced this message at a March 12, 2001 presentation to the Zyprexa sales force, starring Michael Bandick, stating that Lilly "[redacted]" ([redacted]) Further, while noting the desire to

promote Zyprexa to the elderly, Bandick made certain to emphasize that the nursing home population was not the only target the team was after:

[redacted]

268. In a draft internal marketing document, dated April 10, 2001, Lilly focuses on expanding the market of Zyprexa by "[redacted]" The strategy is to establish Zyprexa as a "[redacted]" This is to be done by: "[redacted]" "[redacted]" "[redacted]" The strategy is to provide PCP's with patient profiles: "[redacted]" "[redacted]" "[redacted]" The document goes on to say that "[redacted]", the patient with mood problems, is the future of Zyprexa use by primary care physicians. The internal marketing document also proposes a post-marketing "[redacted]" – a Clinical Trial Not Intended for Registration – with an internally written protocol. Third party vendors Parexcel,

The Lewis Group, and/or Covance are suggested. The document also lists "[redacted]" as: "[redacted]" "[redacted]" "[redacted]" and "[redacted]" ([redacted])

269. Lilly even implied that PCPs had a duty to prescribe antipsychotics as part of "[redacted]" A Lilly slide set dated June 14, 2001 and titled "[redacted]" tells a story of "[redacted]" Lilly insisted that "[redacted]" was necessary for a broad range of symptoms, including "[redacted]" Further, the PCP's "[redacted]" ([redacted])

270. To assist sale representatives in encouraging PCPs to prescribe olanzapine for treatment of symptoms not necessarily caused by schizophrenia, Lilly prepared a "[redacted]", Lilly painted a picture of a good candidate for Zyprexa:

[redacted]

([redacted]) In this manner, Lilly encouraged PCPs to use Zyprexa for the treatment of symptoms rather than diagnoses.

271. In spite of Lilly's suppression of the risks of diabetes, by late 2001, even primary care physicians were raising concerns over the connection to glucose irregularities, hyperglycemia, and diabetes. The September 2001 Hyperglycemia/Diabetes Data on Demand Resource Guide states that it was developed because "[redacted]" Accordingly, the sales force was to emphasize that "[redacted]", that diabetes is common and has lots of risk factors, and that giving a drug should be based on the risks/benefits equation. Further, sales reps should "[redacted]" ([redacted])

272. Lilly encouraged its sales representatives to view physicians as fitting into one of five market segments based on their prescribing patterns: High Flyers; Rule Bounds; Skeptical Experimenters; Selective Majority; or Systematic Conservatives. High Flyers, for example, were those who "[redacted]" while the Selective Majority "[redacted]" Sales representatives were encouraged to provide PCPs in this group with "[redacted]" ([redacted])

273. Lilly recognized that those in the Rule Bound, Systematic Conservatives, and Selective Majority groups would not typically prescribe Zyprexa and that PCPs would have to be coached into writing these prescriptions: "[redacted]

[redacted]" ([redacted]) However, its sales representatives would "[redacted]" ([redacted])

274. Lilly made no secret of its desire to sell Zyprexa beyond its indicated and approved use. In a May 21, 2002 email marked "[redacted]", Robert Graham of Lilly told his colleagues that as a follow-up to recent discussions about the challenges ahead for Zyprexa, it was important to remember that Zyprexa is an "[redacted]" and that "[redacted]" ([redacted])

275. Lilly's efforts to promote Zyprexa for use as a general mood stabilizer in the treatment of depression have resulted in tremendous revenue for the company. Depression-related sales of Zyprexa from 1999 to 2005 reached nearly $3 billion.

4. Manipulation of Studies

276. While Lilly promoted Zyprexa to primary care physicians for a variety of illnesses and down-played the risks of adverse metabolic events, the company also sought to suppress side effect information by manipulating and spinning studies, clinical trials, and reports from academia and the field.

277. Lilly addressed its deficiencies with publications, hoping to hide the severity of Zyprexa's side effects. A Lilly email correspondent said that the focus of the Zyprexa Product Team was to "[redacted]" Studies were treated as marketing tools rather than sincere research efforts into the health risks, leading one

Lilly executive to note in April 2001:

( ) He went on to state the "

" ( )

278. As noted, many of the approximately 125 manuscripts, articles, and chapters already published dealt with treatment of the elderly and adolescents with Zyprexa, evidence of Lilly's continued targeting of those populations. ( )

279. In an attempt to diminish concerns over the cardiac risks of olanzapine, Lilly engaged an international PR firm to ' ' write a paper for the March/April 2001 edition of the Progress in Neurology and Psychiatry supplement. On February 23, 2001, Kerrie Mitchell of Cohn & Wolfe emailed Lilly colleagues to inform them

( )

280. On May 3, 2001, Lilly's Michele Sharp emailed Robert Baker, James Gregory, and others to discuss Zyprexa studies and interactions with the FDA regarding the results of

those studies - particularly whether to hide them or not.

[redacted]

([redacted])

281. Lilly's manipulation of Zyprexa studies is exemplified in a December 19, 2001 email, in which Robert Thompson documented a meeting between Dr. Robert Smith of the NYU Department of Psychiatry and Lilly researchers, who advised Smith on changes to protocol design of proposed study funded by Lilly: "[redacted]" The recommended changes to make the study "[redacted]" included cherry-picking participants, e.g. more stringent exclusion criteria of patients in order to reduce the number and rate of treatment-emergent diabetes as well as terminating certain patients from the protocol early rather than simply switching their medications: "[redacted]" Lilly also encouraged the study to be designed according to marketing needs in determining which antipsychotics to involve in the trial:

[redacted]

[redacted]

([redacted])

5. Off-Label Promotion to the Elderly

282. Following the trend it began in the 1996-2000 period, in the next few years Lilly continued to encourage utilization of Zyprexa in the elderly and for any symptoms that might be categorized as relating to dementia. In an undated overhead training presentation entitled "[redacted]", Lilly identified the "[redacted]" for opening the door to the elderly market for Zyprexa: "[redacted]" ([redacted]) Lilly instructed the sales force that patient profiles "[redacted]" and that the focus should be on "[redacted]" such as "[redacted]" rather than diagnoses. ([redacted]) Further, Lilly directed its sales representatives to misrepresent the uses for which Zyprexa had received FDA approval, stating it was "[redacted]" ([redacted])

283. In October 2000, Lilly emphasized its "[redacted]" to "[redacted]" In particular, Lilly wanted to target elderly patients who are "[redacted]" and "[redacted]". ([redacted])

[redacted])

284. In addition, Lilly's consultants recommended that they target non-Alzheimer elderly patients with dementia. For example, on May 2, 2001, McKinsey & Co. presented their "[redacted]" Identifying at least eleven different patient types, McKinsey included three separate profiles targeting the elderly: Patient 2 with "[redacted]"; Patient 5 with "[redacted]"; and Patient 11 with "[redacted]". The consultants suggested Lilly "[redacted]" in the use of Zyprexa for Patient 2 – elderly patients with non-Alzheimer's mild dementia – leading to the assumption that Lilly already had a large off-label market share among that population. ([redacted])

285. Lilly took this advice to heart. In a June 29, 2001 presentation, Lilly highlighted the "[redacted]" patient profile. Martha, like Donna, is another fictional Lilly character: a widow having "[redacted]" and who "[redacted]". She is "[redacted]", "[redacted]" In other words, Martha may be experiencing dementia or mild Alzheimer's, or any number of health concerns associated with age and declining health, but there is absolutely no indication that Martha is schizophrenic or bipolar. Yet Lilly sees Martha as a great business opportunity because Lilly can persuade primary care physicians to prescribe an antipsychotic to "[redacted]" No doubt there are millions of people in the United States who fit Martha's profile and who are not psychotic, schizophrenic, or bipolar. But one of Lilly's goals was to get as many unsuspecting elderly patients on Zyprexa as possible and Lilly saw marketing to primary care physicians as the optimum way to accomplish that their scheme. ([redacted])

286. Lilly did not let up on the push to prescribe Zyprexa for the treatment of

dementia, noting in an October 31, 2001 brochure that olanzapine is the "[redacted]" ([redacted])

287. A year later, Zyprexa Brand Manager, Michael Bandick, reiterated the dementia-treatment strategy when informing numerous Lilly marketing representatives about a "[redacted]" letter issued by its competitor, Janssen, with regard a Risperdal Cerebrovascular Warning in Canada. Bandick noted that the Risperdal label change was "[redacted]" Bandick's directive provides further evidence of Lilly's off-label promotion of Zyprexa to doctors for treatment patients for dementia - a condition for which Zyprexa was not approved. ([redacted])

6. Changing the Message

288. Despite Lilly's best efforts to encourage utilization of Zyprexa, primary care physicians raised concerns over the connection to glucose irregularities, hyperglycemia, and diabetes. Lilly noted in September 2001 that "[redacted]" ([redacted]) While still instructing the sales force to emphasize the "[redacted]" message and highlight the multiple risk factors for diabetes, the company began to contemplate a message shift.

289. Lilly had been conducting large scale market research into physician prescribing patterns and their perceptions of Zyprexa and its side effects for quite some time. The "[redacted]" tasked with the research conducted polls of 100 primary care physicians and 240 psychiatrists in three different waves, February 2001, July 2001 and January 2002. Following the third wave, the team reported that physicians increasing concern that Zyprexa caused both

weight gain and diabetes was influencing their prescribing habits. ([redacted])

290. In a January 28, 2002 email on "[redacted]" to Thomas Reck, Katharine Armington, Diana Caldwell, Robert Baker, and Donald Hay, Cassandra Mehlman of Marketplace Management writes about "[redacted]" She asks:

[redacted]

([redacted])

291. As Lilly looked to change its message to physicians and psychiatrists about hyperglycemia and diabetes and their relationship to Zyprexa in early 2002, the company engaged consultants at Harper to hold strategy sessions with focus groups. In a report dated March 12, 2002, Harper presented the results of one such strategy session. Stated "[redacted]" included determining "[redacted]", determining "[redacted]", evaluating "[redacted]". The conclusions and recommendations note "[redacted]" and that "[redacted]

[redacted]" Further, "[redacted]

[redacted]" ([redacted])

292. While Lilly contemplated a message change, questions from the field on how to address diabetes and hyperglycemia continued to come in. On June 21, 2002, Kristine Healey sent an email to Vicki Hoffmann stating "[redacted]

[redacted]" Ms. Hoffman's response included the following:

[redacted]

([redacted])

293. On August 12, 2002, Eli Lilly rolled out its' [redacted]. In the plan, Lilly emphasized that "[redacted]" and notes that a substantial number of psychiatrists either do not prescribe or discontinue use of Zyprexa due to association with weight gain and diabetes. ([redacted]) A concurrent strategy brief outlined the short- and long-term plans for continuing sales of Zyprexa, noting that "[redacted]" The

takeaway message on weight gain: "[redacted]" The takeaway message on diabetes: "[redacted]" ([redacted])

294. The overwhelming concerns of doctors over the side effects of Zyprexa compelled Lilly to shift its marketing strategy, though they held fast to the "[redacted]" message. On October 14, 2002, Lilly updated a document entitled "[redacted]" emphasizing: "[redacted]" The strategy directed sales representatives to "[redacted]" ([redacted])

7. Failure to Disclose Adverse Side Effects

295. During 2001-2003, Lilly continued to fail to adequately disclose the mounting evidence and knowledge it had regarding the side effects and lack of comparative efficacy of Zyprexa, both for on-label and off-label purposes.

296. The ongoing refusal of Lilly to make these disclosures was all the more egregious given the mounting evidence known to it.

297. Between August 3, 2000 and July 18, 2003, Lilly made 9 more label changes. For a single drug to undergo as many label changes as Zyprexa underwent is highly irregular. Additionally, the greater the number of label changes the less effective the warnings contained in

those changes are because most doctors do not read the changes to a drug's label after the first one or two. This is known as "[redacted]". The only change made to the label containing a warning about diabetes-related injuries occurred in November of 2001, when "[redacted]" was added, however, it too was buried in the "[redacted]" section. Again, because of the date of this change, the new label did not appear in the upcoming 2002 PDR, but rather was first published in the 2003 PDR.

298. As with the "[redacted]" report, the "[redacted]" reference is again buried deep within the label and is virtually unrecognizable. Further, this reference also fails to include any mention of the mountain of post-market adverse events reports of diabetes, hyperglycemia, diabetic deaths, and ketoacidosis. The egregiousness of this conduct is highlighted when juxtaposed against the fact that during this time, the medical literature continued to identify the connection between the drug and diabetes-related illness and that Lilly's foreign labels were being changed to warn about these very complications.

J. 2001-2002: Major Warning Signs Abroad

1. Japan and UK Label Changes

299. Another reason why Zyprexa's U.S. label should have had a prominent warning of diabetes and diabetes-related injuries and a warning for appropriate monitoring significantly in advance of the disseminated warning in March 2004, is evident from Lilly's labeling changes outside of the United States. Lilly was forced to change its label in the United Kingdom and Japan in April 2002 because of the mounting reports of diabetes-related injuries. Indeed, after only 9 AERs in Japan and 40 AERs in the U.K., Lilly changed its label in those foreign countries to warn about the possible association between these injuries and Zyprexa. However, Lilly failed to change its label in the U.S. at the same time.

300. Additionally, the medical literature indicates that Eli Lilly was or should have

been aware of Zyprexa's association and/or causal relationship and/or potential to cause diabetes-related injuries significantly prior to the forced label change by the FDA. Prior to 2001, there were over 50 articles that showed a likely association between SGAs and the development of diabetes-related injuries.

301. This well documented class effect was ignored by Lilly in its clinical trials, in its label and in its subsequent marketing effects. Articles published since the marketing of Zyprexa demonstrate that the incidence of diabetes-related adverse events is greater with Zyprexa than any other drug in its class – another fact known to Lilly, but ignored.

302. In December of 2000, the British Journal of Psychiatry printed a review of 52 studies involving 12,649 patients. It concluded: "[redacted]." As another example, an April 2001 study entitled *Antipsychotic Metabolic Effects: Weight Gain, Diabetes Mellitus, and Lipid Abnormalities*, concluded that "[redacted]"

303. By January of 2000, Lilly was becoming inundated with reports – particularly from international regulatory authorities –of patients who suffered serious adverse health events after having taken Zyprexa, even for very brief periods of time.

304. For example, on or about January 1, 2000, according to a document produced from the files of Lilly's Julie A. Birt titled, "[redacted]" Lilly responded to a formal inquiry

from Switzerland's Health Authority regarding numerous adverse health events in patients using Zyprexa and undisclosed potential side-effects by reviewing all "[redacted]" information potentially relating to hyperglycemia in patients treated with Zyprexa. Notwithstanding the document cases leading to Switzerland's inquiry, after supposedly analyzing the available AER data, Lilly concluded that no action was warranted, but did concede that "[redacted]" ([redacted])

305. Later that year, in or about July 2000, Lilly had been put on notice from the European Agency for the Evaluation of Medicinal Products, *Human Medicines Evaluation Unit* ("[redacted]"), that it had serious concerns about adverse events reported in connection with Zyprexa use. In particular, the EAEMP emphasized that a periodic safety report covering the period September 26, 1997 through March 1998, revealed, *inter alia*, that numerous adverse reactions to Zyprexa had been reported and that "[redacted]" At the same time, the EAEMP also noted that while Zyprexa is not authorized for use in children, numerous adverse reactions in children had been reported. ([redacted])

306. Notwithstanding, Lilly persisted in refusing to acknowledge and/or disclose Zyprexa's problems in the United States even though the company admitted to these problems overseas after being forced to do so by several foreign governments, including Japan and the UK. For example, in preparation for Zyprexa's launch in Japan in or about June 2001, Lilly representatives, at the direction of the company's senior level managers in Indianapolis, attempted to persuade Japan's Ministry of Health and Welfare ("[redacted]") (Japan's drug regulating authority) not to adhere to its request that Zyprexa's package insert include a warning

that blood glucose monitoring be conducted in certain patients due to the reports of diabetes and hyperglycemia. Lilly's main concern was that such a disclosure would drive down demand for the drug. In fact, in an email dated October 5, 2000, with a caption emphasizing the words "[redacted]", "[redacted]", and "[redacted]", Masashi Takahashi, a Lilly representative in Japan, discussed the MHW's request "[redacted]". Mr. Takahashi goes on to state that "[redacted]" ([redacted])

307. Moreover, in further preparation for Lilly's Zyprexa launch in Japan, Maseo Amano of Lilly's Zyprexa Product Team informed Dr. Charles M. Beasley, Jr., Lilly's "[redacted]", (in an e-mail dated October 11, 2000) that the MHW Evaluation Center ("[redacted]") contacted Lilly's Kobe, Japan office and wanted to know as soon as possible whether Lilly knew of any severe cases of diabetic coma and diabetic ketoacidosis in connection with Zyprexa use. In particular, Mr. Amano informed Mr. Beasley that in response Lilly faxed 3 groups of documents to the EC including: 1) supporting documents for adding diabetic coma and diabetic ketoacidosis to the package insert, 2) ADR reports on Ketoacidosis submitted previously to the EC, and 3) A study titled, "[redacted]", which had already been submitted to the EC. In a subsequent related email, Masashi Takahashi emphasized, "[redacted]"

[redacted]

308. Meanwhile, as Lilly was undertaking damage control in Japan, in November 2000, at the request of the Malaysian Regulatory Authority, Lilly was forced to send a "[redacted]" letter to Malaysian physicians advising them of a change in Zyprexa's package insert and an increased risk of hyperglycemia and/or diabetes as it relates to Zyprexa use. Notably, this "[redacted]" letter advised Malaysian physicians to monitor patients with risk factors for the development of diabetes. ([redacted])

309. By the end of the year 2000, Lilly was regularly receiving reports of new onset diabetes and/or hyperglycemia in connection with Zyprexa use. In response, on or about December 14, 2000, Lilly conducted a three hour meeting at which the company and its senior management discussed how to respond to rising concerns among physicians in the United States about Zyprexa use, Diabetes, and Weight Gain. In discussing its' strategy, Lilly emphasized that were 2 groups of physicians "[redacted]" and that "[redacted]". ([redacted]) During a discussion on "[redacted]", Lilly noted concern about "[redacted]". On the subject of weight gain, Lilly instructed meeting participants to "[redacted]". When discussing "[redacted]" Lilly informed meeting participants of what would become its' strategy. ([redacted]) Namely, that notwithstanding the numerous reports of serious adverse health events from around the world, representatives should emphasize that "[redacted]". ([redacted])