booklets

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CRIMES AND ABUSES of the Pharmaceutical Industry

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In the brief period from 2000 to 2003, almost all the large pharmaceutical companies went before state tribunals in the USA, accused of fraudulent practices. Eight of these firms were fined over 2.2 billion dollars. Four of these eight companies — TAP Pharmaceuticals, Abbott, AstraZeneca and Bayer- admitted criminal responsibility for activities that put the lives and health of thousands of people at risk[1]. What were these activities? And who bore the price? What causes pharmaceutical companies to behave in such a way? What actions have been taken in response to these abuses, and what actions still need to be taken? This booklet will examine the current strategies used by the pharmaceutical industry and the direct impact these strategies have on the way health and illness are defined and on which types of resources are available today to promote health and to prevent or cure disease.

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1. THE CASE OF "FEMALE SEXUAL DYSFUNCTION"

In 1998, Pfizer, the largest and most profitable American pharmaceutical company, introduced a drug known as "Viagra" for the treatment of male sexual dysfunction (defined as erectile dysfunction). By 2001, Viagra had become a "blockbuster" drug with 17 million prescriptions written and a billion and a half dollars in sales[2]. ("Blockbuster" is the term used by the industry to describe a drug with annual sales exceeding the billion dollars mark.) With its stock price soaring, the management of Pfizer turned its attention to women, hoping to identify some sort of female sexual dysfunction for which another lucrative "blockbuster" could be developed. The main obstacle was that while there were seemingly clear and objective criteria to define male sexual dysfunction (erectile problems), female sexual dysfunction was much more difficult to define and, most importantly, much more difficult to quantify and objectively evaluate.

In 1997, only a few months after Viagra had appeared on the market, nine pharmaceutical companies planned, organized and financed a meeting of medical specialists in Cape Cod (Massachusetts). Plainly stated, their goal was to create a new pathology (namely, "female sexual dysfunction") in order to suit the economical interests of the pharmaceutical industry[3]. A year and a half later, in October 1998, the first international conference to develop a clinical consensus on female sexual dysfunction took place in Boston[4], fully financed by eight pharmaceutical companies. Eighteen out of the nineteen authors of the new internationally agreed upon definition had direct economic ties with the companies that financed

the event or with other pharmaceutical companies. One year later, in 1999, an article entitled "Sexual Dysfunction in the USA: Prevalence and Predictors" appeared in the Journal of American Medical Association (JAMA)[5]. The authors of the article asserted, with seeming scientific objectivity, that 43% of the American female population was suffering from this "new illness," an illness in fact created and defined to suit the economic interests of the pharmaceutical industry.

Three steps were used to identify the "affected population." (1) A list of seven "symptoms" was developed, each of them considered significant enough to justify a diagnosis of the new condition if a woman were to present it for two months or more in the previous year, (2) A questionnaire about these seven symptoms was answered by a total of 1,500 women, (3) Results were evaluated in such a way that a single "Yes" response would be seen as sufficient grounds for diagnosing the condition. One of the seven "symptoms" was the lack of sexual desire. In other words, women who reported a lack of sexual desire for two successive months or more over the previous year —not taking into account whether they had been mourning the death of a loved one, stressed with too much work, trapped in an unhappy relationship, enjoying a period of solitary creativity etc.— were *automatically* labeled as "sexually dysfunctional," thus increasing the percentage of potential candidates for the treatment that the pharmaceutical industry hoped to develop in the near future. Two out of the three authors of this article had economic links with pharmaceutical laboratories. In October of the same year, a third meeting on the issue took place, organized by the Medical School of Boston University, but promoted and financed by sixteen pharmaceutical companies. 50% of those present admitted having direct economic links with the pharmaceutical industry[6]. From this meeting came the Forum on Female Sexual Function, which held two more conferences in Boston in 2000 and 2001 thanks to the generous financial contributions of twenty pharmaceutical companies led by Pfizer[7].

In 2003, Ray Moynihan denounced this manipulation of medical criteria to serve commercial interests in the prestigious *British Medical Journal (BMJ)*[8]. Over six weeks, the editors of the magazine received a total of seventy responses to Moynihan's article. Two-thirds of the responses were in support of the article and confirmed the growing indignation of medical professionals in the face of this manipulation although, as one of the replies made very clear, without the help of the same medical professionals, this situation would not have arisen in the first place[9]. If we doctors did not take part in the exploitative abuse carried out by pharmaceutical companies, such situations would not arise.

In December of 2004, the U.S. regulatory agency (the Food and Drug Administration (FDA)) prevented the commercialization of the first drug that was developed to treat "female sexual dysfunction," a testosterone patch offered by Proctor and Gamble[10]. The principal investigators of the clinical trials —all directly financed and supervised by Proctor and Gamble— had presented their results in such a biased manner, that the doubtful

benefits and the likely dangerous side-effects (breast cancer and cardiac disease) were instead advertised as clear benefits and negligible risks.

No other drug has yet been developed to treat female sexual dysfunction, largely because of a growing awareness of all those involved of the detrimental effects that the excessive influence of the pharmaceutical companies exerts on the practice of medicine[11].

There is no doubt that female sexual problems exist, but they (like any other medical condition) need to be studied in relation to the medical needs and the personal concerns of the women affected, and not in relation to the economic interests of some of the richest companies in the world.

2. THE CASE OF DRUGS USED TO COMBAT AIDS IN AFRICA

On March 23rd 2005, the Indian Parliament was obliged to modify its patent law in accordance with the stipulations of an international agency (the World Trade Organization, WTO), which had been created in 1994 to defend the interests of wealthy countries confronting the challenges of globalization. The new patent law required the commercialization of drugs in India be made subject to the international patenting system stipulated by the WTO. Under increasing international pressure, the Indian Parliament had to repeal its own 1970 legislation that had included safeguards to protect against the abusive power of patent holders. For example, if a company imposed prices that were too high for the Indian population, India could, within its own boundaries, legalize the production of generic versions of medicines still protected by patents in other countries.

Under the 1970 law, Indian companies were also permitted to commercialize these (much cheaper) generic medicines in other poor countries. The new international patenting system imposed by the WTO has no mechanism to protect against unaffordable pricing nor does it allow for the commercialization of Indian generics in poor countries. It should also be noted that the generic pharmaceutical industry is a major employer in India. In 2003, this industry provided work for 500,000 people in over 20,000 companies that were themselves able to provide work to another 2.5 million people through subsidiary contracts[12].

Let us examine the effect that such a change in patent law has upon those suffering from HIV in Africa. In 2003 more than 30 million people infected with HIV (out of a total 40 million worldwide) were living in sub-Saharan Africa. In Botswana, for example, 40% of women are infected with the HIV virus, and in Lesotho a third of the total population are infected[13]. Due to the lack of affordable antiretroviral drugs, three million Africans die from AIDS every year. Until 2005, the Indian pharmaceutical companies that produced generic drugs had been able to grant access to essential drugs to an extremely low (less than 1%) but steadily gro-

wing percentage of the population of poor countries. Due to the free market competition allowed in India under the 1970 legislation, the price of the standard antiretroviral treatment had been reduced (in 2004) from 1,500 dollars to 150 dollars per person per year[14]. In addition, the bypassing of the patents allowed the generic manufacturers to combine the different drugs into one single tablet. The astonishing reduction in price together with the simplification in the treatment protocol were already starting to show dramatic effects in the possibility of successfully treating the worldwide AIDS epidemic.

On a global scale, some 350,000 people undergoing antiretroviral treatment are dependent on the production of generic drugs in India. This figure represents half of all those currently undergoing antiretroviral treatment in developing countries. That is to say, less than 2.5% of people who are HIV positive in developing countries are currently receiving treatment. Millions of people die every year because of this. With the move to strengthen international patenting laws, all drugs developed between 1995 and 2005, as well as all those developed after 2005, are now protected by patent laws and therefore cannot enter into free competition, meaning that their price is soon likely to increase (at least) tenfold. This applies to drugs that are essential to treat the HIV virus as well as other very prevalent and potentially fatal diseases such as malaria, tuberculosis, and cancer.

Between 1995 and 2005, 8,926 new patent applications were made to the Indian regulatory agency. Many of these were refused as abusive but now, due to the new law imposed by the WTO, all the refused requests will need to be reassessed and it will be virtually impossible to legally refuse them again. More than 7,000 of these requests come from large foreign multinationals, including the pharmaceutical giant Pfizer. Today, Pfizer is the largest pharmaceutical company in the world and a key player in the US economy. A potent example of Pfizer's power can be seen in the way it prevailed over the French government in 2002. After the French government opposed its abusive prices, Pfizer threatened to withdraw its products from the French market. The French government, after many failed negotiations, ended up yielding to the pressure[15]. If a prominent member of the European Union had to yield in the face of Pfizer's economic threats, then what political power could developing countries possibly hope to use to oppose unfavorable agreements?

The direct link between the introduction of patenting laws and the mortality of the population can be seen in the case of Brazil. Since laws were passed that prohibited the patenting of drugs that had appeared on the Brazilian market before 1997, Brazil was able to locally produce the generic equivalent of eight out of the ten antiretroviral drugs currently available worldwide, with an average reduction in price of 79%. In 2003 it became clear that the Brazilian AIDS epidemic had been stabilized and the mortality rate reduced by half[16]. With the new international legislation, however, the production of generic medicines in Brazil will also be blocked.

Due to its relevant content, we will now reproduce some extracts of the letter which Karim Laouabdia, spokesperson for Médecins Sans Frontières (Doctors

Without Borders), addressed to Pascal Lamy on September 20th 2005, on the occasion of Lamy's election as Director General of the World Trade Organization (WTO).

"The HIV/AIDS crisis has shown the urgent need to ensure that essential medicines are available at affordable prices. Today approximately half of the one million people in the developing world who receive antiretroviral drugs rely on generic production. The fixed-dose combinations, produced in India, greatly simplify the administration of antiretroviral therapy and have been critical to scaling up treatment in resource-poor settings. The 2001 WTO Doha Declaration on TRIPS and Public Health[17] *was a vital step in increasing access to medicines. It provides unambiguous support to any government that needs to protect the health of their people [because these governments are allowed] to use the TRIPS flexibilities to overcome the barriers posed by patents, and helps the least developed countries by extending the transition period for enforcing and granting pharmaceutical product patents until at least 2016. Since then, however, there has been a systematic dismantling of the Doha Declaration through bilateral trade agreements in which much higher levels of intellectual property protection are demanded than [those] required by the WTO. The impact of patent protection on HIV programs will become very apparent in the coming years when large numbers of patients currently on treatment will need to switch to newer, second-line medicines. These drugs are at least 4-10 times as expensive as first-line treatments, and almost all are patented or are likely to be patented in those countries that have capacity to produce them generically such as India, Brazil and Thailand. (...) In addition, the impact of patents is not limited to antiretroviral drugs, but will increasingly be felt across all diseases with all medicines brought to market from now on. (...) The patent system is intended as a stimulus for innovation, but there is no mechanism for directing that innovation, and as a result many diseases are completely ignored. We face the consequences on a daily basis in our projects, for example to diagnose TB [tuberculosis] in HIV patients and in children; to treat tropical diseases like leishmaniasis, which affects 12 million people; to monitor HIV patient progress, and to treat HIV in children"*[18].

Less than three months after submitting this letter, Médecins Sans Frontières exposed a new offense: some well-known pharmaceutical companies, after having prohibited the production of generic drugs in poor countries, were refusing to commercialize in these same countries the drugs that, despite being needed by the population, were not lucrative enough for the producing company[19]. The example used was that of the antiretroviral drug Kaletra, marketed by Abbott. Abbott has introduced a version of Kaletra that does not need to be refrigerated. In spite of the enormous advantages that such a product would represent to African patients (due to the high temperatures and the frequent interruptions in electrical supply which occur in the African territory), Abbot refuses to market this medicine in Africa. Abbot is not alone. Gilead, the pharmaceutical company that owns the patent of tenofovir, another antiretroviral medicine recommended by the WHO, has also refused to commercialize it in Africa.

3. WEALTH AND POWER AGAINST THE POOR

The extraordinary growth in political and economic power of the large American pharmaceutical companies began in 1984 with the law on the extension of patents (Hatch-Waxman Law) approved by the Republican-dominated Congress of the Reagan years. This power was then consolidated in 1994 with the World Trade Organization (WTO), whose creation was intended to prevent the rapidly expanding global economy from hindering the economic interests of the world's wealthiest companies[20].

3.1. CURRENT WEALTH AND POWER OF LARGE PHARMACEUTICAL COMPANIES

The gross profit margins of the pharmaceutical industry range from 70 to 90% and its net income rate is the highest of all industries. (According to *Fortune* magazine, in the year 2000 the net income rate of the pharmaceutical industry stood at 18.6% *versus* the 15.8% rate of commercial banks). In 2004, Pfizer, the largest pharmaceutical company, had a net income rate of 22% of its total sales, which amounted to *53 billion* dollars[21]. In spite of these extraordinary profits, the tax rate imposed on pharmaceutical companies is remarkably *below* average, standing at 16.2% *versus* the 27.3% average rate imposed on other large industries[22]. Such a tax break is shocking when one considers that annual prescription drug price increases routinely outpace the level of inflation (from 6% to 20% each year)[23].

In 2000, the main pharmaceutical lobby in the USA (PhRMA) counted 297 professional lobbyists, that is, one for each two members of Congress[24]. This number —already vastly exceeding the number of any other lobby— has *tripled* in recent years. In 2002, PhRMA financed the work of 675 lobbyists, which means

that in Washington that year there were more people working to promote the interests of pharmaceutical companies than members of Congress[25]. This unrelenting pressure and influence on the legislative process has allowed the industry to obtain the advantageous conditions (see section 3.2) that have permitted it to progressively dominate the global market: today 60% of all drug patents are owned by USA-based companies versus 20% owned by the EU. The USA controls the market of the 50 best-selling drugs, all of them *blockbusters*[26]. In 2002, the total earnings of the ten largest pharmaceutical companies exceeded the combined earnings of the other 490 companies listed in *Fortune*'s top 500 most profitable companies: the ten largest pharmaceuticals together made a total profit of 35.9 billion dollars and the other 490 companies together made a total profit of 33.7 billion dollars[27]. The disproportionate privileges that the pharmaceutical industry is enjoying in the form of tax breaks and advantageous laws and agreements, show clearly that the industry's current power and wealth are not the result of a "free market" but rather of a deliberate policy designed to protect an industry that is as politically strategic to the USA as the petroleum industry.

To highlight the current absence of freedom and fair play and the need to better regulate this market, Marcia Angell, chief editor of the renowned medical review *The New England Journal of Medicine* for almost twenty years, succinctly affirms: "The colossus that is the pharmaceutical industry is today like a five-hundred pound gorilla: it can do what it wants"[28]. And Philippe Pignarre, director for seventeen years of a large pharmaceutical company and currently Professor at the University of Paris-VIII, insists that the market is not and has never been a *natural* reality, but is always a cultural or a social one. That is to say, the concept of *market* necessarily implies norms and agreements whose goal is not to regulate some sort of pre-existing 'natural entity', but instead to *create* the reality we call *market*. The norms are constitutive of the market. The so-called 'free market' (an unregulated market) cannot exist; instead, what can and — most certainly— *do* exist are the 'brutal market,' that is, a market regulated according to the interests of the five hundred pound gorilla, and the 'less brutal market,' that is, a market whose norms attempt to temper the avidity of the weightier[29].

3.2. WAYS IN WHICH THE WEALTH AND POWER OF LARGE PHARMACEUTICAL COMPANIES IS BEING USED

Today large pharmaceutical companies use their extraordinary wealth and power to defend their own interests at the cost of the well-being, health and in some cases even the lives of others. That is why they are accused of *criminal* behavior.

According to the report issued last year (2005) by a committee of experts of the

British House of Commons, it is obvious that the interests of the pharmaceutical industry and those of the general public do not coincide. This committee concluded that it is therefore (1) "essential to set up an effective regulatory regime to ensure that the industry works in the public interest," (2) "the present regulatory system is failing to provide this" and (3) "as a consequence of lax oversight the industry's influence has expanded and a number of practices have developed which act against the public interest"[30].

The authors of the report also pointed out "that the aim of new drugs should be to provide a *real therapeutic benefit for patients*"[31]. What does this mean? If they are not working towards producing *real therapeutic benefits* now, then what are pharmaceutical companies spending their time doing? As the third most profitable industry in the country (after tourism and banking), this very same report called the pharmaceutical industry "a jewel in the English crown"[32]. Whence come the extraordinary profits of this industry if not from producing useful medicines?

The main strategies employed today by the pharmaceutical industry to create their wealth include: (1) orchestrating aggressive and often misleading advertising campaigns and emphasizing propaganda in relation to the drugs they *develop, whether or not they are useful, and in spite of the fact that some may be harmful or even fatal*, (2) seeking to monopolize the markets by exploiting their medicines (including the *essential* ones) in increasingly abusive conditions that do not take into account the objective needs of patients nor their purchasing power, (3) greatly reducing or in some cases completely eliminating their research into illnesses that primarily affect the poor so they can focus their resources on profitable markets and problems that affect populations with a high degree of purchasing power, even when that research does not involve actual diseases (for example, the proliferation of anti-aging "medicines"), (4) forcing national and international laws and agreements even if it is at the expense of millions of lives.

3.2.1. Marketing of useless medicines that might prove harmful or even fatal

Statistics from the FDA show that between 1998 and 2002, eight suicides were reported in the USA among sufferers of epilepsy that were taking the drug *gabapentin* made by Pfizer (its commercial name is Neurontin®)[33]. During the first six months of 2003, the number of reported suicides was 17. A private law firm made these facts public and opened their own investigation of the incidents. During the 12 months from September 2003 to August 2004 they documented 2,700 suicide attempts among patients that were taking *gabapentin*, 200 of which ended with the death of the patient. In November 2004 the *British Medical Journal (BMJ)* reported that since this issue had come to light, neither Pfizer nor the FDA had taken any action not even by indicating on the leaflet the increased risk of suicide[34]. As of the writing of this booklet, the risk of increased suicide caused by Neurontin® is noted on Pfizer's webpage[35].

As for the anti-depressant *sertraline* (Zoloft®), also produced by Pfizer, the sa-

me issue of the *BMJ* reported that the company had hidden information on possible side effects that included suicide attempts and aggressive behavior[36]. The case of Christopher Pittman (a 12 year-old boy who began to display highly aggressive behavior within a few weeks of taking *sertraline* and who, two days after having his dosage doubled, murdered his grandparents and set fire to their house), together with an accumulation of less dramatic evidence along the same lines, was enough to convince the European regulatory agency for medicines to prohibit its prescription to patients under 18 years old[37].

Unnecessary medicines are known in pharmaceutical slang as "me-too drugs." These drugs are designed and marketed with the aim of substituting a previous drug whose patent is about to expire. The therapeutic qualities of me-too drugs are essentially the same as those of the previous drug, but because they are introduced as *new* drugs into the market, pharmaceutical companies have the right to obtain a new patent. The success of such unnecessary medicines can only be explained through the power of advertising to doctors and patients (see section 4.2). One example of this type of drug is *cerivastatin* made by Bayer (its commercial names are Baycol®, Lipobay®, Cholstat® and Staltor®). *Cerivastatin* is an anti-cholesterol medication that had to be taken off the market in 2001 after having been shown to cause 1,100 cases of severe rhabdomyolysis (a muscular wasting condition that can be irreversible) as well as one hundred deaths[38].

Another more recent example is that of the anti-inflammatory drugs Vioxx® (made by Merck), and Bextra® and Celebrex® (made by Pfizer). These drugs had shown no therapeutic benefits in the clinical trials that compared them to other anti-inflammatory drugs already on the market[39]. In 1998 and 1999, the manufacturers were nevertheless given the go ahead by regulatory agencies because it was hoped that these drugs would produce milder side effects than the older anti-inflammatories. In September 2004, Vioxx® (Merck) was taken off the market after it became clear that its side effects were not only not milder but potentially fatal (stroke and heart attack). The FDA reported that Vioxx® was likely to be responsible for 27,785 deaths from heart attack between 1999 and 2003[40]. In April 2005 Bextra® and Celebrex® (Pfizer) were also taken off the market following a long and difficult struggle between the FDA and Pfizer. That such a prolonged struggle ensued for a drug that had shown little or no potential benefit but rather great risk, highlights just how much political power this giant of the pharmaceutical industry really wields[41].

Whenever a new drug is developed, there is always a risk of unwanted side effects that could not be detected at the research phase. This cannot be avoided. But if every medicine has a risk of causing serious side effects and in some cases death, why are new medicines developed that offer no real therapeutic advantage over those already on the market? Why do pharmaceutical laboratories produce them? Why do regulatory agencies approve them? Why do doctors prescribe them?

On the topic of unnecessary medications, we shall mention the drugs that are designed to cure illnesses —such as fe-

male sexual dysfunction as defined above— that the pharmaceutical industry labels as such according to their own interests. Some examples of non-pathological human conditions that are labeled as *illness* so that drugs can be sold to cure them include: menopause (allegedly cured with hormone replacement therapies that have recently shown unacceptable side-effects), appropriate sadness (labeled as depression and allegedly cured by anti-depressants that we have already seen are capable of causing suicide or even murder[42]), and memory loss among the elderly (labeled as "incipient cognitive deficit" and treated with anti-dementia medicines; it is to note that on learning that they might have incipient dementia, the elderly often feel sad and become suitable candidates for anti-depressant therapy).

There is a popular English expression used to denounce this abusive intrusion of the medical model (and the medical business) into non-medical aspects of human life: "*a pill for every ill*.[43]" The 2005 report by the committee of experts of the House of Commons notes that in 2003, 650 million *prescription* drugs were sold in England. This number (to which we should add the blossoming business of the over the counter sales of drugs) reflects an increase of 40% in relation to the amount of prescription drugs sold in the ten years prior to 2003 and means that *each English citizen* takes an average of 13.1 *prescription* medicines each year[44]. The same report remarks that "while the pharmaceutical industry cannot be blamed for creating unhealthy reliance on, and overuse of, medicines, it has certainly exacerbated it. There has been a trend towards categorizing more and more individuals as 'abnormal' or in need of drug treatment"[45].

According to the French network of regional centers of drug-vigilance, every year 1.3 million French citizens are hospitalized due to side effects of medicines they are taking. This figure represents 10% of all hospitalizations per year. A third of this total figure (ca. 400,000) is admitted in a serious condition and 18,000 of them end up dying. This means that, in France, the mortality rate per year due to side effects of medicines is *double* that of road accidents[46].

3.2.2. Exploitation of essential drugs in abusive conditions

In the discussion on the marketing of antiretroviral drugs in Africa, we saw the brutal effect that the new international patent law is having on access to essential drugs in poor countries. According to Pignarre, in the face of direct accusations from humanitarian organizations, the big pharmaceutical companies defend themselves in this way:

The pharmaceutical industry explains that any move against the right to uphold patents in the Third World, and particularly in Africa in relation to drugs used to combat AIDS, would signify the end of the research into such drugs, for nobody will be willing to fund research into drugs that will not be able to be protected by patents. (...) This reasoning implies that tomorrow's theoretical progress can only be pursued at the cost of sacrificing millions of today's lives… it implies a choice in favor of improving the quality of life of the privileged populations of the North at

the cost of immediately cutting short, by several decades, the life expectancy in the South. It is equivalent to condemning to death 90% of those who need essential medicines, in order to maintain the high prices that only the privileged 10% are able to pay. This obscene dialectic —into which the pharmaceutical industry of richer countries unanimously wants to trap us— is the beginning of a reign of terror[47].

During the international controversy that followed the obligation imposed on poor countries to respect —at the expense of the lives of their citizens— the abusive patents on essential antiretroviral drugs, the UN World Intellectual Property Organization (WIPO) developed a propaganda document in favor of the pharmaceutical companies, in which the six main accusations leveled against the patent system by humanitarian organizations from all over the world were labeled as "myths" and were refuted with false arguments.

Here is a summarized version of the six accusations that the WIPO discarded as myths (underlined), followed by some critical comments by Philippe Pignarre[48].

1. *The difficulties of access to health care and the restricted availability of essential drugs are a consequence of the actual patent system*. If this is a myth, why have countries that up until now have not respected the patent system (like India) been able to combat the AIDS epidemic much more successfully than countries that were forced to accept these regulations from the beginning?

2. *The high market price of drugs is mainly caused by a patent system that allows the industry to fix artificially high prices*. If this is a myth, why does fluconazol, a drug used by AIDS patients, have a market price that ranges from $18 to 32 in the countries where Pfizer has maintained its monopoly, and a price of only $1 in countries where a generic equivalent exists? Why does the Indian company Cipla that makes generic drugs offer Médecins Sans Frontières (MSF) an annual charge of $450 per patient for anti-AIDS treatment in contrast to the $13,300 demanded by western laboratories?

3. *The actual patent system favors the interests of private companies at the expense of the common good*. It is clear that there is a conflict of interests between the pharmaceutical companies and the common good and it is as well clear that the market in general —and very particularly the drug market— is not "free", but rather subject to legislation in every country. At the present time, this legislation is aimed at favoring private interests.

4. *The actual patent system prevents real competition*. Nobody claims this. The actual patents system does allow competition, but its rules are not aimed at favoring the common good..

5. *The actual patent system is particularly unfair for developing countries that are facing very complex social and economic situations, and so should therefore be made exempt from such obligations as are linked to the international intellectual property, particularly in relation to certain drugs*. Not only is this not a myth, but a growing large-scale health emergency. An international forum —with no right to veto allowed to the US nor to any other country— should be immediately set up to deal with this question.

6. *Actual international treaties on the protection of patents prevent the exercise*

of the fundamental human right to have access to available drugs that can save one's life. As we have seen, this is indeed the case today. We need a new, more just, international patents system.

The abuse of the current patents system does not solely affect Third World countries. In richer countries, increasing numbers of patients are facing difficulties in paying for the treatments they are prescribed. In order to reduce expenses, some patients take their daily medications every other day or share them with other members of the family. In the USA the cost of taking one drug can reach as high as $1500 per year. On average, elderly US citizens take regularly six different drugs. This represents a total average annual expense for prescription drugs of roughly $9000[49].

3.2.3. Research driven exclusively by economic profit

In 2001, the group set up by Médecins Sans Frontières (MSF) to study neglected illnesses published a report called "Fatal Imbalance". The report concluded that, in spite of the fact that certain illnesses affect millions of people in a significant way and in spite of the fact that they can potentially be cured: a) hardly any research is done into illnesses that *primarily* affect the poor, and b) illnesses that *only* affect the poor are not investigated *at all*.

The name of the report, "Fatal Imbalance," refers to the fact that only 10% of the world's health research projects (including all those undertaken by governments and universities) is dedicated to illnesses that affect 90% of patients worldwide. The scandalous imbalance of wealth in our world is well known: 20% of the global population enjoys and wastes 80% of the planet's wealth, while 80% of the global population struggle and die with the remaining 20% of global resources. One could imagine that with regard to essential medicines, this imbalance could at least be partially ameliorated because this is a sensible topic that moves many to compassion and because of the many international agencies involved. However the opposite is true; the imbalance between rich and poor in our world is made much worse by the inequities involved in the allocation of resources and the availability of essential medicines: 90% of all health resources are committed to researching diseases that affect 10% of patients (those living in the developed world), and 10% of all health resources are committed to researching diseases that affect 90% of patients (those living in the developing world). This is known as the "10/90 gap"[50].

Tropical diseases belong to the category of neglected diseases. Out of a total of 1,393 drugs that were marketed between 1975 and 1999, only 13 (1%) were developed for the treatment of a tropical disease. The forgotten illnesses include: malaria, tuberculosis, sleeping sickness (African Trypanosomiasis), Chagas disease (South American Trypanosomiasis), Buruli ulcer disease, Dengue fever, leishmaniasis, leprosy, filariasis and schistosomiasis. Apart from the first two, the illnesses in this list almost exclusively affect the poor. Of particular note is Chagas disease, currently affecting *16-18 million people*, with some 100 million (25% of the Latin American population) at risk of acquiring it[51] and 50,000 people dying annually from it[52].

The authors of the MSF report, in collaboration with the Harvard School of Public Health, sent a questionnaire to the twenty largest pharmaceutical companies of the world requesting information on their research programs. Only eleven companies replied, including six out of the ten largest companies. Out of the eleven companies that responded, none were researching sleeping sickness and only three had invested some money into Chagas disease and leishmaniasis.

One could argue that private companies have the right to invest their money as they please, but the remarkable point here is the fact that the money that funds the health research carried on by the pharmaceutical industry comes largely from the public: six out of the eleven companies studied by MSF had financed their studies primarily through agreements with public health organizations. A study by *The Boston Globe* on the 50 most widely sold drugs between 1992 and 1997 concluded that 45 of these had received public funding[53]. The public pays first to fund the research and then again to buy the product. It is no surprise then that the earnings of the industry be so spectacular. Of the 17 final clinical trials that led to the approval of the five most widely sold drugs in 1995 (Zantac®, Zovirax®, Capoten®, Vasotec® and Prozac®), only one was financed entirely by the pharmaceutical industry. Of all the research involved in the development of these five drugs, only 15% was financed by the pharmaceutical industry; 55% of the research work was carried out by the National Institute of Health (the public governmental institution of the USA that is financed through tax revenues), and the remaining 30% of the work was carried out by academic institutions outside of the USA almost entirely financed with public money[54].

The MSF report makes clear that responsibility for the *fatal imbalance* lies not only with the pharmaceutical industry but also with all the public and private institutions that participate in a system seemingly driven exclusively by profit with little or no regard for the suffering of patients[55]. According to the same MSF report, in 2001 the majority of financial and intellectual resources invested in health research throughout the world were committed to investigating impotency/erectile dysfunction, obesity and insomnia[56].

In addition to not being taken into account when deciding the priorities of pharmaceutical research, the patients of poor countries —particularly those in Africa— are often used as experimental subjects in unethical clinical trials. In Kenya, for example, towards the end of the 1990's and under the responsibility of the University of Washington, clinical trials were carried out to observe the *natural progression* of AIDS. What that means is that, with the excuse that these patients would have died anyway, hundreds of Africans were submitted to complementary tests in order to document and study how they deteriorated until their death. As the infection advanced they were never offered any of the treatments that could have stopped it[57]. In his 2000 report "The Shame of Medical Research," David Rothman exposed the fact that in 15 of 16 clinical trials that were being carried out in developing countries to study the most cost-effective way to prevent the transmission of the AIDS virus during preg-

nancy, the women enrolled in the control group received a placebo drug (a sugar pill) instead of the AZT treatment that has been shown to reduce the maternal-fetal transmission of the virus. According to the Helsinki Convention on ethical protocols for medical research, a new treatment should always be compared with the most effective treatment available on the market. The study of the Harvard School of Public Health in Thailand was the only ones who honored the Helsinki Convention. The other 15 studies enrolled a total of 17,000 women and allowed half of these women (those in the control groups) to go through multiple blood extractions and through the additional tests required by their study protocol, while giving them daily a useless sugar pill and documenting how their health deteriorated and how the virus infected the child they were carrying[58].

3.2.4. Manipulation of legislation in their own countries and with regard to international agreements

In 2002, 26 of the 675 pharmaceutical lobbyists on payroll were *former members of Congress*, and 342 of them were former employees of Congress (20 of whom had held management roles)[59]. Each lawmaker has assigned to her/him one or more lobbyists who have the time and financial backing to study their psychological profile, personal and employment history, and their weaknesses. This information is used to exert as much pressure as possible upon each lawmaker so as to garner support for legislation favorable to the interests of the pharmaceutical industry and to curtail any measures that would inhibit these interests. As we have seen, these interests are *contrary* to the common good.

In addition to attempting to directly influence the highest levels of the government, pharmaceutical companies in the US have begun to develop a parallel strategy meant to manipulate public opinion. They promote organizations that appear to be spontaneous initiatives and are in reality supported and run by citizens that work for the pharmaceutical companies and are paid to promote their interests "on the ground" as it were, without being noticed[60]. These associations are especially useful when pressure is being exerted to remove a new drug from the market because of its harmful side effects. As the pressure begins to build, these "spontaneously" formed organizations recruit people to loudly and publicly complain and to bombard the media with an avalanche of glowing patient testimonials about the wonderful improvements they have experienced on the new drug.

Today, neither the FDA, nor any other regulatory agency in the world, requires that in order to approve a new drug for sale, proof that this new drug is *better* than the drugs already available on the market be demonstrated. Taking into account that —as we have seen— there is always a possibility that hitherto unknown side effects of a new drug prove fatal, this demand seems only too logical and reasonable. All over the world, however, all that is necessary for a new drug to be approved for sale is that it be shown to be better than taking nothing at all.

The fact that patenting a new medicine does not require proof that this drug represents an improvement over similar drugs already on the market explains the

proliferation of the so-called "me-too drugs", drugs that, as well as being unnecessary, are capable of causing death or other serious or irreversible illnesses. For a pharmaceutical company it is much more profitable to minimally modify an old drug and sell it with a new patent when the patent of the first is about to expire, than to pour money into researching a new drug from scratch. Between 2000 and 2004, 314 new drugs were approved in the USA of which only 32 could actually be considered "new"[61]. As we shall see, this possibility of making the industry profitable by producing drugs that are simply copies of others already in existence is the key factor of the crisis that this industry is currently facing (see section 4.1).

The demand that new drugs prove their worth before being allowed to enter the market is reasonable enough, but more reasonable still would be for drugs to be evaluated by independent organizations rather than by the same companies that will be economically benefiting from them. Today, none of the democratic governments of the world requires that an independent body assess the effectiveness and safety of drugs. The existing regulatory agencies evaluate the data provided by pharmaceutical companies, but do not carry out any research of their own. Pharmaceutical companies make the drugs, validate them, and sell them. The only task left out of their direct control is the approval necessary for the sale of the product. This is the responsibility of the regulatory agencies. The question is: have pharmaceutical companies used their immense power and clout to influence and manipulate the regulatory agencies meant to ensure the safety of the public? The answer is yes. And did they succeed in doing so? Again the answer is largely yes, at least with regard to the USA. Let us examine how this occurred.

In 1992, the US Congress approved a law allowing pharmaceutical companies to accelerate the process of obtaining new patents in exchange for economic compensation[62]. The pharmaceutical company wanting to patent a new drug can —if it so wishes— pay a considerable sum to the FDA so that they hire more workers and in this way decide more speedily whether a new drug should be approved. Of course this is not supposed to be a matter of buying governmental approval, but rather a question of economically contributing to the improved functioning of the regulatory agency. In practice, however, what occurs is that the very salary of some of the FDA employees responsible for evaluating a new drug comes ultimately from the pharmaceutical company interested in obtaining its patent[63]. Under these conditions, it is not surprising that since this law was passed, there has been a marked increase not only in the *total number* of patents approved (a logical consequence after having increased the number of workers), but also in the *percentage* of patents approved (i.e., other things being equal, if 10 workers reject 5 patents and approve 5, 100 workers should reject 50, and approve 50, not *more* than 50; the total number of approved patents should increase, the percentage should remain stable).

This irregular situation that compromises the neutrality of the FDA, would not have been allowed to arise had the pharmaceutical industry not controlled the nomination of the director of the FDA. In 2002, the candidacy of the respected pro-

fessor of pharmacology Alastair Wood was blocked in favor of Mark McClellan, who, besides being the brother of the press secretary of the White House, had as his greater asset the fact of being unreservedly in favor of the politics of the pharmaceutical lobby PhRMA and its fraudulent practices. McClellan held the highest position in the FDA between the years 2002 and 2004[64].

There are more irregularities. In 1997, Congress passed a law allowing a company known as "Drugdex" to develop and distribute an official list of recommended uses for medicines much broader than that approved by the FDA. One might wonder whether it is ever possible to prescribe a medicine to treat a condition for which it has not been approved by the regulatory agency. The answer is yes, because physicians are entitled to make use of medicines in the way and at the doses they deem appropriate for they patient, always under their direct responsibility and understanding that they can be sued if their use of the medicine proves wrong. "Wrong use" is not the same as "use not sanctioned by the regulatory agency". Physicians need to have leeway in prescribing and this is acknowledged and respected by all. However, it is one thing to allow a physician to use her/his clinical judgment as she/he sees fit, and it is another —very different— thing to create, with the support of government, a second much longer list of official uses of a medication parallel to the list given by the regulatory agency.

The benefit to the pharmaceutical industry is clear: the more conditions a drug can treat, the greater its potential market. Not being directly part of the pharmaceutical industry, Drugdex (a subsidiary of Thomson Corporation, a company which offers courses and training to physicians) serves their interests in the following way: (1) a pharmaceutical company wants to increase the list of conditions that can be treated by one of their drugs (drug X), (2) it contacts Drugdex to request that certain conditions be included in their official list of indications for drug X, (3) Drugdex includes them without too strictly assessing the information submitted by the pharmaceutical company, (4) in return, the pharmaceutical company finances a continuous education course offered by the professionals from Thomson Corporation to which Drugdex belongs, and (5) the subject of the course offered is, naturally enough, "New indications of drug X." As the course is being offered in more and more medical centers, Thomson Corporation benefits because it is offering a course and is being paid for it, and the pharmaceutical company benefits because the physicians trained by Thomson start prescribing drug X to treat the new set of ailments, thus increasing its sales and its profits. Another convenient consequence of this cooperation is that physicians who prescribe drugs for the additional ailments listed by Drugdex are legally covered, should any complications arise. And, last but not least, Medicare, the public program in the USA that helps the elderly pay for medical care and prescriptions, is *obliged by law* to at least partially reimburse prescriptions if the conditions for which they are written are listed in Drugdex[65]. This abuse of the Medicare system translates into a substantial and direct transfer of public money to pharmaceutical companies.

The dangers of such an indiscriminate broadening of the medical indications of a

drug cannot be underestimated. The drug Neurontin®, for instance, in addition to being used to treat epilepsy, which is the official condition recognized by its patent, can also —according to Drugdex's list— be appropriately prescribed to treat 48 other conditions. Its additional indications include conditions as common as hiccups, migraines, and smoking cessation. In section 3.2.1, we have seen that Neurontin is a "me-too drug" with a potential risk for inducing suicide[66]. How is it possible that a drug with such a profile be officially approved in the US to treat 48 different medical conditions including hiccups?

To avoid such abuses, the committee of experts of the English Parliament recommended that their public health system be funded to carry out independent studies on drugs and also be given the necessary authority to compel pharmaceutical companies filing for patents to carry out clinical trials comparing their new drug with the drugs already on the market[67].

With regard to international politics, the influence of the large pharmaceutical companies is mediated in two ways: (1) through the pressure the US government exerts on other countries by threatening them with economic sanctions if they don't accept devastating bilateral agreements contrary to their national interests and favorable to the American pharmaceutical industry, (2) through the WTO[68], one of whose first agreements was the TRIPS[69], which, apart from imposing an abusive patent system to all countries —including developing countries— lengthened the validity of pharmaceutical patents from 17 to 20 years. Before the creation of the WTO and the imposition of the TRIPS (both took place in 1995), the majority of countries in the world did not even acknowledge the patenting of medicines, given that they were not considered commercial products but rather items of "first necessity" that should be made available to all patients, regardless of their economic status.

The WTO regulations regarding generic drugs were approved in 1995, but poorer countries were given until 2005 to prepare for these new laws. The South African government, realizing that the introduction of the new legislation would make it impossible to treat their population due to a lack of funds, and that this in turn would bring about an increase in the AIDS epidemic, announced at the end of the nineties that they would begin producing generic antiretroviral drugs in their own laboratories. In response, the pharmaceutical industry pressured the American government, and the Clinton administration threatened South Africa with crippling commercial sanctions if they dared to produce their own drugs *in order to fight the AIDS epidemic*.

Where is the *free market* in all this?

On February 17th 2006, the English newspaper *The Independent* published an article which further illustrates the extent to which the actions of pharmaceutical companies are abusive towards poorer countries, and in particular towards Africa[70]. The article denounced the fact that pharmaceutical companies are prospecting the African continent to obtain natural resources that could be used to benefit their own industry, with a complete disregard for the UN convention on biodiversity that establishes the inviolable

sovereignty of a country over its own natural resources[71]. The pharmaceutical company SRPharma used a micro-bacteria discovered in Uganda in the seventies in order to develop a drug that would treat chronic viral illnesses, including HIV/AIDS. The Managing Director of SRPharma acknowledged that his company had offered no economic compensation to Uganda in return for this discovery. SRPharma did not respect international law and did not compensate Uganda for using the country's natural resources for their own benefit. Neither did they allow Uganda to use the drug that was made from this discovery to treat Ugandan patients. In the same article, the Managing Director of SRPharma complained that the drug had not brought about the anticipated benefits, and yet remained silent about the 20 million dollars that had been received to finance its development. For its part, the Bayer Company benefited from the discovery of a bacterial strain found in Lake Ruiru in Kenya, from which it was able to create a drug used to treat diabetes (Precose® or Glucobay®). This drug generated more than 380 million dollars in sales. The Bayer group flouted the same international conventions as SRPharma and did not offer Kenya anything in return for this discovery. Bayer acknowledged this, but defended itself by saying that in spite of the fact that the origin of the drug lay in the bacterial strain found in Kenya, its biotechnological development meant that the end product was completely different, concluding that "*we patented the end product, and not the bacterial strain*." However, the investigators responsible for studying the violations to the convention on biodiversity in Africa[72] reached a very different conclusion: "We find ourselves facing a new form of colonialism". International agreements are forced upon the poor and are flouted by the wealthy.

4. AN INTERNAL CRISIS

INNOVATIONS IN TREATMENT REPLACED BY ADVERTISING

Between 1994-96, the large pharmaceutical companies were willing to pay up to 59 million dollars to smaller companies for a new molecule that had successfully completed pre-clinical trials, so that they could then carry on the required clinical trials and hopefully end up reaping the benefits of patenting a new medicine and introducing it into the market. Between 2000-02, the figure that these same companies were willing to pay had risen to 148 million dollars[73].

4.1. CURRENT CRISIS OF PHARMACEUTICAL COMPANIES

The information above brings to sharp light the hidden cause of the current crisis of the pharmaceutical industry: its innovatory capacity has practically disappeared. And without capacity for innovation the industry has no future. The alarm was first sounded by *The Wall Street Journal* in 2003 when consultants at IBM studied the twenty largest pharmaceutical companies and revealed a dramatic decline in shareholder return[74]: "The return that the twenty largest pharmaceutical companies were able to offer to their shareholders, which had averaged 28% from 1993-1998, fell to an average 4-5% in the following five years, 1998-2003"[75].

Another significant fact is the growing frequency and volume of mergers taking place between larger pharmaceutical companies in recent years. In 2002, Pfizer became the largest pharmaceutical company after merging with Warner-Lambert and Pharmacia (not long after Pharmacia had bought Upjohn and Monsanto). Following this merger, Pfizer controlled 11% of the global market. Five years earlier, Merck had been the No. 1 pharmaceutical company, but theirs was only a 5% share of the global market[76].

This extraordinary concentration of capital creates gigantic corporations that are very difficult to manage and more importantly, breaks up consolidated research groups and places their leading-scientists under non-scientific administrators that interfere with their research projects. Jürgen Drews, an ex-researcher with Hoffmann LaRoche, states: *All in all, the pharmaceutical industry is replacing its old investigative structure with a technical apparatus that is still able to carry on analysis, animal research, and chemical synthesis of molecules, but that is proving utterly unable to develop new ideas. The research departments of the large laboratories are not any more autonomous and the scientists working for them cannot manage their own affairs; their creativity is being curtailed by lawyers, economists, businessmen and top-ranking administrators unable to imagine the future other than as a lineal development of what we already have (...). The pharmaceutical industry has created conditions that destroy originality, creativity and freedom and favor consensus, imitation, submission and repetitiveness*[77].

In 1990, an efficient researcher could test the reactive capacity of 2,000 molecules per year. In 2000, a robot, like the ones that are currently used in large research laboratories, could test 6,000 molecules in a single day[78]. But this exciting quantitative increase has not brought about an increase in innovation; rather it seems to have caused the opposite. In the five years between 1998 and 2002, a total of 415 new drugs were approved in the USA. Out of these, only 133 (32%) were based on new molecules and of these 133, only 58 were new molecules that produced new effects (effects different from those of the drugs already available on the market). The yearly distribution of these 58 genuinely new drugs was as follows: 16 were developed in 1998; 19 in 1999; only 9 in year 2000, and only 7 each in 2001 and 2002. This is the real productivity of the —up to now— most profitable industry in the US. Such meager productivity is particularly shocking considering the money invested during this period (around 30 billion dollars), and the size of the 35 companies involved (in 2003 Pfizer alone owned more than 60 laboratories in 32 different countries)[79].

The consequences of the industry's misguided politics are becoming evident to all involved. The patent controversy over antiretroviral drugs in Africa has drawn attention to the policies and privileges enjoyed by pharmaceutical companies, and these are now being questioned at an international level. In the US, the two most important factors that have raised the awareness on this issue have been: (1) the growing difference in prices between US and Canada with regard to drugs that are protected by patents, and (2) the superfluous and potentially hazardous nature of "me-too drugs." Let's have a look at these two factors in a little more detail.

The price of a medicine protected by a patent is in Europe or in Canada one half or even one third the price of the same medicine in the US. Since1987, it is illegal in the US to import medicines from Canada. Despite this prohibition, in 2002 over a million American citizens were regularly buying their medication from Canadian pharmacies. In several areas close to the border buses were even organized to transport them. By 2003, 7%

of American citizens were buying their medication from Canada over the Internet (the number of on-line Canadian pharmacies rose between 1999-2003 from 10 to 140). The city of Springfield, Massachusetts, in an open act of defiance meant to denounce the unfair price differential, decided to lower its administrative costs by purchasing all drugs for its public officials through Canadian pharmacies. The city of Boston and governmental representatives from 12 other states followed the protest made by Springfield and are currently seeking alternative ways of buying drugs at more reasonable prices[80].

With regard to the growing awareness of the unnecessary character and potential dangers of the "me-too drugs," it should be noted that the largest insurance companies and a growing number of states have developed and approved formularies that exclude them. These insurance companies will not reimburse the prescription expenses of their clients if they are prescribed drugs that are not included in their list of useful medications. On their part, some states have begun to pass legislation ruling that their Medicare program (the program that partly covers the cost of medication for those over 65 years of age) will only cover the cost of those drugs included in their state formulary, and not those that appear in the official Drugdex list (ultimately controlled, as we have seen, by the pharmaceutical companies themselves). In 2001 only 2 states had enacted this legislation; by 2003, half of all American states had[81].

4.2. A DECREASE IN INNOVATION AND A RISE OF MARKETING

A study carried out by a committee of experts selected by the US Congress estimated that the cost of producing a new drug in 1993 stood at 802 million dollars[82]. The center for the Study of Responsible Legislation in Washington released a counter-report calling this figure into question after assessing the cost of producing the so-called *orphan drugs*. *Orphan drugs* are drugs that —having a potential market too small to motivate the investors — are co-financed by pharmaceutical companies and public funds. They represent 20% of the US drug market. The total cost of production of co-financed drugs is *three times lower* than the cost of drugs financed by pharmaceutical companies alone. How is it possible? This disparity arises because under production expenses, the pharmaceutical companies routinely include the greatest proportion of their marketing expenses. In the case of orphan drugs, the companies are obliged to make available and correctly differentiate their *production expenses* from their *marketing expenses* in order that the government can pay its share. That marketing —and not research or production— is the greatest investment of today's pharmaceutical companies is not a fact openly acknowledged because only the disguise of marketing costs as research and pro-

duction costs, allows the pharmaceutical companies to pass the enormous cost of advertising to the consumers in the form of higher drug prices.

Pharmaceutical marketing is directed in the first place to physicians. In 2001, American doctors were regularly visited by a total of 88,000 representatives of the pharmaceutical industry. These drugs representatives distributed a total of 11 billion dollars worth of free samples of new medications to doctors so that they could "test them" on their patients. In addition, they offered personal gifts, all-expenses paid holidays and other forms of remuneration.

The advertising of *prescription* drugs is also increasingly being directed to the patients themselves, in the hope that physicians can and will be persuaded to write prescriptions if pressured to do so by their patients. The USA and New Zealand allow the direct advertising of prescription drugs to patients. All the other industrialized nations —despite being pressured by the pharmaceutical industry— still explicitly prohibit such advertising, recognizing the vulnerability and susceptibility of patients looking for relief from serious conditions[83].

The following are two examples of how a patient's vulnerability can be exploited: (1) advertising directly to hospitalized patients through the *patient channel*. The *patient channel* is a US TV channel only transmitted in hospitals. Patients lying in their hospital bed, maybe severely ill, are targeted for the delivery of biased information on new drugs that promise them relief or even a cure. These ads are presented by famous television and sports figures that give moving (usually false) testimonies; (2) targeting college and university students for massive promotion campaigns of anti-depressants. In return for large sums of money, some educational centers have allowed physicians paid by pharmaceutical companies to give conferences to their students with the goal of encouraging them to ask their doctors for prescription antidepressants that could *cure* sorrows and mood-swings common among normal healthy adolescents and young people.

By way of personal testimony, I remember the impact that one of these conferences had on medical interns. It was offered a few months after our arrival at Buffalo, New York, where we were to complete our three-year medical residency. We were told that the suicide rate among first-year residents was very high, and that we should look for treatment for our depression as soon as possible (we were all quite logically exhausted from our long shifts). They also told us that a new treatment had just come out that seemed to prevent depression. I was lucky enough to have a medical tutor who warned me about the economical interests hidden behind this "academic act." I could have become ill or died from the side effects of a drug that I did not need and that had been: (1) produced solely with the intention of making money, (2) tested and approved too hastily, and (3) promoted to me at a very vulnerable moment. I didn't take the medicine and nothing happened to me, but other people —thousands of other people— have not been so lucky.

5. AN OPPORTUNITY TO DISMANTLE THE SYSTEM

The sources consulted in preparing this booklet agree that the pharmaceutical industry is in urgent need of immediate and substantial reform. Such reform is possible and necessary above all in the interest of patients (be they in the first or third world countries), but also to ensure the future of the industry itself. Below is a summary of the conclusions of the main sources consulted.

MAIN CONCLUSIONS OF M. ANGELL, 2005*

1. Pharmaceutical companies are producing too many "me-too drugs" and too few drugs that are genuinely new.
2. The most influential regulatory agency in the world (the American FDA) is too closely linked to the industry that it is supposed to be regulating.
3. Pharmaceutical companies have too much control over the clinical tests that assess the effectiveness and safety of their own products.
4. The current 20-year period of validity of drug-patents is unjustified and its present regulation is detrimental to the

* Marcia ANGELL. A *The Truth about Drug Companies*, Random House, 2004. For almost 20 years Marcia Angell has been editor-in-chief of the most influential medical review, the *New England Journal of Medicine*.

quality of clinical research. Drugs today are patented before having completed the clinical tests necessary to prove their effectiveness and safety. This means that the 20-years period of validity of a drug-patent includes the years necessary for its clinical testing. To avoid the pressure to shorten clinical studies, the law should be modified so that the clock starts ticking once a drug can be sold and not before. The total length of the patent could then be reduced to 6 years. Legislation should also be enacted to eliminate the current legal loopholes used by pharmaceutical companies to block the arrival of generic drugs on the market for 30 months following the expiry of their own patent.

5. Pharmaceutical companies have an undue influence over medical schools curricula (2/3 of US university hospitals have direct economical links to this industry).
6. Important information on research, development, marketing, and pricing of drugs is kept secret from the public.
7. Drug prices are too high and too inconsistent.

MAIN CONCLUSIONS OF P. PIGNARRE*

In order to achieve the necessary reform of the pharmaceutical industry (see below), citizens have to be involved in:

1. The establishment of priorities for research and for the allocation of resources.
2. The development of research (particularly on the design of clinical trials) and,
3. the commercialization of drugs (patent rights and pricing policy)

Objectives of the reform of the pharmaceutical industry:

1. Setting up democratically agreed national and international priorities (highly lucrative rewards / sales conditions could then be offered to those advancing research in those areas).
2. Highlighting the active principle of a drug rather than its commercial name (medical packaging should show the generic name of the drug clearly visible and the commercial brand name in smaller print, the reverse of the current situation).
3. Rewarding the real worth of a drug rather than its promotional value (a 5%

* Philippe Pignarre worked as director of a large pharmaceutical company for seventeen years and is currently working as a Professor at the University of Paris-VIII.

increase in therapeutic effect does not need to imply a 10, 15 or even 100 fold increase in price).

4. Reconsidering the length of patents; they could be extended in richer countries in return for eliminating them in poorer countries.

5. Creating a research observatory to maintain an independent registry of all the processes leading to the discovery of each new drug in order to be able to rationalize investment and avoid dishonesty. This could be easily done because this information is already available in specialized magazines.

6. Taking decisions democratically. This should be at the heart of all economic practices, but is particularly feasible in the case of drug development because no new drugs can be developed without clinical trials and no clinical trials can be carried on without the written consent of the patients. As the association "Act Up" has demonstrated in the case of AIDS, the power to stop the current abuses is in the hands of the citizens.

MAIN CONCLUSIONS OF THE MSF REPORT "FATAL IMBALANCE", 2001

1. Diseases that mainly affect poor people are not researched because they are not profitable for the pharmaceutical industry.
2. The WHO should develop an effective plan to solve this problem.
3. The governments of rich and poor countries should redress the unfairness of the current global market.
4. A complete and independent analysis of the real cost of producing a new drug should be carried out.
5. In return for the investment of public money poured into the research and development of new drugs, they should be made accessible and economically available to all patients.
6. The capacity for drug-research and production in poor countries should be fostered.
7. An independent assessment of the long-term impact on global health of current patent policies should be urgently carried out.
8. A new international body needs to be created to address the problem of neglected diseases (MSF have already initiated the process with the DND NfPI (Drugs for Neglected Diseases Non-for-Profit Initiative)).

MAIN CONCLUSIONS OF THE COMMITTEE OF EXPERTS SET UP BY THE BRITISH HOUSE OF COMMONS, 2005:

1. "Me-too drugs" are a real problem.
2. An independent center to carry out clinical research should be set up, because the current system is too biased.
3. The aggressive direct marketing campaigns that accompany the launch of a new drug, the avalanche of information that is distributed, and the disguising of this information as medical fact all contribute to the fact that medicines are inappropriately prescribed.
4. The falsification of scientific reports and the hiding of unfavorable results gained in clinical research by the industry bring about the proliferation of these inappropriate prescriptions.
5. The responsibility for inappropriate prescriptions does not lie with the pharmaceutical industry alone, but also with doctors and other professionals who show too much willingness to accept gifts from pharmaceutical companies and to take at face value the clinical information they provide.
6. The marketing strategy of the pharmaceutical industry is relentless and pervasive and is not directed at professionals alone, but also at patients and the general public.
7. A leaflet for patients should be developed containing general and comprehensive information clarifying the important but limited role drugs play in the treatment of illnesses. Drugs are not the only therapeutic alternative available and patients should know it.
8. Advertising that is directed specifically at patients is inappropriate and unnecessary in the UK. This sort of advertising has a highly emotional content. The laws that prohibit it should be reinforced.
9. Indirect advertising made through so-called educational campaigns is not sufficiently regulated.
10. Often, the remuneration offered by pharmaceutical companies to patients' groups is not revealed. This information should be made public.
11. The monitoring of drugs already on the market is insufficient.
12. The government should finance the study of alternative forms of non-pharmacological treatment that are currently being ignored by the pharmaceutical industry because they are not profitable.
13. Doctors and other professionals who can prescribe medication should acknowledge their responsibility for the problems caused by the inappropriate prescriptions of SSRI anti-depressants and COX-2 anti-inflammatories. These drugs have been prescribed indiscriminately on a large scale. This was due in part to the huge promotion they received, particularly at their launch onto the market, but is also due to the fact that important information was kept secret while the propaganda of the pharmaceutical companies was taken at face value without much hesi-

tation. Aggressive marketing campaigns have led too many health professionals to prescribe inappropriately. No effective mechanism exists to moderate the explosion of prescriptions that follows the launch of a new product. As well as being the most crucial time to promote a product, it is also the time at which the least is known about the drug's potential side effects.

14. We recommend that an independent body keep a record of all clinical trials and that the results of all trials related to a given drug —whether favorable or not— be made public, as a precondition to its being launched on the market.
15. The number of free samples received by professionals should be reduced, particularly during the first six months of the appearance of the product on the market.
16. The decisions of the regulatory agency and the information and criteria used to reach conclusions should be made public. Ordinary citizens should be involved at the clinical research stage and should be offered training and sufficient support so that they can play an active role in the making of decisions.
17. Improved research into side effects of medication should be carried out. The observations made in clinical trials prior to launching a drug are insufficient.
18. The regulatory agency should employ more people in the monitoring of new drugs during their first six months on the market. We recommend that all new drugs be systematically and throughly re-assessed five years after their original launch on the market.
19. We recommend that the regulatory agency, besides authorizing the sale of a drug, also be made responsible and given due authority for restricting its uses.
20. We recommend that an improved system of registering the side effects of drugs be set up throughout the country, that all these cases should be duly investigated and that this should be carried out with transparency and without giving false assurances.
21. We recommend that public proceedings should always take place when a drug is withdrawn from the market due to its side effects.
22. Excessive marketing leads to inappropriate prescriptions. Current strategies to provide unbiased information to the public are insufficient. We recommend that the regulatory agency should have the right to veto any promotional material belonging to a new medicine as well as limiting (by specialty for instance) the right to prescribe new drugs during their first two years on the market.
23. We recommend better coordination and promptness in the area of investigating complaints on illegal advertising. Illegal advertising is a criminal offense and the punishment should reflect this. In cases where it is necessary to correct false information, the correction such receive as much publicity as the initial information.
24. The existing market of generic drugs is useful and important. Large pharmaceutical companies should be prevented from damaging this market by manipulating the legislation in order to unduly lengthening patent rights.
25. We recommend that medical students be better taught to critically evaluate the results of clinical trials, to recognize the side effects of medications, and

to have an appropriate relationship with the representatives of the pharmaceutical companies. Obligatory post-graduate courses should exist for all health professionals allowed to prescribe drugs so that they are always up to date. The prescription practices of these professionals should be more strictly regulated.

26. We recommend that professional associations keep a public record of any gifts, money, honors or other benefits that these associations and their members may have received from pharmaceutical companies. Each member should be responsible for keeping this record up to date. The professional associations should clearly and publicly state the level of favors that they consider acceptable for its members to receive.
27. The standards of health campaigns promoted by laboratories should be toughened so that it is always required to clearly state which company is financing these campaigns and which are the medications commercialized by this company.
28. Patients' groups should make public their sources of funding as well as all the favors they receive from pharmaceutical companies.
29. The incidence, cost and implications of illnesses caused by medication should be investigated in a systematic way by the Department of Health along with the regulatory drug agency.
30. The government should create a new program that grants all patients access to medication, and that adequately guarantees the safety and effectiveness of these medications as well as their appropriate use. Comparative studies of pharmacological versus non-pharmacological treatments should routinely be carried out.
31. The national health system should modify their current legislation so that effective non-pharmacological treatments are considered in the same category as pharmacological treatments.
32. The responsibility of representing the interests of the pharmaceutical industry should be transferred to the Department of Trade and Industry so that the Department of Health can commit itself exclusively, as is its obligation, to dealing with the regulation of drugs and the promotion of health.

* * *

The study of the current crimes and abuses of the pharmaceutical industry should have helped us move beyond the fallacious discussion between those who favor the free-market and those who favor greater government regulations. It is clear that without the unduly favorable laws of the US Congress and without the unduly favorable agreements of the WTO, the pharmaceutical industry would not have thrived the way it has. The market is always necessarily regulated by policies. What is needed is that the policies that today regulate the pharmaceutical market be reassessed and brought into line with the above recommendations, so that the industry can survive its present crisis and, most importantly, so that the patients can be better served by it.

NOTES

1. Angell, Marcia. *The Truth about the Drug Companies: how they deceive us and what to do about it. Is the Party Over?* pp. 217-36.
2. Pfizer. *Annual report 2001*. www.pfizer.com quoted by Moynihan, R. "The making of a disease: female sexual dysfunction". *BMJ* 2003; 326: 45-47.
3. Special Supplement. Int J Impotence Res 1998; 10 (supl 2): S 1-142 (*The Cape Cod conference: sexual function assessment in clinical trials*, 30-31 May, 1997. Hyannis, Massachusetts, USA), quoted by Moynihan 2003.
4. Basson R, Berman J, Burnett A, Derogatis L, Ferguson D, Fourcroy J, et al. "Report of the international consensus development conference on female sexual dysfunction: definitions and classifications". *BMJ* 2005; 330: 192-94.
5. Laumann E, Paik A, Rosen R. "Sexual dysfunction in the United States: prevalence and predictors". *Urology 2000*; 163: 888-93.
6. Kaschak E, Tiefer L, eds. *A new view of women's sexual problems*. Binghamton, NY: Haworth Press 2001: 70, quoted by Moynihan 2003.
7. Moynihan, 2003: 45.
8. Moynihan, Ray. "The making of a disease: female sexual dysfunction". *BMJ* 2003; 326: 45-47.
9. Tonks, Alison associated editor *BMJ*. "Summary of electronic responses. The making of a disease". www.bmj.com 2003.
10. Moynihan, Ray. "The marketing of a disease: female sexual dysfunction". *BMJ* 2005; 330: 192-194.
11. Many articles and books have been recently published on this topic. Besides the excellent reviews by Pignarre and Angell frequently quoted in this booklet, see also: *The $800 Million Pill* by M Goozner; *Powerful Medicines* by J Avorn; *Overdo$ed America* by J Abramson or *On the Take* by J Kassirer.
12. Pignarre, p. 124.
13. Pignarre, Philippe. *El gran secreto de la industria farmacéutica*. Barcelona: Gedisa, 2005 (original in French, 2003), p.117.
14. Press release from the coordinators of the Médecins Sans Frontières (MSF) Campaign for Access to Essential Medicines. Prognosis: short term relief, long-term pain. The future of generic medicines made in India. April 21 2005.
15. Pignarre, p.140.
16. Pignarre, p.127.
17. In response to stark international criticism, the Doha's Declaration (Qatar, 2001) modified the scandalous 1994 WTO agreement on the reinforcement of patents (Trade-Related Aspects of Intellectual Property Rights, TRIPS). Some of the most abusive clauses from TRIPS are: an obligation on the part of the laboratory wishing to produce generic drugs to buy not only the patent right of that medication but also of any other products chosen by the patent owner as "linked sales"; the right of the patent owner to determine the way in which the laboratory buying the product must produce the generic drug; the obligation on the part of the buyer to inform the patent owner of any improvements carried out on the product; the limitation or prohibition of exporting the product (cf.

Lecourieux A. “Patents that Kill”. In *Le Monde Diplomatique*. December 2005).
18. www.essentialdrugs.org/edrug/archive/-200510/msg00001.php. Last accessed on November 9, 2006.
19. Lorenz J, Berman D. “Companies not selling new AIDS drugs in Africa”. *MSF*, December 8 2005.
20. Pignarre, pp.13-14.
21. “The Fortune 500”, *Fortune* April 18 2005 (F28). Quoted by Angell, p. xv.
22. “The Fortune 500”, *Fortune* April 18 2005 (F28). Quoted by Angell, p. xv.
23. The price of the well-known anti-allergy medication Claritin (Schering-Plough) was allowed to rise 13 times in 5 years with a total increase of 50% of its initial price. This represents a four-fold increase above inflation (cf. Angell, p. xx).
24. Pignarre, p. 19.
25. Angell, p. 198.
26. A "blockbuster" is a drug with annual sales exceeding the billion dollars mark.
27. Pignarre, p. 129.
28. Angell, p. 3.
29. Pignarre, p. 129.
30. House of Commons. *The Influence of the Pharmaceutical Industry*. March 22, 2005. p.5.
31. House of Commons, p.5.
32. House of Commons, p.3.
33. Food and Drug Administration (FDA).
34. Eaton, Lynn. “More surveillance of drugs is needed to protect public”. *BMJ*, 2004; 329:1124.
35. www.pfizer.com/pfizer/download/uspi_neurontin.pdf.
36. Lenzer, Jeanne. “Documents missing from a 10 year old murder case sent to the BMJ”. *BMJ*, 2004; 329: 1365.
37. Eaton, Lynn. “Regulator restricts use of SSRIs in children”. *BMJ*, 2005;330:984.
38. Pignarre, p. 37; Angell, p. 81; see also www.humanite.fr.
39. Angell, p. 269; Pignarre, p. 143.
40. A study by David Graham, Associate Director of Science at the Office of Drug Safety of the FDA. Quoted by www.consumeraffairs.com and in the House of Commons report, p. 4.
41. Angell, pp. 270-72.
42. House of Commons, p. 8. It states that: a) 65% of patients taking anti-depressants clearly do not need them; b) 65% to 95% have a doubtful diagnosis; and c) only for the remaining 5% can the prescription of anti-depressants be medically justified.
43. House of Commons, p. 4, p. 10 and p. 102.
44. House of Commons, p. 7.
45. House of Commons, p. 4.
46. Pignarre, p. 147. In England, hospitalizations due to side effects of medicines represent 5% of all hospitalizations (cf. House of Commons, p. 8).
47. Pignarre, p. 121.
48. Pignarre, pp. 125-27.
49. Angell, pp. xxi-xxii.
50. Fatal Imbalance MSF, p.10.
51. WHO. Chagas. Last accessed 20 September 2006.
52. Carlier,Y. “Chagas Disease (American Trypanosomiasis)”. *eMedicine* (27 February 2003).
53. Angell, p. 65.
54. Angell, p. 65.
55. MSF, p. 10.
56. MSF, p. 12.
57. Pignarre, p. 150.
58. Rothman, David. “The shame of medical research”. *The New York Review of Books*, November 30, 2000. Quoted by Pignarre, p. 150.
59. Angell, p. 198.
60. Angell, p. 201.
61. Angell, p. 234.
62. Prescription Drug User Free Act, 1992.
63. Angell, pp. 208-11.
64. Angell, pp. 211-14.
65. Angell, pp. 202-06.
66. During the 12 months from September 2003 to August 2004 there were 2,700 suicide attempts among patients that were taking gabapentin, 200 of which ended with the death of the patient (see section 3.2.1 of this booklet).
67. House of Commons p. 116 (recommendations 18-20). See a summary of the 32 recommendations of the Experts Committee in section 5 of this booklet.

68. World Trade Organization (WTO).
69. Trade-Related Aspects of Intellectual Property Rights (TRIPS).
70. Buncombe, Andrew. “African bio-resources 'exploited by West'”. *The Independent*. February 17, 2006.
71. International Convention on Biodiversity. ONU, 1992.
72. Mariam Mayet from The African Center for Biodiversity and Beth Burrows from Edmonds Institute.
73. Pignarre, p. 39.
74. At the time of writing this booklet, news has come out that the value of activities of the pharmaceutical company SkyePharma has been reduced by half in the last 5 years, and that last year the company could not find a financial partner that would promote its new anti-asthmatic medicine Flutiform (Kollewe, J. “SkyePharma rebels lose vote to appoint Thian on board”. *The Independent March* 10, 2006).
75. Lorelle, Véronique. “Les industriels devront accelérer le lancement de médicaments plus ciblés”. *Le Monde*, January 15, 2003., quoted by Pignarre, p. 29.
76. Pignarre, p. 85.
77. Drews, Jürgen. *In Quest of Tomorrow's Medicines*. Springer: Nova York, 1998. p. 221, quoted by Pignarre, p. 91.
78. Pignarre, p. 105.
79. Angell, p. 221.
80. Angell, pp. 220-21.
81. Angell, p. 227.
82. "OTA Study". *Marketletter*. January 13 1997, pp.24-25, quoted by Pignarre, p. 24.
83. House of Commons, recommendation n.8.