2.1.2. Big Pharma and conflicts of interest

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Introduction

During the 1980s mergers between firms led to the creation of huge transnational companies in almost all industrial sectors. Big Pharma, as the handful of European and US transnational drug companies that dominate the market is known, grew in the same fashion and their turnover is currently estimated at about 400 billion dollars per year[1]. Big Pharma expanded with the help of a series of favourable US Laws, such as the Bayh-Dole Act of 1980, which granted pharmaceutical companies the right to give exclusive license concessions; and the Hatch-Waxman Act of 1984, which effectively made it possible to extend the period a patent on drugs was valid for, an advantage which was applied worldwide in 1994 with the TRIPS (*Trade Related aspect of Intellectual Property rights*) Agreement. The enormous increase in profits that resulted from this has made Big Pharma so economically powerful that it can now further its own commercial interests regardless, unchallenged by business competition or governments, thanks to a concurrent decline in the increasingly impoverished public sector and weakening of political credibility and control in many areas of the world.

Conflicts of interest

The conflict of interests between the pharmaceutical market and the defence of people's right to health is easy to see in low income countries, where it has been, and is, doing enormous harm to people's health. Just think of the way patents are being defended *"à l'outrance"*, which restricts people's access to affordable treatments, impedes importation and prevents local production of low cost drugs. Defended even when Governments take legal action against the pharmaceutical companies, as has happened in India, over a drug against cancer, and in South Africa, over drugs to treat AIDS. The same is happening in higher income countries, where the effects are often masked by the complexity of the social structures and mechanisms which, apparently, grant an acceptable, overall level of well-being. But today the conflict is getting increasingly bitter everywhere and it is harder and harder to contain the power and influence of Big Pharma over all key points in the chain of drug development and production: from research to scientific knowledge and information; or from prescriptions to the laws concerning medicines. This general conflict of interests between working for the good of the market or the good of people's health is being played out

in many diverse personal or institutional conflicts of interests, often associated with the professions or social roles of the different subjects who, in some way or another, come into contact with the pharmaceuticals industry and the drugs market.

Research and scientific information

A large proportion of bio-medical research is funded by the pharmaceutical industry. This has serious consequences, in that the results concerning the efficacy of drugs are often far more favourable to the drug when it has been tested in clinical trials directly sponsored by the industry[2]. As the saying goes, "He who pays the piper calls the tune", Big Pharma pays and can, effectively, decide the direction and subject of research. The result is that 90% of research today is on drugs and all other health needs are neglected. Added to which, in most cases, the drugs developed are usually those required to treat diseases prevalent in high-income countries, where more products can be sold and at higher prices too.

The literature abounds with studies on the influence of the pharmaceutical companies on research, but an editorial published jointly by the main scientific journals in 2001, launched a true cry of alarm[3]. More recently, Richard Smith, former director of the *British Medical Journal*, declared that medical research had, for the most part, become unreliable[4]. There are safeguards to ensure the integrity of research: for example, authors are obliged to declare any conflict of interests they may have. But the question of what exactly is meant by "conflict of interest" has never been answered. Does it depend on the amount of money received from the industry, or on other personal interests, or something else entirely? Dennis Thompson defines conflicts of interest as "a set of conditions for which professional judgement concerning a primary interest tends to be unduly influenced by a secondary interest"[5]. But very few researchers are prepared to admit that they are being unduly influenced by anything or anyone. However, it is well known firstly, that most researchers receive funds from the pharmaceutical companies and, secondly that there are neither controls nor sanctions for those who make false declarations about what they give or receive.

A more effective line of defence for free sharing of information is by publishing independent information in *Open Access Journals* or Drug *Bulletins*: but this is not entirely satisfactory as these all have to survive on public funding. Some French doctors have resolved the problem by contributing directly, out of their own pockets, to producing an independent journal: *Revue Préscrire.*

Drug prescriptions

Big Pharma is spending more and more on marketing. In 2004, such spending accounted for about one third of its overall budget: twice as much as was invested in research[6]. Investment in research is low because innovative molecules are not produced in great numbers, while photocopy (me-too) drugs are. Total spending

on marketing in 2004 was 57.5 billion dollars, i.e. about 61,000 dollars per doctor[7], but it is very difficult to get an accurate breakdown of where all this money is going. A survey among US doctors revealed that 83% receive free meals; 78% free drug samples; 35% are reimbursed for expenses when they go to conferences or training events and 28% receive honorariums for conferences, teaching or for enrolling patients in studies[8]. The 2007 Consumers *International Report* offers documentary evidence that even in the poorest countries, the pharmaceutical companies offer doctors gifts of every kind in order to influence prescriptions. One consequence of this practice is that 50% of the drugs turn out to have been prescribed, dispensed or acquired in an inappropriate manner[9].

All over the world, training, which shapes and conditions doctors' approaches to disease and their choice of prescription drugs, is with rare exceptions financed by the pharmaceutical industry which means, that, effectively, they select the experts, the opinion leaders. Many doctors do not know about the tactics being used by the pharmaceutical industry to influence behaviour, and even if they do know they will still, even in the teeth of the evidence, continue to deny that their professional judgement could, in any way, ever, be deliberately manipulated. Curiously enough, many suspect that sometimes their colleagues may well have been influenced[10].

Disease mongering

One other aspect that should be discussed is the phenomenon of *disease mongering* (inventing and selling diseases), which is changing our perception of sickness and health. Thirty years ago the director of a pharmaceutical company, Merck, declared that his dream was "to be able to sell drugs and pharmaceuticals to healthy people, because in that way you could sell to everyone"[11]. His dream may well have come true already. A well known advertiser in New York, Vince Perry, wrote a disconcerting article entitled "The art of inventing diseases", in which he revealed that he had collaborated with pharmaceutical companies to create "new ideas about ill-health and disease" and to encourage "a new way of thinking about things" in order to maximise sales of drugs[12]. It seems he has succeeded. Today, many of the formerly normal, natural events of people's lives have been transformed into diseases, like menopause or reduced libido due to age, or dysfunctions, such as personality traits like shyness or poor concentration, that should be treated with drugs. The thresholds for blood sugar, cholesterol and pressure too, have been progressively lowered, which means that millions of essentially well people have now been re-classified as "sick". Curt Furberg, professor at Wake Forest University, argues that the whole debate on blood pressure is being influenced by what he calls "the hypertension Mafia"[12]. Disease-mongering mechanisms have triggered a huge increase in unnecessary consumption of drugs, drugs which often have serious side effects that must be treated. This cycle is transformed into the hardly reassuring perception that almost all of us are ill almost all of the time and, in the final analysis, almost all of us are unhappy.

What is to be done?

The first thing to be done would be to sever the link, the umbilical cord that puts doctors in debt to the pharmaceutical industry through a series of gifts and unearned funds. Various proposals have been put forward as to how to deal with this problem and all sorts of solutions tried, running from setting a limit on the value of any gift a doctor can accept, to establishing a public register, to forcing doctors to refuse all gifts or funds. This latter position is supported by many doctors all over the world: *No free lunch* in the United States and Great Britain, *No grazie pago io* (No thanks, I'll pay) in Italy, *Non merci* (No thanks) in France, *Healthy Skepticism* in Australia[13]. Even some US universities have begun to take the same line[14], as has the *American Medical Student Association*, which organises an information campaign for students on the tactics adopted by the pharmaceutical industry[15].

Something should also be done about the agencies that regulate the drugs market. The task of evaluating the efficacy and safety of a drug is entrusted to the *Food and Drug Administration* (FDA) in the USA and to the *European Medicines Agency* (EMEA) in Europe. Clearly such agencies have a very delicate and strategically important role in protecting citizens' health, and should be protected from the influence of drug producers in pursuit of profit. But there have been serious problems. In 2004, Vioxx® was withdrawn from the market because of serious cardiovascular side-effects, which the manufacturer had known about but kept hidden, thus directly causing the death of tens of thousands of people. This highlighted the often deep conflicts within the FDA and severely damaged its credibility[16]. It is widely agreed that the role of the FDA, as guarantor for public health, must be reinforced, but so far the problem has not been solved. As for the EMEA, there is cold comfort in the fact that it is 70% funded by the pharmaceutical industry and that it comes under the aegis of the EU Commissioner for Industry rather than that for Public Health. But the repeated appeals of Silvio Garattini, Director of the Mario Negri Research Institute in Milan, to tackle the danger that these conflicts of interest pose for the health of European citizens, and his demand that Governments should increase the quota of public investment in pharmaceutical research, have so far fallen on deaf ears.

Certainly it is important to educate citizens about drugs, but to let them receive information only from one side, from the people who actually produce the drug – as some propose – is a risk that should not be run. Experiences in the only two countries in the world where this does happen, the USA and New Zealand, have shown that the benefits claimed by the drug industry rarely materialise, but this type of advertising can still influence both patients' requests and doctors' behaviour when prescribing for their patients, neither of which can be controlled yet both are dangerous. For example, advertising increases the consumption of new drugs even when there is not really enough data available about them, as happened with Vioxx®[17]. Furthermore, it sends costs rocketing. Notwithstanding this, Europe is currently discussing whether to introduce the same practice and should have come to a decision by the end of 2008.

Another critical point in the relationship between Big Pharma and citizens is the

financial aid given to Patients' Associations. These funds can become a Trojan horse. There are several examples of the pressure that has been exerted by the industry through these associations, to introduce a new drug or to broaden the range of its indications. The most clamorous episode concerns a drug for Alzheimer's Disease for which the UK *National Institute for Clinical Excellence* (NICE) had to go as far as the Supreme Court to defend its evaluation regarding a rejected request by the producer to broaden the range of the drug's indications, which was aggressively supported by the Association for people with Alzheimer's, financed by the pharmaceutical company that produces the drug[18]. It is important that people should both be warned regarding the insidious nature of this "financing mechanism" and should demand greater transparency about how much and who finances exactly what among these associations.

In the US there has been a sharp increase in investment in lobbying activities on members of the government and Congress. It has been estimated that from 1998 to 2005, the pharmaceutical industry spent a total of around 900 million dollars between them and that for the period January 2005 to June 2006 alone, they spent more than 180 million dollars on employing a total of around 1100 lobbyists[19]. Many of the laws in the sights of the lobbyists concerned drug safety and prices. Some of the laws sought greater powers for the FDA in evaluating and watching over the drug safety, others were those that would permit *Medicare** to bargain over the price of drugs, or laws which would allow lower cost versions of drugs imported from other countries[20]. Even though there is no parallel data currently, it would be very naive to think that similar mechanisms for putting pressure on politicians do not exist in other countries too.

Conclusions

The conflict of interests between the pharmaceutical market and the defence of people's right to health involves four important players: citizens are the main subjects, then there are Big Pharma, politicians and doctors. It is a complex picture, sometimes it is difficult to see what determines the conflicts and even where they are. However the underlying mechanism seems to produce a weakening of knowledge of the roles and responsibilities of each of the different players. These roles and responsibilities must be re-defined, re-stated clearly and soon, to avoid confusion. The current cultural climate encourages aggressive, sometimes ruthless, defence of personal or group interests, indeed, it nourishes conflicts of interests instead of helping to prevent them. A change in culture and attitudes will take a long time and will require a lot of determination to carry it through. The best solution would be to start by setting clear rules, rules for all parties involved, and then, above all, to check that they are being fully respected. This will be the most difficult task.

* USA public programme that guarantees health insurance cover for the elderly.

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