

Monopoly v. Openness: two sides of IP coin in the pharmaceutical industry

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Abstract

The pharmaceutical industry extensively relies on the patent system. It actively lobbies for the strengthening of patent protection of its medical products and the results of its efforts may be found in the majority of bilateral and multilateral agreements, including the TRIPS and the most recent TPPA, augmented by private patent strategies pursued by pharmaceutical companies. However, some recent developments show the emerging tendency of implementing different business models by pharmaceutical companies that may mark the beginning of transformation of this industry. Among these developments is an 'open innovation' model, which has increasingly been followed by some research institutions and pharmaceutical companies aiming at facilitating the creation of new and affordable medicines, as well as providing transparency in order to enhance safety and efficacy of drugs. This article will discuss these two current developments in the pharmaceutical industry, i.e. strong IP protection against open innovation.

Keywords: *patents; the pharmaceutical industry; access to medicines; open innovation.*

Introduction

Traditionally, intellectual property is seen as a monopoly granted by the state in order to reward the creator/inventor and to facilitate dissemination of knowledge that otherwise would be kept secret. Out of all types of intellectual property rights, patents are the strongest monopoly one can obtain over the results of his intellectual creations. Possession of such a monopoly controls the use of a product protected by the patent; most importantly, its price.

A classic example of patent monopoly may be found in the pharmaceutical industry, where the unique role of intellectual property is due to the industry's specific features. On the one hand, pharmaceutical companies invest significant financial resources and time into the R&D process, and further transformation of the resulted invention into an effective and safe medicine. On the other hand, the development and marketing of drugs are under vigilant control of the state. Within this complex

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environment, the crucial need for strong patent protection, as it is claimed by the industry,¹ stems from the nature of the product: the development of a successful drug requires substantial time and resources, but considerably less time and investments to copy it. Therefore, for the purpose of protection of their inventions and prevention of free-riding, pharmaceutical companies extensively rely on the patent system.

One of the main arguments for strong patent protection, which is actively articulated by the pharmaceutical industry, is the high cost of R&D that amounts to between US\$ 800 million² (Angell, 2005; Frank, 2003; Light and Warburton, 2001; Morgan *et al.*, 2011; the Pharmaceutical Sector Inquiry, 2009) and US\$ 2.6 billions (DiMasi *et al.*, 2015).³ According to the industry figures, as few as 1 in 5,000 to 10,000 tested compounds are successfully launched (The Pharmaceutical Sector Inquiry, para 161). Some studies go as far as claiming that 60% of the pharmaceutical inventions made between 1981 and 1983 would not have been developed at all and 65% of those inventions would not have been introduced into commerce if patent protection had been unavailable (Mansfield, 1986).

Hence, it is accepted that the pharmaceutical industry is the IP monopoly oriented industry with the need of strong patent protection. It actively lobbies this idea and the results of its efforts may be found in the majority of bilateral and multilateral agreements, including the TRIPS and the most recent TPPA.

This is in contrast with other industries that rely on other forms of protection, such as trade secrets⁴ (Kulakowski and Chronister, 2006), trade marks, copyrights and design rights. Despite such an attractive advantages of the monopoly power provided by the patent, such a business model may not be of a great interest to other industries. The software-based industry, for example, has increasingly used intellectual property in a different way. Instead of restricting access to their intellectual property, some companies open it to their users (e.g. Linux), sometimes on a royalty-free basis, deriving their income from a service support and a tailor-made software. These developments have created the antipode of the traditional copyright, the so-called ‘copyleft’.

However, some recent developments in the pharmaceutical industry may mark the beginning of the transformation of this industry, proving that monopolistic patent strategies may not be the best business models after all. Among these developments is an ‘open innovation’ model, which has increasingly been followed by some research institutions and pharmaceutical companies aiming at facilitating the creation of new and affordable medicines, as well as providing transparency to enhance safety and efficacy of drugs.

This article discusses these two current developments in the pharmaceutical industry, i.e. strong IP protection against open innovation. It will be explained that pharmaceutical companies can use their intellectual property restrictively in order to protect market monopoly of their products. Intellectual property can also be used as an open source, facilitating the creation of new medicines through providing free access to IP protected information. This article will outline these different models of drugs development. It will first discuss the traditional position of the pharmaceutical industry, which is aimed at strengthening patent protection by means of international and bilateral instruments, as well as private business practices. The article will then turn to the emerging tendency towards implementing ‘open innovation’ models in the drugs development process with some recent examples of how these models are facilitated by international organisations, state authorities, individual initiatives and pharmaceutical companies themselves.

1. Strengthening of Monopoly Power

1.1. *When drugs were not protected by patents*

Once upon a time, when drugs were not protected by patents ... The modern pharmaceutical industry is relatively young and is considered to be an offspring of the dyestuff and chemical industries. The establishment of the pharmaceutical industry is closely linked to an incidental discovery made by William Henry Perkin, a young scientist at the Royal College of Chemistry in London (Greenwood, 2008, pp. 49-50; Firn, 2010, p.40; Myers, 2003, p. 295). In 1856, he was given a task to synthesise quinine from coal-tar, an industrial waste product of gas lighting (Dutfield, 2009, p.11). Although unsuccessful in his initial task, he nevertheless discovered the dyeing properties of mauve that eventually led to the development of several completely new industries, including the synthetic dyestuff, chemical and pharmaceutical industries (p. 12). The dyestuff and chemical industries were dominated by German companies such as Bayer, Hoechst, BASF and AGFA, some of which became more famous for drugs than dyes (p. 12). Later, companies like Merck, Eli Lilly and Roche, which supplied natural products such as morphine, quinine and strychnine, also started a large-scale production of drugs (Taylor, 2015).

Despite the importance of this scientific development and the establishment of an entirely new industry, patent protection of drugs had not been available in most of the countries until recently. In nineteenth century Europe, typically only the process of producing a drug was patentable⁵ (Boldrin and Levine, 2005). This meant that, after a drug had been discovered, other companies were free to manufacture and sell it using a different process of making it. The pharmaceutical industry, therefore, invested considerable time and efforts in order to convert its products from non-patentable subject matter to the invention that has arguably the strongest patent protection compared to inventions in other industries.

1.2. *Further strengthening of pharmaceutical patent protection on the international level: TRIPs and TPPA*

The signing of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (the TRIPs agreement) in 1994 became a grand victory of the 'Big Pharma'. Heavily lobbied by the industry, this agreement finally set a minimum standard of patent protection on an international level⁶ (Matthews, 2002). Article 27 of the TRIPs agreement establishes the rules on patentable subject matter and provides that:

'... patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application.' (emphasis added)

Such a mandatory minimum standard resulted in the protection extended to all inventions, including pharmaceuticals. As a result of this international treaty, every signatory Member State undertook an obligation to introduce patent protection for drugs in their national legislations, as well as implement relevant mechanisms for their registration and enforcement.

Such changes were particularly detrimental to developing countries that could not afford the burden of pharmaceutical patents: they had no administrative resources and knowledge in order to implement an

adequate examination and registration process, and they were also lacking the necessary financial resources to bear the cost of expensive patented medicines. While understanding the challenges of developing countries, a few flexibilities were introduced into the TRIPs agreement, such as parallel importation, compulsory licensing and the possibility for the Member States to frame their own rules on IP exhaustion and patentability requirements.

However, despite the great value of these flexibilities, they are increasingly curtailed by free trade agreements signed between developing and developed countries (Dutfield, 2001; So, 2004; Trade and Development Report, 2006, p.195; United Nations High Level Panel on Access to Medicines Report, 2016; WHO, WIPO, WTO Report, 2013, p.83). These free trade agreements tend to strengthen the IP protection of medical products on the bilateral and regional levels. These so-called ‘TRIPs-plus’ provisions usually set a higher level of intellectual property protection than is required by TRIPs.⁷ It is believed that such provisions delay generic market entry and lead to higher prices and restricted access to medicines in the signatory countries (UNITAID, 2014).

The concerns over access to medicines and excessive pricing are particularly relevant to the Trans-Pacific Partnership Agreement (the TPPA) signed in 2016.⁸ It is described as a model agreement for the twenty-first century, implying that similar provisions will appear in future trade agreements (Voon, 2013). This regional agreement substantially elevates the patent protection of medicines comparing to the TRIPs agreement standards (Correa, 2015). For instance, the TPPA provides the extension of the 20 year patent term for pharmaceutical patents as a compensation for ‘unreasonable or unnecessary delays’ during marketing authorisation of drugs,⁹ as well as provides a patent term adjustment for ‘unreasonable’ delays by the patent office.¹⁰ (Matthews, 2015 (a))

Further, Article 18.37 of the TPPA provides that:

‘Each Party shall make patents available for any invention, whether a product or process, in all fields of technology, provided that the invention is new, involves an inventive step, and is capable of industrial application.’

Thus, this provision mirrors Article 27 of TRIPs agreement. However, it goes further adding the following section:

‘... each Party confirms that patents are available for inventions claimed as at least one of the following: new uses of a known product, new methods of using a known product, or new processes of using a known product.’

These provisions, therefore, provide pharmaceutical companies with the opportunity to engage in the evergreening practices that allow them to extend the protection of a drug beyond the term of a basic patent¹¹ (The Pharmaceutical Sector Inquiry, 2009, paras 20 and 138).

Moreover, previous version of the TPPA’s Intellectual Property Chapter, proposed by the US and leaked in February 2011, contained an additional sentence in this Article, which guaranteed a patent for new uses or methods of using a known product: ‘... *even if such invention does not result in the enhancement of the known efficacy of that product*’ (emphasis added)¹² (Love, 2014). Although this phrase was deleted in the subsequent version of the Chapter, it shows the unprecedented level of protection lobbied by the US for its pharmaceutical corporations.¹³ Despite the withdrawal of the US from the TPPA, the discussions of its ratification by the remaining members continue.¹⁴ Therefore, such a favourable

provisions towards the pharmaceutical industry is likely to have a significant effect on access to medicines should this agreement come into force.

As can be seen from the above discussion, the level of intellectual property protection gained by the pharmaceutical industry by means of introducing the patent protection for drugs into national laws, free trade agreements and international treaties has substantially increased during the last few decades. Such development has led to the strengthening of market power by pharmaceutical companies and increased the entry barriers for competitors.

1.3. Further strengthening of patent protection by business strategies

Strengthening of international and national intellectual property laws, which enable pharmaceutical companies to increase protection of their products and enhance their market power, is not the only tool in the arsenal of the pharmaceutical industry. Individual business strategies of pharmaceutical companies may also be very effective, which, when used together with the strong IP protection and other regulatory rules, may substantially extend market exclusivity of a drug beyond the terms and scope of initial patent protection. Such a dual strategic approach to the protection of drugs can substantially delay or even block generic competition, as well as stifle the development and introduction of innovative drugs.

The particular interest to such individual practices in the EU was raised by the *AstraZeneca* case, when, in 2005, the company was found by the EU Commission to abuse its dominant position.¹⁵ In this case, the originator company AstraZeneca was accused of two abuses. The first concerned the abuse of the patent system by providing misleading information to the patent office and obtaining a supplementary protection certificate that led to the unlawful extension of the patent protection of the company's product Losec (omeprazole). The second abuse related to the misuse of marketing authorisation procedures. The company employed several strategies in order to deter a generic version of its product from entering the market when its patent for the original product Losec was about to expire. Due to the success of this strategy, the company was able to keep generics off the market in some countries. In 2005, AstraZeneca was fined EUR 60 million by the EU Commission. In 2010, the General Court upheld the Commission's decision.¹⁶

The EU Commission, concerned about the anticompetitive practices of pharmaceutical companies, as well as the evident market failure, launched an inquiry into the pharmaceutical industry. In 2009, after its in-depth investigation, the Commission released a report, which outlines several practices of pharmaceutical companies that are likely to cause delays of both generic and innovative competition (The Pharmaceutical Sector Inquiry, 2009). The Commission found that brand-name pharmaceutical companies protect their market share by employing a tool-box of practices, which enable them to block generic competition and deter innovative competitors.¹⁷ These practices include *inter alia* patent thickets¹⁸ (Gurgula, 2017), life-cycle strategies for follow-on products (Bansal *et al.*, 2009; Granstrand and Tietze, 2015; Hemphill and Sampat, 2012), defensive patenting (The Pharmaceutical Sector Inquiry, para 1117) and patent settlement agreements¹⁹ (Federal Trade Commission Staff Study, 2010).

Despite the Commission referring to these strategies as a reason for the delays of generic entry, they have not become the focus of its attention. For instance, practices such as patent settlement agreements, while heavily litigated by the US FTC for more than a decade, have only recently raised the interest of

the EU Commission. Moreover, strategic patenting, although being claimed in the Commission's Report as a reason for the delay of generic competition, has not been investigated by the competition authorities at all. The lack of control of these particular practices by the competition authorities results in the (ab)use of the patent system by pharmaceutical companies for the detriment of consumers leading to excessive prices and restricted access to medicines (Matthews and Gurgula, 2016(b)).

2. Open access to IP in the pharmaceutical industry

As the FTC acknowledged in its seminal 2003 Report: '[e]ver greater intellectual property protection is not necessarily socially beneficial' (The FTC Report, 2003). Hence, on the other side of the IP fence erected by the pharmaceutical industry, there is a growing understanding of the importance of open innovation and open access for the benefit of society. The changes in the way the drug development process is perceived have occurred as a result of, among other things, a significant decrease in the development and approval of innovative drugs on the one hand; and a lack of transparency and restricted access to the data, which has raised considerable concerns about the safety and efficacy of medicines, on the other hand. 'Open innovation' or 'open science' is an emerging trend in drugs development, the most important features of which are that 'all data and ideas are freely shared, anyone may participate and there are no patents' (Robertson *et al*, 2014; Shaw, 2017; Wells, 2016). The benefits of this approach compared to the traditional models of the drugs development process is its speed, access to a wide network of experts, disclosure of both positive and negative data and a reduction in unnecessary duplication of research worldwide (Robertson *et al*, 2014). Open science in the pharmaceutical industry mimics the open source movement in software development acknowledging its significant achievements (*ibid*).

At present, such changes are mainly driven by academics, NGOs and public research institutions. However, a number of pharmaceutical companies have also shown some interest in these new business models of drugs development moving towards collaboration and open access. By way of example, this section will outline several initiatives pursued by public and private organisations in the recent years aiming at achieving transparency and open innovation in the pharmaceutical industry.

2.1. Initiatives on the international level

In September 2016, after completing the extensive discussion and reviewing numerous submissions from various stakeholders, the UN High-Level Panel on Access to Medicines released its Report on 'Promoting innovation and access to health technologies'(Matthews and Gurgula, 2016(a); United Nations High Level Panel on Access to Medicines Report, 2016). The aim of this UN initiative was to 'review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies'(United Nations High Level Panel on Access to Medicines Report, 2016, p. 7). The UN High-Level Panel recommended, among other things, that the results of the publicly-funded research should be made freely and widely available (p. 9), that the data on all completed and discontinued clinical trials should be made publically available (p. 11), and that patent information on medicines and vaccines should be made available through publicly accessible databases (*ibid*).

This initiative was upheld by eleven major funders of medical research and international non-governmental organisations, including the UK Medical Research Council, Médecins Sans Frontières, the Bill and Melinda Gates Foundation, and the Wellcome Trust.²⁰ On 18 May 2017, these organisations signed a joint statement agreeing on ‘new standards that will require all clinical trials they fund or support to be registered and the results disclosed publicly’ (Joint statement, 2017). Such an initiative was a result of the concerns that about 50 per cent of clinical trials are unreported, often because their results are negative (WHO Press Release, 2017). Such ‘unreported trial results leave an incomplete and potentially misleading picture of the risks and benefits of vaccines, drugs and medical devices, and can lead to use of suboptimal or even harmful products’ (ibid).

The WHO also actively discusses the alternative incentives for innovation in health products, in particular how to incentivise more R&D in order to meet global health needs with the focus on the importance to delink ‘the costs of R&D from the price of the end product’, as well as to facilitate ‘open knowledge innovation’ (WHO Report, 2012). In 2016, the WHO launched a global health research and development observatory²¹ in order to monitor and analyse relevant information on health research and development, the function of which will include the integration of available information on funding for health research and development, health products in the pipeline, clinical trials and research publications, etc (ibid).

In 2011, WIPO, in collaboration with BIO Ventures for Global Health (BVGH), and with the participation of a number of pharmaceutical companies and other private and public sector research organisations, established the WIPO Re:Search, a database in which public and private sector organisations share their intellectual property and expertise with the global health research community. The aim of this initiative is to promote the development of new drugs, vaccines and diagnostics in the fight against neglected tropical diseases, malaria and tuberculosis by means of granting access to intellectual property, including pharmaceutical compounds, technologies, know-how and other data for further research and development.²²

Open access initiatives are also taken by the EU, which is also determined to examine alternative mechanisms in order to enhance access to medicines (Oxfam Briefing Paper, 2014). Thus, under Horizon 2020 (the EU’s €80bn research and innovation funding programme adopted in 2013), some important developments have been undertaken, including mandating open-access publishing, facilitating the dissemination of research results and encouraging the use of prizes.²³ Another EU initiative under Horizon 2020 is the Innovative Medicines Initiative (IMI) that is aimed at facilitating R&D through a public-private partnership with the European Federation of Pharmaceutical Industries and Associations (EFPIA), to enhance knowledge sharing and create tools and methods that will facilitate the development of better medicines (IMI; Europe 2020 Flagship Initiative, 2010).

2.2. Public initiatives on ‘missing data’

As was discussed above, there is a considerable concern about the bias in pharmaceutical trial literature (Angell, 2005; Jones *et al.*, 2013; Risin *et al.*, 2008; Turner *et al.* 2008), in particular regarding ‘missing data’ in pharmaceutical research²⁴ (Dziura *et al.*, 2013; Goldacre, 2013; Molenberghs and Kenward, 2007). It is claimed that a large proportion of evidence from human trials is unreported, and much of what is reported is done inadequately.²⁵ The unpublished trials are the trials that show the pharma companies' new products in unfavourable lights and may contain evidence that the new drugs are not

as effective as being claimed, are not effective at all, or are harmful. The fact that pharmaceutical companies withheld such data undermines the confidence in the safety and efficacy of medicines that are prescribed by doctors as many of the drugs have been promoted as safer and more effective than they really are. This endangers people's lives and wastes public funds.

A few initiatives tackling this problem have been launched recently. One is launched by AllTrials²⁶ and requires that 'all trials past and present should be registered, and the full methods and the results reported'.²⁷ Also, in 2013, *The BMJ*²⁸ announced that it will no longer publish any trial where the authors do not commit to making the relevant anonymised patient level data available, on reasonable request. Moreover, the journal published a number of *The BMJ*'s coverage of adverse outcomes associated with hidden clinical trial data. For instance, in 2014, *BMJ Open* published the first RIAT (Restoring invisible and abandoned trials) paper on an abandoned randomised controlled trial that remained unpublished for 20 years, and their reanalysis casts doubt regarding the survival benefit of further surgery after curative resection of colorectal cancer.²⁹ Another independent investigation was done with respect to Study 329, the infamous trial of paroxetine (Paxil, Seroxat) that was claimed to show that the drug was well tolerated and effective in the treatment of major depression in adolescents (Noury et al., 2015). Study 329 was subsequently dubbed by the US Food and Drug Administration a 'failed trial', as neither treatment was found to be better than placebo (*The BMJ*, Open Data Campaign). The examination showed that the paper was not prepared by the authors claimed in it, but by a writer paid by the manufacturer (ibid). However, the disturbing fact was that reports emerged of serious adverse effects of paroxetine in adolescents, including self-harm and suicidal ideation (ibid). In 2012, the US Department of Justice investigated a failure to report safety data and other misconduct by GSK, and commenced criminal and civil proceedings with a record \$3bn fine (ibid).

2.3. State initiatives

The problem of unpublished data is exacerbated by the fact that even those clinical trial documents that are submitted to the marketing authorisation bodies are not available to the public. Most of the countries, including the US, consider clinical trial reports and other parts of the dossier submitted by pharmaceutical companies as commercial confidential information and, therefore, not releasable. However, the European Medicines Agency (EMA) is the only regulator that has started to give access to clinical trial data (Doshi and Jefferson, 2016).

Thus, in October 2014, after a considerable discussion among stakeholders, the EMA published its new policy: *Publication of Clinical Data for Medicinal Products for Human Use*, which came into force on 1 January 2015 (EMA, 2014). It allows the EMA to proactively publish clinical data. The main objectives of the new policy are, by making clinical data available proactively, to enable public scrutiny and application of new knowledge in future research in the interest of public health (ibid). As a result of these developments, the current approach of the EMA to transparency covers both the reactive (upon the request from third parties) and proactive release of clinical data (proactive release of clinical study result summaries on the EU Clinical Trials Register) (Cameron *et al.*, 2014; GIPC Report, 2015; Matthews, 2015(b)).

2.4. Initiatives of the pharmaceutical industry

Understanding the value of collaboration with other experts in the field, pharmaceutical companies have started to implement new models of drugs development more actively in the recent years. Such new models are implemented through collaboration with public research institutions and other originators. This collaboration may diverge in terms of IP related aspects, spanning from the traditional IP protection of the research results to open innovation with no IP protection at all and free open access to the generated data. The latter model of open innovation, the so-called ‘precompetitive collaboration’, has proven to be successful in the early stages of R&D (United Nations High Level Panel on Access to Medicines Report, 2016, p. 27). Such collaboration helps to enhance the research in new fields of science and expand the knowledge for all, facilitating the progress in development of innovative medicines in a shorter period of time (ibid). While such business practices of pharmaceutical companies were perceived as an exception in the past, they are increasingly becoming an emerging tendency, rather than an isolated practice.

A well-known example of private-public collaboration is Medicines for Malaria Venture (MMV) that was established in 1999 with the financial support of the Rockefeller Foundation, Gates Foundation, and three European governments³⁰ (Gabriel *et al.*, 2017, p. 31). Its goal is to ‘reduce the burden of malaria in disease-endemic countries by discovering, developing and delivering new, effective and affordable antimalarial drugs’.³¹ The intellectual property over the results of the research belongs to Novartis, which has obliged to distribute medicines at affordable price to the public sector in countries where malaria is endemic (Gabriel *et al.*, 2017, p. 31). MMV has also initiated open source research in drug discovery for malaria and neglected diseases, including the Pathogen Box, which contains 400 diverse, drug-like molecules active against neglected diseases available free of charge.³² Further, the most recent example of private collaboration is the 2016 agreement between GSK and Google's parent company Alphabet on collaboration aiming at the development of bioelectronic medicines - miniature electronic implants for the treatment of chronic disease such as asthma, diabetes, arthritis and other conditions (GSK Press Release, 2016).

A gradual shift towards open access research can be seen in a launch of partnerships with public institutions by a number of pharmaceutical companies. These partnerships make freely available all information generated as a result of such joint collaboration. Such free and open access is anticipated to facilitate further research on the basis of the released information. An example of a partnership, on the basis of the open innovation model in the pharmaceutical industry, is the Structural Genomics Consortium (SGC),³³ the members of which are Abbvie, Bayer, Boehringer Ingelheim, Canada Foundation for Innovation, the São Paulo Research Foundation, Genome Canada, Janssen, Merck, Novartis, The Ontario Ministry of Research and Innovation, Pfizer, Takeda, and The Wellcome Trust.³⁴ Although the SGC receives funding mainly from private pharmaceutical companies, it has undertaken to release and make freely available all generated output to the public (Pearson, 2012). There are also several individual proposals to share clinical trial data at patient level, including the GlaxoSmithKline Data Transparency Initiative and Roche Global Policy on Sharing of Clinical Trial Data. According to these proposals, researchers may receive access to patient-level data after requests have been reviewed by an independent panel of experts.³⁵

2.5. *Public initiatives*

Perhaps one of the most important and active elements that guard public interest are various public initiatives, such as non-governmental organisations, patients groups and individuals, which are vigorously fighting against abuses of pharmaceutical companies and for transparency and the enhanced access to effective and affordable medicines. Numerous examples of such public pressure have forced pharmaceutical companies to provide licences (sometimes even on a royalty-free basis) to generic companies on their medicines, or to decrease prohibitive prices to affordable.

One of the examples of a successful public pressure relates to Gilead's innovative drug Sovaldi (sofosbuvir) that is used in the treatment of HCV (Hepatitis C). This new generation of medicines offers more efficiency, with many boasting sustained virologic response (SVR) in more than 90% of patients and fewer side effects than previous treatment options. It was included in the 2015 Model List of Essential Medicines (Mezher, 2015). However, the company has set a prohibitive price for the drug of \$1,000 per pill, or \$84,000 for a 12-week treatment. In the first quarter of 2014, the company sold \$2.27bn of Sovaldi. (Hoofnagle and Sherker, 2014; Associated Press, 2014; Hensley, 2014)

As 75 percent of the estimated 150 to 180 million people infected with Hepatitis C live in LMICs, this means that they cannot afford this essential medicine (Douste-Blazy, 2014; Knox, 2014; The Lancet, 2014). This triggered outcry and debate throughout the world from patient advocacy groups, which demanded that Gilead lower the price for Sovaldi and criticised the company for its licensing practices (Oxfam Briefing Paper, 2014). As a result, Gilead has entered into licensing agreements with several generics manufacturers in India (ibid).

Some activists, like James Love, argue that the best solution against the abuses of pharmaceutical companies are to forfeit the patent protection on medicines, and that public health would be better served by systems where essential public health research is publicly funded, monopoly protections of IP are suspended, and information is freely exchanged as in the open source software movement (Love, 2004). As an alternative, he refers to the Medical Innovation Prize Fund, a legislation proposed in the US Congress, which would allocate part of the US government's budget to pay substantial cash rewards to researchers who create innovative drugs or vaccines, but remove the monopoly protections of IP. He says that this will divorce the market for the product from the market for innovation.³⁶

Conclusions

Starting from its establishment in the nineteenth century, the modern pharmaceutical industry has gone through several stages of development. It began with a minimum level of protection afforded by intellectual property and has culminated into the international and bilateral treaties with the highest level of IP protection that hardly any inventions receive nowadays. Such a protection is supplemented by private business strategies of pharmaceutical companies, the most effective of which are the active use of the patent system and regulatory rules. Moreover, although these strategies may be abusive, competition authorities are reluctant to act fearing that this may affect incentives to innovate.

Strong proprietary position of the pharmaceutical industry, achieved as a result of changes in the law, as well as aggressive IP strategies by pharmaceutical companies, often lead to prohibitively high prices of drugs, making them unaffordable not only to the patients in developing countries, but also in developed countries. As a result, some authors believe that the pharmaceutical industry has forgotten

its initial objective of creating new and innovative medicines to cure diseases and save lives (Angell, 2005). Instead, it has become a mega business, or as it is now called, the 'Big Pharma', with the sole purpose of reaping the yield and increasing it further.

It is, nevertheless, apparent that the global scene in which the pharmaceutical industry operates is changing again. The open access initiatives from various stakeholders are now framing the new reality in the pharmaceutical industry. Companies have to adapt their business strategies to this new reality. Some of them shift to the open access model, sharing their proprietary information with the public institutions or collaborating with other pharmaceutical companies. Of those, some are genuinely driven by willingness to combat poverty, facilitate creation of new orphan drugs, and enhance access to affordable medicines. Others either are forced to adapt, or are acting voluntarily with the understanding that it is the only way to survive. Although it is too soon to salute the defeat of the patent monopoly dominance, there are clear signs that the ice has cracked and there will be no way back.

To conclude, the pharmaceutical industry is experiencing today a major tension between two powerful interests - private business interest that strives for IP monopoly in order to protect its revenues, and public interest that advocates for open access in order to facilitate access to medicines. Although it is hard to predict which of these interests will prevail, it is, however, clear that the pharmaceutical industry has to adapt to the current realities and business models, including clinical data transparency, joint collaboration and constant public pressure.

Notes

1. See, however, Angell, A. (2005) *The Truth About the Drug Companies. How they Deceive Us and What to Do About It*. Random House Trade, 37; Ouellette, L.L. (2010) 'How Many Patents Does It Take to Make a Drug - Follow-On Pharmaceutical Patents and University Licensing', *Mich. Telecomm. & Tech. L. Rev.*, 17, 299 Available at <<http://repository.law.umich.edu/mtrlr/vol17/iss1/7>> [Accessed on May 2017].
2. However, this cost is subject to a heated debate. See e.g., Angell, A. (2005) *The Truth About the Drug Companies. How they Deceive Us and What to Do About It*. Random House Trade 37; Frank, R.G. (2003) 'New Estimates of Drug Development Costs', *J. HEALTH Econ.*, 22, 325, 325 (stating that the \$802 million estimates 'have been a matter of heated debate since they were first made public in 2001'); Light, D.W. and Warburton, R (2011) 'Demythologizing the high costs of pharmaceutical research' *BioSocieties*, 6(1), 34-50; Morgan, S., Grootendorst, P., Lexchin, J., Cunningham, C., and Greyson, D. (2011) 'The cost of drug development: A systematic review', *Health Policy*, 100, 4-17.
3. A recent Tufts Center for the Study of Drug Development (CSDD) estimated that costs could reach \$2.6 billion. See DiMasi, J. A., Grabowski, H. G. and Hansen, R. W., (2015) 'The Cost of Drug Development' *New England Journal of Medicine* 372, 1972-1972, doi:doi:10.1056/NEJMc1504317.
4. The most famous trade secret is the Coca-Cola Company's formula for making its nearly 100-year old product Coca-Cola. See Kulakowski, E.C., and Chronister, L.U. (2006) *Research Administration and Management*. Jones and Bartlett Publishers, 856.
5. Boldrin, M. and Levine, D.K. (2005) *Economic and Game Theory. Against Intellectual Monopoly*. Available at <<http://levine.sscnet.ucla.edu/general/intellectual/against.htm>> [Accessed on May 2017]. The authors explain that, for example, French law of 1844 forbade patents on pharmaceutical inventions, with subsequent permission of process patents; limited patents on drugs from 1966; and eventual withdrawal of the ban in 1978. In Germany, pharmaceutical process patents were allowed under the law of 1877 with the prohibition of product patents. However, in 1891, patent protection was extended to products obtained through the patented process, and starting from 1967, pharmaceutical product patents were also allowed. In Switzerland, patents on pharmaceutical products were prohibited by constitution. Limited protection for process patents was introduced in 1907 due to the constant pressure from German pharmaceutical companies, while product patents were allowed as recently as 1977. In Italy, after the pressure of foreign pharmaceutical companies, product patents were introduced in 1978. In Spain, product patents for pharmaceuticals were prohibited under the law of 1931 and only after the country joined the EEC, starting from 1992, drugs became patentable. In the United States, by contrast, drugs have always been patentable both in the form of a process and product as they were considered to be chemical products.

6. For the details on the negotiation preceding the conclusion of the TRIPs agreement see Matthews, D. (2002) *Globalising Intellectual Property. The TRIPs Agreement*. Routledge.
7. For example, the US-Korea Free Trade Agreement establishes prohibition on pre-grant patent opposition (Article 18.8.4) and allows patents for new uses or methods of using a known product (Article 18.8(1)). The US-Australia Free Trade Agreement also allows patents for new uses or methods of using a known product (Article 17.9(1)), establishes data exclusivity periods (Article 17.(10)(1)), patent term extensions for 'unreasonable' regulatory or marketing delays (Article 17(9)(8)) and restrictions on compulsory licensing (Article 17(9)(4)).
8. The IP Chapter on the TPPA is available at <https://www.mfat.govt.nz/assets/_securedfiles/Trans-Pacific-Partnership/Text/18.-Intellectual-Property.pdf> [Accessed on May 2017].
9. Article 18.48 of the TPPA 'Patent Term Adjustment for Unreasonable Curtailment'.
10. Article 18.46 of the TPPA: Patent Term Adjustment for Patent Office Delays. Section 4 of this article explains that 'for the purposes of this Article, an unreasonable delay at least shall include a delay in the issuance of a patent of more than five years from the date of filing of the application in the territory of the Party, or three years after a request for examination of the application has been made, whichever is later.'
11. According to the pharmaceutical industry jargon, acknowledged by the EU Commission in its Pharmaceutical Sector Inquiry Report, 2009, paras 20 and 138, a basic patent protects an active compound of the drug, while secondary patents protect various features of a drug, such as formulation and method of production.
12. For the discussion of the previous versions of the TPPA's IP Chapter see Love, J (2014) 'New leak of TPP consolidated text on intellectual property provides details of pandering to drug companies and publishers' Available at <<http://www.keionline.org/node/2108>> [Accessed on May 2017].
13. The complete text of the US proposal for the TPPA's IP Chapter (10 February 2011) is available at <<http://keionline.org/node/1091>>.
14. Press Release (2017) 'The United States Officially Withdraws from the Trans-Pacific Partnership' Available at <<https://ustr.gov/about-us/policy-offices/press-office/press-releases/2017/january/US-Withdraws-From-TPP>> [Accessed on May 2017].
15. Case T-321/05 *AstraZeneca AB v Commission* [2010] ECR II-2805.
16. The Court decreased the fine from 60 to 52.5 million euros. The appeal against that decision by AstraZeneca was rejected by the European Court of Justice in 2012.
17. According to the Pharmaceutical Sector Inquiry Report (2009) other practices that may delay competition to the patent-related exchanges and litigation, oppositions and appeals, interventions before marketing authorisation and/or pricing and reimbursement bodies.
18. For the critic of the Commission's approach to patent thickets in the pharmaceutical industry see Gurgula, O. (2017) 'Strategic Accumulation of Patents in the Pharmaceutical Industry and Patent Thickets in Complex Technologies — Two Different Concepts Sharing Similar Features'. *IIC* doi:10.1007/s40319-017-0551-8.
19. Case T-472/13 *Lundbeck v Commission*; Case AT.39612 - Perindopril (Servier) (2014); *FTC v Actavis, Inc.*, 570 US ___(2013), slip op. See also the FTC Press Release (2015) 'FTC Settlement of Cephalon Pay for Delay Case Ensures \$1.2 Billion in Ill-Gotten Gains Relinquished; Refunds Will Go To Purchasers Affected By Anticompetitive Available at <<https://www.ftc.gov/news-events/press-releases/2015/05/ftc-settlement-cephalon-pay-delay-case-ensures-12-billion-ill>> [Accessed on October 2016]; Federal Trade Commission Staff Study (2003) 'Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions'. p. 3 Available at <http://www.ftc.gov/os/2010/01/100112_payfordelayrpt.pdf> [Accessed on October 2016].
20. These includes the Indian Council of Medical Research, the Norwegian Research Council, the UK Medical Research Council, Médecins Sans Frontières and Epicentre (its research arm), PATH, the Coalition for Epidemic Preparedness Innovations (CEPI), Institut Pasteur, the Bill & Melinda Gates Foundation, and the Wellcome Trust.
21. The observatory was established according to the Resolution WHA66.22 adopted by the Sixty-sixth World Health Assembly adopted (May, 2013).
22. WIPO Re:Search, available at <http://www.wipo.int/cooperation/en/multi_stakeholder_platforms/> [Accessed on October 2016].
23. The H2020 and FP7 reference documents page available at <http://ec.europa.eu/research/participants/portal/desktop/en/funding/reference_docs.html#h2020-legal-basis-fp> [Accessed on October 2016].
24. Goldacre, B. (2013) *Bad Pharma: How Medicine is Broken, and How We Can Fix It*. Fourth Estate (arguing that about half of the clinical trials undertaken by the pharmaceutical industry are never published).
25. As reported by the *BMJ* (formerly the *British Medical Journal*) available at <http://www.bmj.com/content/344/bmj.d8158> [Accessed on October 2016].
26. AllTrials is an international initiative of Ben Goldacre (author of *Bad Science* and *Bad Pharma*), the *BMJ*, Centre for Evidence-based Medicine, Cochrane Collaboration, James Lind Initiative, *PLOS* and Sense About Science and is being led in the US by Sense About Science USA, Dartmouth's Geisel School of Medicine and the Dartmouth Institute for Health Policy & Clinical Practice. The AllTrials petition has been signed by 88741 people and 682 organisations (as of September 2016).
27. See <<http://www.alltrials.net/find-out-more/all-trials/>> [Accessed on October 2016].
28. The *BMJ* is a weekly peer-reviewed medical journal. It is one of the world's oldest and influential general medical journals. Originally called the *British Medical Journal*.
29. See <<http://www.bmj.com/open-data>> [Accessed on October 2016].

30. For more details see <<https://www.mmv.org/>> [Accessed on May 2017]; see also Gabriel, M., Stanley, I. and Saunders, T. (2017) 'Open innovation in health: A guide to transforming healthcare through collaboration' 31 Available at <<http://www.nesta.org.uk/publications/open-innovation-health-guide-transforming-healthcare-through-collaboration>> [Accessed on May 2017].
31. See 'MMV Boilerplate 2017', available at <<https://www.mmv.org/newsroom/boilerplate>> [Accessed on May 2017].
32. See 'The Pathogen Box', available at <<https://www.mmv.org/research-development/open-source-research>> [Accessed on May 2017].
33. The SGC website states that the SGC (Structural Genomics Consortium) is a not-for-profit, public-private partnership with the directive to carry out basic science of relevance to drug discovery. The core mandate of the SGC is to determine 3D structures on a large scale and cost-effectively - targeting human proteins of biomedical importance and proteins from human parasites that represent potential drug targets. In these two areas respectively, the SGC is now responsible for >25% and >50% of all structures deposited into the Protein Data Bank each year; by September 2011 the SGC had released the structures of over 1200 proteins with implications to the development of new therapies for cancer, diabetes, obesity, and psychiatric disorders. Available at <http://www.thesgc.org/about/mini_faq#faq_1> [Accessed on May 2017].
34. See <<http://www.thesgc.org/about/partners>> [Accessed on October 2016].
35. In 2013, a joint statement was issued by EFPIA and PhRMA on 'Principles for Responsible Clinical Trial Data Sharing'. Available at <<http://www.phrma.org/press-release/joint-efpia-phrma-principles-for-responsible-clinical-trial-data-sharing-become-effective-today>> [Accessed on October 2016].
36. See <<http://www.iavireport.org/Back-Issues/Pages/IAVI-Report-9%285%29-inventionsinnovatethyself.aspx>> [Accessed on May 2016].

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