

# Corporate crime in the pharmaceutical industry is common, serious and repetitive

by

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## Abstract

**Objectives:** To study whether large drug companies routinely break the law.

**Design:** Literature review, using Google searches combining the names of the ten largest drug companies with "fraud."

**Results:** I found recent examples (2007 to 2012) of serious crimes committed by each company. The crimes included marketing drugs for off-label uses, misrepresentation of research results, hiding data on harms, and Medicaid and Medicare fraud. Doctors were often complicit in the crimes, as kickbacks were common. The crimes were repetitive.

**Conclusions:** The crimes persist because crime pays. Harder sanctions are therefore needed, including prison sentences for CEOs and other senior executives. Doctors and their organisations should consider carefully whether they find it ethically acceptable to receive money that may have been partly earned by crimes that are harmful to patients.

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In recent years, numerous articles and books have described serious cases of research misconduct and marketing fraud committed by drug companies.<sup>1-9</sup> When a company has been caught, the standard response from the drug industry is that there are a few bad apples in any enterprise. The interesting question is whether we are seeing a lone bad apple now and then, which might be excusable, or whether the companies routinely break the law.

## Methods

I did ten Google searches on 19 June 2012 combining the names of the ten largest drug companies as of March 2010<sup>10</sup> with "fraud." There were between 0.5 and 27 million hits for each company and I selected the most prominent case described in the ten hits on the first Google page. To ensure that the information I found was trustworthy, I supplied or substituted it using more reliable sources in three cases.

## Results

The ten cases I selected were recent ones, from 2007 to 2012, and were all related to the United States<sup>11-20</sup> The most common criminal offences were illegal marketing recommending drugs for non-approved (off-label) uses, misrepresentation of research results, hiding data on harms, and Medicaid and Medicare fraud. I describe the cases in descending order according to the size of the company.<sup>10</sup>

### 1. Pfizer agreed to pay \$2.3 billion in 2009<sup>11</sup>

This was the largest healthcare fraud settlement in the history of the US Department of Justice at the time. A subsidiary of the firm pleaded guilty to misbranding drugs "with the intent to defraud or mislead," and the firm was found to have illegally promoted four drugs for uses which had not been approved by the drug regulators: Bextra (valdecoxib, an anti-arthritis drug), Geodon (ziprasidone, an antipsychotic drug), Zyvox (linezolid, an antibiotic) and Lyrica (pregabalin, an epilepsy drug). Part of the fine (\$1 billion) was levied to resolve the allegations that Pfizer paid bribes and offered lavish hospitality to healthcare providers to encourage them to prescribe the four drugs. Six whistleblowers would receive \$102 million of the civil fines. Pfizer would have to enter a Corporate Integrity Agreement with the Department of Health and Human Services (which means that good behavior is required for the next five years).

### 2. Novartis agreed to pay \$423 million in 2010<sup>12</sup>

The payment concerned criminal and civil liability arising from the illegal marketing of Trileptal (oxcarbazepine, an epilepsy drug approved for the treatment of partial seizures, but not for any psychiatric, pain or other uses). The company unlawfully marketed Trileptal and five other drugs causing false claims to be submitted to government health care programs. The agreement resolved allegations that the company paid kickbacks to health care professionals to induce them to prescribe Trileptal and five other drugs, Diovan (valsartan, for hypertension), Zelnorm (tegaserod, a drug for irritable bowel syndrome and constipation, which was removed from the market by US Food and Drug Administration (FDA) in 2007 because of cardiovascular toxicity), Sandostatin (octreotide, a drug that mimics a natural hormone), Exforge (amlodipine + valsartan, for hypertension) and Tekturna (aliskiren, for hypertension). The whistleblowers, all former employees of Novartis, would receive payments totaling more than \$25 million. Novartis signed a Corporate Integrity Agreement.

### 3. Sanofi-Aventis to pay more than \$95 million to settle fraud charge in 2009<sup>13,21</sup>

According to the settlement, Aventis had overcharged US and local health agencies for medications destined for indigent patients. The Justice Department said they would ensure that programs for the most vulnerable portions of the population did not pay any more for pharmaceutical products than they should under the law. Aventis acknowledged that it misreported drug prices for patients in the Medicaid Drug Rebate program for poor patients. The firm deliberately misquoted the prices, underpaying rebates to Medicaid and overcharging some public health agencies for the medications. The fraud occurred between 1995 and 2000 and concerned steroid-based nasal sprays containing triamcinolone, Azmacort, Nasacort and Nasacort AQ.

### 4. GlaxoSmithKline to pay \$3 billion in 2011<sup>14,22,23</sup>

This is the largest healthcare fraud settlement in US history. GlaxoSmithKline pleaded guilty to having marketed a number of drugs illegally for off-label use, including Wellbutrin (bupropion, an antidepressant), Paxil (paroxetine, an antidepressant), Advair (fluticasone + salmeterol, an asthma drug), Avandia (rosiglitazone, a diabetes drug), and Lamictal (lamotrigine, an epilepsy drug). The company paid kickbacks to doctors, failed to include certain safety data about rosiglitazone in reports to the FDA, and sponsored programs suggesting cardiovascular benefits from Avandia despite warnings on the FDA-approved label regarding cardiovascular risks. Allegations of Medicaid fraud by misreported prices were also covered by the agreement. The whistleblowers were four employees of GlaxoSmithKline, including a former senior marketing development manager and a regional vice president. The company entered into a Corporate Integrity Agreement.

### 5. AstraZeneca to pay \$520 million in 2010 to settle fraud case<sup>15</sup>

The charges were that AstraZeneca illegally marketed one of its best-selling drugs, the antipsychotic drug Seroquel (quetiapine), to children, the elderly, veterans and inmates for uses not approved by the FDA, including aggression, Alzheimer's, anger management, anxiety, attention-deficit hyperactivity disorder, dementia, depression, mood disorder, post-traumatic stress disorder and sleeplessness. Further, the company targeted its illegal marketing towards doctors who do not typically treat psychotic patients and paid kickbacks to some of them. Other doctors were sent to lavish resorts to encourage them to market and prescribe the drugs for unapproved uses. The whistleblower would get more than \$45 million.

### 6. Roche convinces governments to stockpile Tamiflu<sup>16,24-26</sup>

In preparation for the mild 2009 influenza epidemic, the US government spent \$1.5 billion and the European governments billions of Euros on the purchase of Tamiflu (oseltamivir).<sup>16,24</sup> Based on unpublished trials, Roche had claimed that Tamiflu reduced hospital admissions by 61%, secondary complications by 67%, and lowered respiratory tract infections requiring antibiotics by 55%.<sup>24</sup> Roche had omitted publishing most of their clinical trial data and refused to share them with independent Cochrane researchers. The company had convinced the European Medicines Agency (EMA) to approve the drug for prevention of influenza complications,<sup>26</sup> whereas the FDA required Roche to print a disclaimer to the contrary on the labels: "Tamiflu has not been proven to have a positive impact on the potential consequences (such as hospitalizations, mortality, or economic impact) of seasonal, avian, or pandemic influenza". There is no convincing evidence either that Tamiflu

prevents influenza complications or reduces the spread of influenza to other people.<sup>24-26</sup>

Guidance from the WHO had concealed that the authors had received payment from Roche,<sup>16</sup> and Roche also used ghostwriters. One of them said: "The Tamiflu accounts had a list of key messages that you had to get in. It was run by the marketing department and you were answerable to them."<sup>24</sup> Tamiflu reduces the duration of influenza by 21 hours,<sup>25</sup> which can probably be obtained with far cheaper drugs like aspirin and paracetamol. Furthermore, Tamiflu has important harms, but they were concealed to such an extent that the Cochrane researchers could not report on them.

#### 7. Johnson & Johnson fined more than \$1.1 billion in 2012<sup>17</sup>

A jury found that the company and its subsidiary Janssen had downplayed and hidden risks associated with the antipsychotic drug Risperdal (risperidone). The judge found nearly 240,000 violations under Arkansas' Medicaid-fraud law. Jurors returned a quick verdict in favour of the state, which had argued that Janssen lied about the potentially life-threatening side effects of Risperdal which, like similar antipsychotic drugs, include death, strokes, seizures, weight gain and diabetes. The FDA had ordered Janssen to issue a letter to doctors correcting an earlier letter saying the drug didn't increase the risk of developing diabetes. Janssen continued to maintain after the verdict that it did not break the law. Previous verdicts against the company a few months earlier included a \$327 million civil penalty in South Carolina and a \$158 million settlement in Texas.

#### 8. Merck to pay \$670 million over Medicaid fraud in 2007<sup>18</sup>

Merck had failed to pay the appropriate rebates to Medicaid and other government health care programs, and had also paid kickbacks to doctors and hospitals to induce them to prescribe various drugs. The allegations were brought in two separate lawsuits filed by whistleblowers; one of them would receive \$68 million. From 1997-2001, Merck's sales force used approximately 15 different programs to induce doctors to prescribe its drugs. These programs primarily consisted of excess payments to doctors that were disguised as fees paid to them for "training," "consultation" or "market research." The government alleged that these fees were illegal kickbacks intended to induce the purchase of Merck drugs. Merck agreed to a Corporate Integrity Agreement.

#### 9. Eli Lilly to pay more than \$1.4 billion for illegal marketing in 2009<sup>19</sup>

Eli Lilly entered into a settlement with the Department of Justice concerning a wide-ranging, off-label marketing scheme for its top-selling antipsychotic drug, Zyprexa (olanzapine), with worldwide sales of nearly \$40 billion between 1996 and 2009. In the settlement, Eli Lilly would pay \$800 million in civil penalties and plead guilty to criminal charges, paying an additional \$600 million fine. The allegations were raised by six whistleblowers from Lilly who would share in approximately 18 per cent of the federal and qualifying states' recoveries. All six whistleblowers were eventually fired or forced to resign by the company. According to the Complaint, one sales representative had contacted the company hotline regarding unethical sales practices but received no response.

Eli Lilly successfully marketed Zyprexa for numerous off-label uses including Alzheimer's, depression and dementia, particularly in children and the elderly, although the harms of the drug are substantial, inducing heart failure, pneumonia,

considerable weight gain and diabetes. Eli Lilly sales people were posed as persons in the audience who were interested in Zyprexa's expanded use and asked "planted questions" during off-label lectures and audio conferences for physicians. Another tactic was that, while knowing the substantial risk for weight gain posed by Zyprexa, the company minimized the connection between Zyprexa and weight gain in a widely disseminated videotape called "The Myth of Diabetes" that used "allegedly scientific studies of questionable integrity as well as the haphazard reporting of adverse events." The settlement agreement included a Corporate Integrity Agreement.

#### 10. Abbott to pay \$1.5 billion for Medicaid fraud in 2012<sup>20</sup>

Abbott settled allegations of Medicaid fraud for the company's illegal marketing of the epilepsy drug Depakote (valproate); part of the settlement would be paid to the whistleblowers. Abbott would pay \$800 million in civil damages and penalties to compensate Medicaid, Medicare, and various federal healthcare programs for harm suffered as a result of its conduct. Abbott also pled guilty to a violation of the Food, Drug, and Cosmetic Act and agreed to pay a criminal fine and forfeiture of \$700 million.

The states alleged that Abbott promoted the sale and use of Depakote for uses that were not approved by the FDA as safe and effective; that Abbott Laboratories made false and misleading statements about the safety, efficacy, dosing and cost-effectiveness of Depakote for some unapproved uses; improperly marketed the product in nursing homes; and paid kickbacks to induce doctors and others to prescribe or promote the drug. Abbott entered into a Corporate Integrity Agreement.

### **Discussion**

Even though my search strategy was simple, it was very easy to find recent examples of serious crimes and other misdeeds committed by each of the ten largest drug companies. It was also easy to find additional crimes committed by the same ten companies (see selected cases in table 1)<sup>27-38</sup> Six of these cases appeared on the first Google page in the original search, one on a subsequent page, and three were found using "crime" instead of "fraud." Sometimes many crimes were listed in the first ten hits in the original search and an example is shown in table 2 for GlaxoSmithKline.<sup>39-43</sup> I decided *a priori* to use "fraud" as my search word, but I could also have used "criminal," "illegal," "FBI," "kickback," "misconduct," "settlement," "bribery," "guilty" and "felony," for example, which would have revealed many additional, recent crimes. It was also easy to find crimes committed by the drug companies outside the United States.

Thus, there can be no doubt that the crimes are widespread and repetitive, which suggests they are committed deliberately. The obvious reason is that crime pays, and a well-researched example is Neurontin (gabapentin) (table 1). Warner-Lambert, later bought by Pfizer, paid doctors to allow sales people to sit with them as they saw patients and to suggest using gabapentin to patients with a wide array of ailments, including bipolar disorder, pain, migraine headaches, and drug and alcohol withdrawal,<sup>27</sup> although the drug was only approved for treatment-resistant epilepsy.<sup>2,8,44</sup> At some Neurontin meetings, the company paid not only the speakers but also the listeners, treating them to luxury trips to Hawaii, Florida or the 1996 Olympics in Atlanta<sup>27</sup> and a physician-whistleblower has testified that he was trained to distort the scientific evidence.<sup>8</sup> Of 40 influential thought leaders identified as potential speakers in Northeastern USA, 35 participated in company-sponsored

activities, and 14 requested or were allocated \$10,250 to \$158,250 in honoraria or grants.<sup>45</sup> One doctor received almost \$308,000 to tout Neurontin at conferences.<sup>27</sup> The speakers were updated on the company's promotional strategies,<sup>45</sup> and Warner-Lambert tracked high-volume prescribers and rewarded them as speakers or consultants, or for recruiting patients in studies. Doctors were paid to lend their names to ghostwritten articles purporting to show that Neurontin worked for unapproved conditions.<sup>2,46</sup>

Pfizer agreed in 2009 to pay \$430 million to resolve criminal and civil charges, but as the sales of gabapentin were \$2,700 million in 2003 alone, and as about 90% was for off-label use,<sup>27,44</sup> such fines are far too small to be expected to have any deterrent effect. When Pfizer was fined \$2.3 billion for off-label use of four other drugs,<sup>11</sup> part of the settlement with the Justice Department was that Pfizer entered a Corporate Integrity Agreement with the Department of Health and Human Services to avoid and detect such problems in future. Such agreements may have little teeth, as Pfizer had previously entered into three such agreements,<sup>47</sup> and Merck at least two (table 1). As five of the ten companies had entered a Corporate Integrity Agreement in relation to the ten first cases I selected, I looked the other five companies up. Of the top 10 pharma companies, only Roche was not bound by such an agreement in July 2012.<sup>48,49</sup>

#### The companies' views of themselves

The Pharmaceutical Research and Manufacturers of America (PhRMA) claims its members are “committed to following the highest ethical standards as well as all legal requirements.”<sup>50</sup> Its Code on Interactions with Healthcare Professionals<sup>51</sup> states that:

*“Ethical relationships with healthcare professionals are critical to our mission of helping patients ... An important part of achieving this mission is ensuring that healthcare professionals have the latest, most accurate information available regarding prescription medicines.”*

The disconnect between the proclamations of “highest ethical standards” and the reality of big pharma’s conduct is vast. The ten largest companies are all signatories to the code, apart from Roche,<sup>51</sup> which was the largest corporate fraudster worldwide in the 1990's<sup>52</sup> (table 1). Further, the top executives' views of themselves are not shared by their employees. An internal survey of Pfizer employees showed that about 30% didn't agree with the statement, “Senior management demonstrates honest, ethical behavior.”<sup>9</sup>

#### The public's views of the companies

The general public has a more sober view of what the companies are doing. In an opinion poll that asked 5,000 Danes to rank 51 industries in terms of the confidence they had in them, the drug industry came second to the bottom, only superseded by automobile repair companies.<sup>53</sup> A US poll also ranked the drug industry at the bottom, together with oil and tobacco companies.<sup>54</sup>

#### The consequences of the crimes are huge

In relation to AstraZeneca's off-label marketing of its antipsychotic drug, Seroquel (quetiapine), described above,<sup>15</sup> the US Attorney General said:

*"These were not victimless crimes - illegal acts by pharmaceutical companies and false claims against Medicare and Medicaid can put the public health at risk, corrupt medical decisions by health care providers, and take billions of dollars directly out of taxpayers' pockets."*

Doctors are complicit in the crimes when they accept kickbacks and engage in other types of corruption, often in relation to illegal marketing. When drugs are marketed to non-approved uses, we don't know whether they are effective, and they could also be more harmful, e.g. if used in children. This practice has therefore been described as using the citizens as guinea pigs on a large scale without their informed consent.<sup>27</sup>

Even when doctors use drugs only for approved indications, the crimes have consequences for the patients. Doctors only have access to selected and manipulated information,<sup>1-9,43</sup> and they therefore believe drugs are far more effective and safe than they really are. Thus, both legal and illegal marketing leads to massive overtreatment of the population and a lot of harm that could have been avoided.

As many of the crimes I identified were related to psychiatry, I shall use this specialty as an example. Psychiatry is a lucrative area for the industry, as most definitions of psychiatric disorders are vague and easy to manipulate. In Minnesota, psychiatrists collected more money from drug makers from 2000 to 2005 than doctors in any other specialty, and those who took most money tended to prescribe atypical antipsychotics to children most often.<sup>55</sup> In Denmark, the sales of selective serotonin reuptake inhibitors (SSRIs) are now so high that 7% of the entire population could be in treatment with an adult dose every day.<sup>56</sup> Obviously, such massive use of drugs that affect the brain cannot be healthy,<sup>5</sup> and it is clear that the drug companies have caused this overtreatment. From 1992, the sales of SSRIs increased almost linearly by a factor of 18, which was closely related ( $r = 0.97$ ) to the number of products on the market (and therefore the marketing pressure), which increased by a factor of 16.<sup>56</sup> The psychiatrists are aware of the problem. A 2007 survey of 108 Danish psychiatrists showed that 51% felt they used too much medicine and only 4% felt they used too little.<sup>57</sup> In the United States it is even worse. The most sold class of drugs in 2009 (in dollars) was antipsychotics and antidepressants came fourth, after lipid lowering drugs and proton pump inhibitors.<sup>58</sup> It is hard to imagine that so many Americans can be so mentally disturbed that these sales reflect genuine needs.

### What should be done?

To tackle a problem effectively, we first need to describe and name it. In 2004-5, The British House of Commons Health Committee examined the drug industry in detail<sup>59</sup> and found that its influence was enormous and out of control.<sup>60</sup> The drug industry is clearly playing hardball, running calculated risks and corrupting people on a large scale, which lead to the unnecessary loss of thousands of lives every year and great costs for our national economies.<sup>1-9,41,59,61</sup>

I therefore believe that what we are seeing has similarities to organized crime. A previous global vice president of marketing at Pfizer turned whistleblower when the company wouldn't listen to his complaints about illegal marketing<sup>9</sup> holds a similar view.<sup>62</sup>

*"It is scary how many similarities there are between this industry and the mob. The mob makes obscene amounts of money, as does this industry. The side effects of*

*organized crime are killings and deaths, and the side effects are the same in this industry. The mob bribes politicians and others, and so does the drug industry ... The difference is, all these people in the drug industry look upon themselves - well, I'd say 99 percent, anyway - look upon themselves as law-abiding citizens, not as citizens who would ever rob a bank ... However, when they get together as a group and manage these corporations, something seems to happen ... So there's something that happens to otherwise good citizens when they are part of a corporation. It's almost like when you have war atrocities; people do things they don't think they're capable of. When you're in a group, people can do things they otherwise wouldn't, because the group can validate what you're doing as okay."*

I also suggest we view marketing of drugs as drug pushing. Between the two World Wars, Hoffman-La Roche supplied morphine to the underworld, and other companies in the United Kingdom, Germany, Japan, Switzerland and the United States also participated in the trade with opium, morphine and heroin.<sup>61,63,64</sup> Pushing drugs people don't need is a highly lucrative business. Valium (diazepam), another Roche product, was once the top-selling drug, many indications for its use were highly doubtful, and the wholesale prize was 25 times the price of gold.<sup>61</sup> It took many years before it became accepted that tranquilizers are strongly addictive, but the hard lessons were forgotten, as we now witness a similar explosion in dubious indications for SSRIs, although these drugs are also addictive,<sup>5,59,65</sup> and for antipsychotics. The fact that some drugs affecting the brain are legal and others are illegal is not important, as the drugs are pushed in both cases. After having examined the drug industry in detail, John Braithwaite published a book in 1984 where he said:<sup>61</sup>

*"People who foster dependence on illicit drugs such as heroin are regarded as among the most unscrupulous pariahs of modern civilisation. In contrast, pushers of licit drugs tend to be viewed as altruistically motivated purveyors of a social good."*

When a crime has led to the deaths of many people, we should view it as a crime against humanity. Whether hundreds or thousands of people are killed for personal gains by arms or by pills should make no difference for our perception of the misdeed.

We need much harder sanctions for the crimes. Even the large fines in the United States are insufficiently large. To deter bad behavior, they would need to be so large that the companies would risk going bankrupt, but unfortunately, this is unlikely to happen. The largest companies earn so much money to their home country that the governments wouldn't dare run such a risk. In 2010, the ten largest companies sold drugs for \$303 billion,<sup>10</sup> which is more than the Gross National Product for all but the richest 34 countries in the world.<sup>66</sup> US federal law requires that any company found guilty of marketing fraud be automatically excluded from Medicare and Medicaid, but government prosecutors decided that this exclusion would lead to the collapse of "too big to fail" Pfizer.<sup>67</sup>

To bring the crimes to light also outside the United States, we need laws that protect whistleblowers and ensure they get a fair proportion of the fines. It is curious and unfortunate that very little happens to the offending companies outside the United States. When Merck had withdrawn rofecoxib (Vioxx) from the market in 2004 after its marketing frauds<sup>68</sup> had caused tens of thousands of cardiovascular deaths,<sup>69,70</sup> Pfizer Denmark grabbed the opportunity and wrote to the doctors that its



Cox-2 inhibitor, celecoxib, did not cause thrombosis.<sup>71</sup> The fine for this blatant misinformation was a mere DKK 12,000 (about \$2,000). Three months later, Pfizer US denied that celecoxib causes heart attacks at an FDA hearing FDA,<sup>72</sup> despite having unpublished evidence to the contrary.<sup>73</sup> Indeed, independent researchers who had access to FDA data confirmed the cardiovascular harms of celecoxib.<sup>73</sup>

Top executives should be held personally accountable for the crimes so that they would need to pay attention to the risk of going to prison when they consider performing or acquiescing in crimes. Merck produced a pamphlet to its sales force in 2001 indicating that rofecoxib was associated with 1/8 the mortality from cardiovascular causes of that found with other nonsteroidal, anti-inflammatory drugs.<sup>74</sup> This was *after* the FDA had raised concerns about a five-fold increase in myocardial infarction in a pivotal trial of rofecoxib! Even so, the same year Merck pulled rofecoxib off the market, its CEO received performance-based bonuses worth over \$36 million in addition to his base salary<sup>75</sup> and he was never indicted. This complacency with even lethal crimes may be about to change in the USA. In 2010, the Justice Department charged a former vice president for GlaxoSmithKline (see table 2).

We need to avoid the situation that, by settling accusations of crimes, the drug companies can pretend they are innocent, claiming that they have not been convicted of a crime. AstraZeneca, for example, denied the charges of fraudulent marketing and its general counsel said that moving forward and resolving the case was "in the best interest" of the company.<sup>15</sup> And although part of the civil settlement with GlaxoSmithKline included claims that the company overcharged the US government for drugs, GlaxoSmithKline did not admit any wrongdoing.<sup>23</sup>

We also need laws requiring firms to disclose all knowledge about their drugs and research data,<sup>43</sup> and that not only allows, but requires drug agencies to publish what they know. Currently, the companies may not disclose anything even when they know that their drugs are more harmful than originally thought. In 2004, the WHO sent GlaxoSmithKline an alert about cardiac events caused by rosiglitazone, and the company performed a meta-analysis that confirmed it, which it sent to the FDA and the European Medicines Agency in 2006, but the drug regulatory agencies did not make the findings public because of the proprietary nature of companies' trial results.<sup>76</sup> This is an absurd interpretation of ownership to data and results, which is untenable,<sup>43</sup> and it allows the companies to "push the drug aggressively and hope they can make a billion dollars before someone finds out," as former editor of the New England Journal of Medicine, Jerome Kassirer, expressed it.<sup>15</sup>

A standard response from the drug industry to crimes is that the activities revealed in recent settlements or verdicts occurred many years ago, and practices have changed radically since then.<sup>23</sup> That may be true but not in the way the drug industry wants us to believe, as the crimes seem to be *increasing*. Three-quarters of the 165 settlements comprising \$19.8 billion in penalties during the 20-year interval from 1991 to 2010 occurred in just the past five years of that period.<sup>77</sup>

Doctors and their organisations should consider carefully whether they find it ethically acceptable to receive money that may have been partly earned by crimes that have harmed those people whose interests doctors are expected to take care of. Many crimes would be impossible to carry out, if doctors weren't willing to participate in them.

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**Table 1. Selected additional crimes for each of the ten largest drug companies**

<p><u>1. Pfizer.</u> Agreed to plead guilty in 2004 to two felonies and pay \$430 million in penalties to settle charges that it fraudulently promoted Neurontin (gabapentin) for unapproved uses.<sup>27</sup> A company whistleblower would receive \$27 million. See also main text.</p>
<p><u>2. Novartis.</u> Agreed to pay \$150 million in 2001 to settle lawsuits filed by the states of Florida and California, as well as a whistleblower, to settle charges that it deliberately misreported pricing information in order to hike reimbursements from Medicaid.<sup>28</sup></p>
<p><u>3. Sanofi-Aventis.</u> In 2007, the FDA slammed Sanofi-Aventis over its failure to act on known instances of fraud during a pivotal clinical trial of its antibiotic Ketek (telithromycin).<sup>29</sup> The firm continued to deny the accusations, although one of the investigators had been convicted of fraud over the enrolment of patients and faking consent forms and was sentenced to 57 months in prison. During a review by Congress, a former employee said that the company was aware of fraudulent data but didn't take any action. The imprisoned investigator had enrolled over 400 patients, at a pay of \$400 per patient, whereas another site had enrolled just 12. In addition, no patients had withdrawn from the study or were lost to follow up, which is also highly suspicious given the number of patients. Ketek is still available in the USA, but carries a black box warning, as it can cause liver failure, and it is no longer approved for less serious illness.</p>
<p><u>4. GlaxoSmithKline.</u> In 1999, US psychiatrists Charles Nemeroff and Alan Schatzberg published a drug pushing psychiatry textbook that was ghostwritten by GlaxoSmithKline (GSK).<sup>30</sup> The company withheld scientific studies showing that Paxil (paroxetine) was ineffective in children and adolescents with depression,<sup>30</sup> but in 2001, GSK published a ghostwritten study, trial 329, which became widely cited and believed. In 2004, the Attorney General of New York State sued GSK for repeated and persistent consumer fraud, which opened the company's archives. GSK lied to its sales force telling them that trial 329 showed "REMARKABLE Efficacy and Safety."<sup>31</sup> In internal documents, the company admitted that the study didn't show Paxil was effective, but after extensive data manipulations, the published paper reported positive effects.<sup>31</sup> Eight children became suicidal on the drug versus one on placebo. The publication, however, listed only one headache as being related to the drug, and the suicidal thoughts and behaviour were called emotional lability or hospitalisation.</p>
<p><u>5. AstraZeneca.</u> Paid \$355 million in 2003 after pleading guilty to charges that it encouraged physicians to illegally request Medicare reimbursements for its drug against prostate cancer, Zoladex (goserelin), and bribed doctors to buy it.<sup>15</sup></p>

6. Roche. High-level executives in Roche led a cartel that, according to the US Justice Department's antitrust division, was the most pervasive and harmful criminal antitrust conspiracy ever uncovered.<sup>32</sup> For a full decade, top executives at some of the world's largest drug companies, largely from Europe and Asia, met secretly in hotel suites and at conferences, and working together in a coalition they brazenly called 'Vitamins Inc.,' they carved up world markets and carefully orchestrated price increases, in the process defrauding some of the world's biggest food companies. Roche alone had revenues of \$3.3 billion in the United States while the conspiracy was running, and during that time, Justice Department investigators say the conspirators gradually and artfully raised the prices of raw vitamins, so as not to attract notice; they also rigged the bidding process. After the conspiracy collapsed, those involved agreed to pay nearly \$1 billion to settle Federal antitrust charges, and virtually every big vitamin maker in the world was on the brink of agreeing to pay an additional \$1.1 billion. Roche was hit the hardest, agreeing to pay \$500 million to settle charges, equivalent to about one year's revenue from its vitamin business in the United States. Two Roche executives were sentenced by Federal courts to prison terms of a few months. Roche had gone this route before. In the early 1970's, it was fined by antitrust officials in Europe for engaging in anticompetitive behaviour in the sale of its two tranquilizers, Librium (chlordiazepoxide) and Valium (diazepam).

7. Johnson & Johnson. Was to pay more than \$75m to UK and US authorities in 2009 to settle corruption charges spanning three European countries and Iraq.<sup>33</sup> The charges related to alleged payment of bribes to doctors in Greece, Poland and Romania to encourage them to use the company's products and to hospital administrators in Poland to award the company contracts. In April 2012, the US Government stated in a motion in a potential multi-billion healthcare fraud case against Johnson & Johnson, which began with a whistleblower lawsuit, that Alex Gorsky, who was set to become Johnson & Johnson's next chief executive officer, was actively involved and had firsthand knowledge of the alleged fraud.<sup>34</sup> The allegations were that Johnson & Johnson paid kickbacks to induce Omnicare, the nation's largest nursing home pharmacy, to purchase and recommend the antipsychotic drug, Risperdal (risperidone) and other of the company's drugs. The government's motion stated that Gorsky, being Vice President of Marketing, was in a position to know why the company chose not to inform Omnicare or members of Janssen's sales staff that the FDA had warned the company that marketing Risperdal as safe and effective in the elderly would be false and misleading because the drug had not been adequately studied in that population, and that the FDA had rejected the company's attempt to get approval to market Risperdal for treatment of psychotic and behavioral disturbances in dementia (by far the most prevalent use of Risperdal in Omnicare-served nursing facilities) because of inadequate safety data. Despite the weight of federal and state investigations of the Risperdal allegations, Johnson & Johnson's board of directors rewarded Gorsky by selecting him to be the next CEO.

8. Merck. Pleaded guilty in 2012 to a criminal violation of federal law related to its promotion and marketing of the anti-arthritis drug, Vioxx (rofecoxib), and to pay nearly a billion dollars in a criminal fine and civil damages.<sup>35</sup> The crimes involved off-label marketing of Vioxx and false statements about the drug's cardiovascular safety. As part of the settlement, Merck agreed to enter into an expansive Corporate Integrity Agreement (Merck entered a similar agreement in 2007,<sup>18</sup> see main text).

9. Eli Lilly. Agreed to pay \$36 million in 2005 to settle criminal and civil charges related to the illegal marketing of Evista (raloxifene, a drug against osteoporosis) for the prevention of breast cancer and heart disease in letters sales people sent to doctors.<sup>36</sup> The company had also concealed data that showed an increased risk of ovarian cancer. Eli Lilly entered into a Corporate Integrity Agreement. Eli Lilly's antidepressant, Prozac (fluoxetine), was promoted off-label for several ailments, e.g. shyness, eating disorders and low self esteem, and the company concealed the increased risk of suicide and violence associated with the drug.<sup>5,36</sup> The British Medical Journal had received a series of internal Lilly documents and studies on Prozac from an anonymous source, which the BMJ sent to the FDA. These documents were made available in a litigation case in 1994, after which they disappeared. Throughout the 1990s, while swearing publicly that Prozac did not increase the risk of suicide or violence, Lilly quietly settled lawsuits out of court and was able to keep the incriminating evidence hidden by obtaining court orders to seal the documents, just as it had been doing with Zyprexa until the latest batch of documents was leaked to the press.<sup>36</sup>

10. Abbott. In 2001, TAP Pharmaceuticals, a joint venture of Abbott and Takeda, paid \$875 million, pleading guilty to criminal charges of fraud for inducing physicians to bill the government for drugs that the company gave for free or at a reduced price to doctors.<sup>2,37,38</sup> In 2003, Abbott paid \$622 million to settle an investigation into sales practices for liquids to feed the seriously ill.<sup>37</sup> Abbott gave tubes and pumps to deliver the liquid food directly into the patient's digestive tracts in exchange for large orders of the liquids.



**Table 2. Some of the alleged crimes and other misdeeds identified in the first ten hits of a Google search combining GlaxoSmithKline with fraud**

In 2010, the Justice Department charged a former vice president and top lawyer for GlaxoSmithKline (GSK) with making false statements and obstructing a federal investigation into illegal marketing of the antidepressant Wellbutrin (bupropion) for weight loss.<sup>39</sup> The indictment accused the vice president of lying to the FDA, denying that doctors speaking at company events had promoted Wellbutrin for uses not approved by the agency, and of withholding incriminating documents.

A manufacturing plant in Puerto Rico was closed down in 2009 because it produced defective drugs.<sup>40</sup> The plant had not only sent out batches of Paxil (paroxetine) containing two different doses, it had also mixed different drugs, e.g. Avandia (rosiglitazone) with Tagamet (cimetidine) and with Paxil. GSK pleaded guilty to felony-fraud and was fined \$750 million, \$96 million of which would go to the whistleblower, the company's global quality assurance manager, whose documented concerns were ignored by senior management that fired her.<sup>41</sup> GSK lied to federal investigators about the problems, despite pharmacists calling the plant directly when patients showed up with different coloured pills in their medicine. In pleading guilty to the felony, GSK admitted that it had distributed adulterated drugs, but the company lied to the public when it indicated that it went voluntarily to the FDA in 2002 out of safety concerns about the plant and when it said that, 'The plant was closed in 2009 due to a declining demand for the medicines made there.' Blockbusters such as Avandia, Paxil, and Tagamet could hardly be said to be in declining demand.

In 2007, a meta-analysis showed that the antidiabetes drug Avandia (rosiglitazone) causes myocardial infarction and cardiovascular death.<sup>42,43</sup> This had been known by GSK for many years but the company failed to warn the regulatory authorities and the public and intimidated physicians raising uncomfortable questions.<sup>43</sup> In 1999, the company, then known as SmithKlineBeecham, completed a trial that found more cardiac problems with rosiglitazone than with pioglitazone, but an executive stated in an email that, 'These data should not see the light of day to anyone outside of GSK.' When another GSK trial was published, it showed the same risk of complications for rosiglitazone as for the comparator, but this result was false.<sup>43</sup> An FDA scientist who had access to the case reports found many missing cases of cardiac problems that favored rosiglitazone four to one and an increased risk of myocardial infarction. Rosiglitazone was suspended in Europe in 2009 whereas it remained on the market in the USA.

GSK marketed paroxetine in 1992 and falsely claimed for the next ten years that it was 'not habit forming.'<sup>42</sup> In 2001, the BBC reported that the World Health Organization had found Paxil to have the hardest withdrawal problems of any antidepressant drug. In 2002, the FDA published a warning about the drug, and the International Federation of Pharmaceutical Manufacturers Associations declared the company guilty of misleading the public about paroxetine on US television.

In 2006, GSK would pay \$14 million to resolve allegations that state-government programs paid inflated prices for the firm's anti-depressant drug Paxil because the firm engaged in patent fraud, anti-trust violations and frivolous litigation to maintain a

monopoly and block generic versions from entering the market.<sup>42</sup>

In 2003 GSK signed a Corporate Integrity Agreement and paid \$88 million in a civil fine for overcharging Medicaid for Paxil, and the nasal-allergy spray Flonase (fluticasone).<sup>42</sup>

In 2003, GSK faced a demand for \$7.8 billion in backdated taxes and interest, the highest in the history of the US Internal Revenue Service.<sup>42</sup>

In 2006, GSK settled a tax dispute agreeing to pay \$3.1 billion in a case that concerned intracompany 'transfer pricing'.<sup>42</sup>