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Public health and the interests of the pharmaceutical industry: how to guarantee the primacy of public health interests?

Report[1]
Committee on Social Affairs, Health and Sustainable Development
Rapporteur: Ms Liliane MAURY PASQUIER, Switzerland, Socialist Group

Summary

The pharmaceutical industry is one of the key players in the health field, due to its important role in research on and development of new medicines. However, in recent years, only a few medicines with a real therapeutic benefit have come onto the market, some of which are sold at prohibitive prices. In terms of public health, this is far from optimal. Measures should therefore be taken with a view to gearing the system to public health needs, including by adopting stricter marketing authorisation policies, by ensuring full transparency regarding the real costs of research and development and, where necessary, by having recourse to mandatory licensing.

The industry's interactions with health-sector stakeholders should also be better regulated, as they may lead to conflicts of interest and biased decisions. Despite considerable progress in this area, both by regulators and the industry itself, a lot more remains to be done. In particular, member States should introduce a mandatory levy on the promotional activities of the pharmaceutical industry, ensure absolute transparency regarding the linked interests of experts working with the health authorities, and make sure that persons with a conflict of interest are excluded from sensitive decision-making processes.

1. Reference to committee: Doc. 13148, Reference 3950 of 26 April 2013.

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A. Draft resolution[2]

1. In the 20th century, humankind saw the most spectacular medical advances in its history. Scientific progress helped us to identify the origin of countless illnesses and to develop treatments which have significantly improved the population's state of health. The pharmaceutical industry has played an indisputable role here by investing massively in research and development for new medicines. It continues to do so and is therefore one of the key players in the health field and at the same time a very important sector of activity in many countries.

2. For a long time, questions have been raised about the possible negative effects of the interaction between the pharmaceutical industry and health sector stakeholders. This interaction may well give rise to conflicts of interest, have an influence on the knowledge and behaviour of the players involved and result in biased decisions. In its Resolution 1749 (2010) "Handling of the H1N1 pandemic: more transparency needed", the Parliamentary Assembly had expressed its concern at the risk of conflicts of interest among experts involved in sensitive health-related decisions.

3. Despite the considerable progress made in preventing and dealing with conflicts of interest, this is still today largely a matter of hit-and-miss. By means of a self-regulation policy, the pharmaceutical industry is now adopting a much more ethical approach and legislation lays down rules in this area. However, self-regulation is not binding and the implementation of legislation leaves much to be desired.

4. Research and development for new therapeutic molecules is a costly and lengthy process. In return for this investment, pharmaceutical companies benefit from an intellectual property right on the molecules they develop, protected by a patent. This innovation model has led to the discovery of thousands of medicines. However, more and more voices are now being heard arguing that this is not the optimal approach in public health matters.

5. In recent years, in spite of the increase in the number of new medicines placed on the market, there have been very few that present a real therapeutic benefit, satisfying real health needs. In addition, we have seen an upsurge in the price of medicines, allegedly justified by the cost of research and development, which nonetheless remains opaque and broadly disputed. The exorbitant price of cancer and hepatitis C treatments is of particular concern. Public health systems are faced with constant cost increases in this area, jeopardising their ability to fulfil their role.

6. In the light of these considerations, the Assembly calls on the Council of Europe member States:

6.1. with regard to the interaction between the pharmaceutical industry and the health sector players, to:

6.1.1. incorporate into the curriculum for health-care professionals specific, mandatory training to foster awareness of the influence of pharmaceutical promotion and how to respond;

6.1.2. introduce a mandatory levy on the promotional activities of the pharmaceutical industry and use it, *inter alia*, to finance a public fund to be used for the independent training of health-care professionals;

6.1.3. place an obligation on pharmaceutical companies to declare their linked interests with all health sector players, to make these declarations accessible to the public, and to establish an independent authority responsible for monitoring this matter;

6.1.4. ensure absolute transparency regarding the linked interests of experts working with the health authorities and make sure that persons with a conflict of interest are excluded from sensitive decision-making processes;

6.1.5. ensure that health-related decisions, including decisions on criteria for defining illnesses and thresholds for treatment, are taken on the basis of individual and public health considerations and are not profit-driven;

6.1.6. introduce strict regulations governing the movement from a position in the public sector to one in the private sector (and vice versa), between the health authorities and the pharmaceutical industry;

6.1.7. increase the funding of patients' associations from public funds in order to avoid over-reliance on private funding.

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2. Draft resolution adopted unanimously by the committee on 11 September 2015.

6.2. with regard to research and development for new therapeutic molecules, to:

6.2.1. oblige pharmaceutical companies to ensure absolute transparency regarding the real costs of research and development, particularly in relation to the public research portion;

6.2.2. adopt a stricter marketing authorisation policy, by:

6.2.2.1. introducing criteria such as added therapeutic value (in relation to existing treatments), or a “need clause”, implying that a drug must also be assessed in relation to medical need;

6.2.2.2. making it mandatory to publish the results of all clinical tests relating to the medicine for which authorisation is being requested;

6.2.2.3. where appropriate, considering restricting reimbursement by the social security system to only those medicines which satisfy such criteria and requirements;

6.2.3. ensure that medicines whose effectiveness has been established remain on the market by having recourse, where necessary, to mandatory licences in return for the payment of royalties;

6.2.4. set up a public fund to finance independent research geared to unmet health needs, including in the field of rare and paediatric diseases.

7. The Assembly calls on member States to prohibit any agreement between pharmaceutical companies which aims to delay, for no medical justification, the marketing of generic medicines.

8. The Assembly calls on member States to impose dissuasive penalties for any illegal practices carried out by pharmaceutical companies, where appropriate by imposing fines of a given percentage of their turnover.

9. In order to ensure the viability of health systems and the accessibility of affordable and innovative medicines in the long term, the Assembly calls on the World Health Organization to put forward alternatives to the current patent-based pharmaceutical innovation model.

10. Lastly, the Assembly calls on the pharmaceutical industry, including companies and associations, to step up its efforts to increase transparency and co-operate more closely with the public authorities in the health sector.

B. Explanatory memorandum by Ms Maury Pasquier, rapporteur

1. Introduction

1.1. Dual role of the pharmaceutical industry

1. In the 20th century, humankind underwent the most spectacular medical advances in its history. Scientific progress helped us to identify the origin of countless illnesses, some of which had previously been incurable, and to discover vaccines and effective medicinal treatments to prevent and cure them. Inevitably, these advances led to improvements in the quality of life and the life expectancy of millions of people.

2. The rise of the pharmaceutical industry coincided with this scientific boom period, during which the major laboratories, working with academies and universities, invested massively in the research and development of new medicines. Today, the industry is one of the key players in public health and one of the most powerful and lucrative economic sectors in the world.[3] This dual public-private role requires a healthy balance to be maintained between the legitimate commercial interests of the pharmaceutical industry and public health interests, bearing in mind that they do not necessarily correspond. This, moreover, is the underlying philosophy of this report, which upholds the principle that in no circumstances should the private interests of the pharmaceutical industry interfere with public health interests. This places a requirement on us, as politicians, to keep a close eye on the activities of this industry.

3. On this basis, it was initially planned to consider mainly the interaction between the pharmaceutical industry and various players in the field of health, so as to examine the possible conflicts of interest and the biased decisions likely to result. However, it quickly became clear that medicines research and development (R&D) by the pharmaceutical industry deserved just as much, if not more attention, because of their implications for public health, particularly as regards the accessibility of medicines.

1.2. Procedure

4. In the drafting process of the report, it seemed vital to me to meet the main players concerned in order to gather information at first hand and to ascertain their viewpoint on the issues of concern to us. To this end, I made two fact-finding visits, the first to Geneva (Switzerland) on 19 and 20 November 2014, and the second to London (United Kingdom) on 26 and 27 February 2015. In Geneva, I had talks with representatives of the World Health Organization (WHO), the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), a biotechnology company (Geneva Biotech Center) and the non-governmental organisation (NGO) Bern Declaration (DB).[4] In London, I had talks with representatives of the European Medicines Agency (EMA),[5] the International Alliance of Patients' Organisations (IAPO) and Health Action International (HAI).[6]

5. Following the same line of thinking, the Committee on Social Affairs, Health and Sustainable Development held a public hearing on 24 June 2014, with the participation of Mr Peter Beyer, Senior Advisor in the Essential Medicines and Health Products Department of WHO, Mr François Bouvy, Director in the Market Access Department of the European Federation of Pharmaceutical Industries and Associations (EFPIA), and Mr Patrick Durisch, Health Programme Co-ordinator at DB. At this hearing, the committee focused mainly on R&D and the accessibility of medicines. I should like to thank all the parties to whom we spoke for making themselves available and providing us with valuable information.

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3. In 2014, the revenue of the seven largest pharmaceutical firms reached US$276 billion.
4. The DB combats the causes of poverty, as well as the human rights violations suffered by the world's disadvantaged populations. It condemns the irresponsible activities of companies based in Switzerland and takes action to get political and economic decision-makers to fulfil their social and environmental responsibility. It is a member of the Health Action International Network.
5. The EMA is responsible, amongst other things, for the scientific evaluation of applications for marketing authorisations for medicines. When authorisation is given (by the European Commission), commercialisation is allowed in the 28 States of the European Union and in Iceland, Lichtenstein and Norway.
6. HAI works for, *inter alia*, better access to essential medicines, greater transparency for decisions about pharmaceutical products and better control of the promotion of medicines.

2. Interaction between the pharmaceutical industry and the various players in the health field

6. Initially, I should like to concentrate on the pharmaceutical industry's interaction with the various players in the health field, and analyse whether, and if so to what extent, that interaction is likely to influence the knowledge, attitudes and behaviour of the players concerned and to give rise to biased decisions or practices which are not in the interest of public health.

2.1. Ubiquitous interaction

7. Today, interaction between the pharmaceutical industry and the different players in the health field is ubiquitous: it exists at every level of the medical system, from research to consumer, and involves all its players, including universities, hospitals, doctors, nurses, pharmacists, scientific publishers, health authorities, health insurance funds and patients' associations.

8. In the case of health-care professionals, especially doctors, nurses and pharmacists, that interaction often starts at an early stage, as soon as their medical studies begin, and continues throughout their career. The increasing dependence of research and medical training on the pharmaceutical industry makes such interaction inevitable. In this context, it may be noted, for example, that the industry organises and sponsors the great majority of symposia, congresses and seminars – which are regarded as vocational training – which it often invites researchers and health professionals to address (for which they are paid). Those congresses are also, for doctors and researchers, an opportunity to join pharmaceutical firms' advisory boards. Similarly, the medical sales representatives systematically promote medicines to doctors, as well as pharmacists.

9. In the case of health authorities, for example medicines agencies, it is the very nature of the relationship that makes interaction ubiquitous. In fact, in order to obtain marketing authorisation for its medicines, the pharmaceutical industry has to submit a file to those agencies. In this context, the industry's interaction with experts working for these agencies is an important factor to be taken into account as experts often have linked interests with the industry.

10. A third case is that of patients' associations. These associations play a fundamental role in patients' lives, providing them and their families with psychological, practical, financial, social and legal assistance. They also have strong lobbying power. The pharmaceutical industry makes a considerable contribution to the funding of these associations, in return for which it enjoys certain advantages. Taking the IAPO as an example, those advantages are determined by the level of financial support given by each of the pharmaceutical companies termed "Industry Partners". Those partners are divided into three categories (gold, silver and bronze) enjoying advantages ranging from expressions of gratitude for their financial contribution on IAPO's website to bilateral meetings with Alliance representatives. IAPO considers the industry to be a significant source of information.

11. The interaction briefly described above is legitimate, necessary and valuable. These are natural partnerships based on common interests bringing mutual benefits and important collaboration for innovation and public health. It is not a question of challenging the very principle of this interaction. Rather it is about whether, in the absence of any appropriate regulatory framework, this interaction could have adverse effects with serious implications for public health. In my view, one merely has to look at the example of the Mediator case in France to realise that the answer to this question is unfortunately a resounding "yes". This case highlights the dangerous collusion between health authorities and pharmaceutical companies, in which the malfunctions were due, amongst other reasons, to the conflicts of interests of certain experts.[7]

2.2. Where do conflicts of interest begin?

12. What is common to all the interaction mentioned above is that they create a link between the interests of the pharmaceutical industry and those of the players concerned. Linked interests, of course, are not the same as a conflict of interest. Political science Professor Dennis Thompson, from Harvard University, gave the following definition of a conflict of interest: "A set of conditions in which professional judgment concerning a primary interest (such as patients' welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)." Accordingly, a link between interests is not in itself awkward, but entails the risk of a slide into problematic behaviour if the secondary interest prevails over the primary one. But it is not an easy matter to determine where conflicts of interest begin.

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7. "… the AFSSAPS, which is a health safety agency, is at present structurally and culturally in a conflict-of-interests situation. Not because of …, but because of institutional co-operation with the pharmaceutical industry which led to a form of joint production of expert opinions and the decisions taken as a result." Extract from the Mediator investigation summary report by the General Social Affairs Inspectorate.

13. In the case of doctors, for instance, the daily presence of the industry by their side creates both links and trust. These come to be regarded as normal, even routine, and the risks that may ensue from such apparently inoffensive interaction are underestimated. Indeed, health professionals often believe that product promotion does not influence them. They have little awareness of the influence of promotional activity, which is more effective than they imagine. Health professionals commonly take the view that "promotional activity has no effect on me".

14. Yet the pharmaceutical industry's marketing activities result in sales because they are able to influence health professionals' decision-making process, and therefore the prescription and supply of medicines.[8] For example, studies have shown that doctors are more likely to prescribe medicines that have been promoted to them by pharmaceutical companies, and not necessarily for the right reasons. This can at times result in the irrational prescribing of medicines, with harmful effects not only for patients, but also for the budgets of health systems which have to reimburse the cost of those medicines.

15. With regard to the health authorities, there have been recurring revelations[9] and criticism in connection with the problem of conflicts of interest among experts working with these authorities. In the case of the EMA, for example, the scientific evaluation system operates through a network of external experts. Those experts serve as members of the Agency's scientific committees, working parties or scientific evaluation teams. In 2012, the audit report by the European Court of Auditors on the management of conflicts of interest within four European Union agencies, including the EMA, concluded that "none of the selected Agencies adequately manages conflict of interest situations". At the end of November 2014, the EMA announced the adoption of a more balanced policy on managing conflicts of interest, which came into effect on 30 January 2015.

16. The case of patients' associations is particularly sensitive. Most of them very much depend on the industry for their funding. They seem well aware of the danger that this dependency may create, potentially going as far as manipulation by the industry. Indeed, the pharmaceutical industry has been accused of attempting to mobilise patients to lobby against the revision of the European Directive on clinical trials regarding certain proposals advocating the transparency of such trials[10]or of using patients' associations to bypass the ban on direct advertising to consumers of prescription drugs.

2.3. Prevention and management of conflicts of interest

17. There is a wide range of rules governing interaction between the pharmaceutical industry and the different players in the health field, the aim of which is to ensure the transparency of relations and avoid conflicts of interest which may occur as a result.[11] A major proportion of those rules comprises non-binding texts, such as principles or codes of good practice drawn up by the pharmaceutical industry itself (self-regulation).

18. The IFPMA Code of Practice is a good example of self-regulation. It includes rules on ethical promotion of medicines to health professionals and ensures that interaction with health professionals and other stakeholders, such as patients' organisations, is appropriate and perceived as such. Membership of the IFPMA requires the associations concerned to comply with the ethical standards laid down in it. The Code provides for a monitoring mechanism whereby genuine complaints about infringements thereof are encouraged. The IFPMA may handle such complaints, on condition, *inter alia*, that the alleged infringement is not already the subject of an investigation by one of the member associations. The decision is taken by an ad hoc group of persons experienced in the application of national codes and selected from IFPMA member associations. To date, the IFPMA has dealt with three complaints.[12]

8. Practical guide: "Understanding and Responding to Pharmaceutical Promotion", edited by the WHO and HAI.
9. According to an article published on the *Mediapart* website on 24 March 2015, the members of the marketing authorisation committee of the French agency for the safety of medicines and the members of the transparency committee of France's supreme authority for health care gave members of several pharmaceutical laboratories advice on how to present files in order to obtain marketing authorisation or a higher rate of reimbursement more easily.
10. www.theguardian.com/business/2013/jul/21/big-pharma-secret-drugs-trials.
11. At European Union level, Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use lays down, amongst other things, rules regarding the advertising of medicinal products. In France, the Bertrand Law of 2011 on strengthening sanitary safety of medicines and health products was passed following the Mediator scandal.
12. www.ifpma.org/ethics/ifpma-code-of-practice/cases.html.

19. The EFPIA also has codes of good practice covering interaction with health-care professionals and patients' associations. In addition, it has recently embarked upon a series of initiatives to enhance the transparency of the pharmaceutical industry. One of these initiatives will result in EFPIA member companies publishing, with effect from 2016, their financial relationships with health-care professionals and organisations.[13]

20. The new EMA policy on managing conflicts of interest (see paragraph 15) evaluates conflicts of interest according to the different types (direct/indirect) and levels of interest (level 1, 2 or 3). The restrictions are applied on the basis of the nature of the interest, the time that has elapsed since the interest and the type of activity concerned within the EMA.

21. It remains to be seen whether this wide range of instruments is truly effective in preventing and managing conflicts of interest. Self-regulation demonstrates the commitment of the industry to adopt a more ethical approach, which is undoubtedly laudable, but in my view it is inconceivable to be content merely with self-regulation in such a sensitive field as public health.[14] Indeed, this is not binding and, therefore, not dissuasive. The HAI representatives told me that national legislation and European regulations were often too lenient and that their implementation left much to be desired.

22. What is more, there seems to me to be a degree of confusion between transparency and the management of conflicts of interest. In practice, financial or other interests are now to a greater or lesser extent systematically declared by experts, doctors, etc., and in certain countries these declarations may be viewed on line.[15] But the fact of transparency does not in itself solve the problem of conflicts of interest. First of all, how can we be sure that declarations are full and reflect the facts? When we put the question to the representatives of the EMA, they replied, with good reason, that it was quite simply impossible for them to investigate every expert. Second, who is to manage all these declarations and how is this to be achieved if conflicts are to be avoided? Without any appropriate response to these questions, there is the risk that we shall reach a point where too much transparency will end up killing transparency.

2.4. How can we be more effective in preventing and managing conflicts of interest?

23. I realise that excessively strict regulations totally severing links between the industry and the health sector players would hardly be feasible, or even desirable. However, other less radical solutions are possible.

24. In Resolution 1749 (2010) "Handling of the H1N1 pandemic: more transparency needed", the Parliamentary Assembly had expressed its concerns about the lack of transparency in decision-making processes linked to the pandemic and the risk of conflicts of interest between experts involved in sensitive decision-making on health matters. It had put forward specific recommendations for health authorities, calling for the publication, without exception, of the declarations of interest of the experts concerned and for all persons subject to a potential conflict of interest to be excluded from sensitive decision-making processes. I believe that these recommendations are totally relevant to the questions that concern us in this report. In addition, strict measures should prevent a revolving door policy, namely the movement from a position in the public sector to one in the private sector, in other words between the health authorities and the pharmaceutical industry which they are supposed to regulate and monitor.

25. Bearing in mind the adverse effects of promotion activities on doctors, one might wonder if they should simply be banned. This is undoubtedly a legitimate question, but I would suggest a more pragmatic measure: introducing a mandatory levy on promotion activities to finance a public fund to be used for the independent training of health-care professionals and independent research. This type of funding already exists in some European countries, such as Italy. In fact, since 2005 each year, pharmaceutical companies have paid the Italian Medicines Agency (AIFA) a sum equivalent to 5% of the total amount spent on promotion activities. Such a measure could also encourage pharmaceutical companies to reduce their advertising expenditure, which would kill two birds with one stone.

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13. Code on disclosure of transfers of value from pharmaceutical companies to health-care professionals and health-care organisations.

14. And unfortunately, the recurring astronomical fines imposed on pharmaceutical companies for illegal practices, including promotion, do not inspire confidence.

15. In France, the "transparence.gouv.fr" website publishes online all the information declared by companies about their linked interests with health sector players.

26. Moreover, it is absolutely essential to overcome the reluctance of health-care professionals to accept that they are indeed susceptible to promotion, right from the very start of their training. Specific training to foster greater awareness of the influence of pharmaceutical promotion and how to respond should therefore be included as a mandatory aspect of the university curriculum of health-care professionals. In addition, as far as possible, their vocational training should be financed by public funds.

27. With regard to the funding of patients' associations, first the financing received from public funds should be increased, and second, thought should be given to setting up a joint fund to help finance them. Pharmaceutical companies could contribute to this joint fund, the management of which should be entrusted to an independent authority. This would enable the industry and the associations to continue their collaboration, while giving the latter greater independence.

3. Medicines research and development by the pharmaceutical industry

28. Research and development for new therapeutic molecules is a costly and lengthy process.[16] In return for this significant investment in terms of both time and money, pharmaceutical companies benefit from an intellectual property right to the molecules that they develop, protected by a patent. During a limited period, generally comprising between 15 and 20 years, no company may copy the molecules concerned. Once that period is over, their formulation comes into the public domain, and "generic products" may be brought to the market.

29. It follows that the model of pharmaceutical innovation is based on a system of patents which enables the industry to retain the monopoly over its products for a limited period of time, negotiate their prices without being subject to competition and in this way gain a return on its investment. This system is considered necessary, if not vital, for creating incentives for the pharmaceutical industry to invest in R&D for new medicines. Indeed, the major pharmaceutical laboratories explain that the funding of R&D for new molecules is extremely costly, and that only the system of patents can offset that expenditure.

30. While the system described above has enabled thousands of medicines to be discovered which have brought about outstanding improvements in public health, its efficiency is increasingly called into question today, in terms of both pharmaceutical innovation and economic sustainability.

3.1. Erosion of the pharmaceutical innovation process

31. In Europe, there is a growing number of new medicines being introduced and spending on R&D in the pharmaceutical sector has more than tripled since 1990. It may therefore seem absurd to speak of an erosion of pharmaceutical innovation, except that innovation must not be measured solely in terms of the number of medicines placed on the market, but above all in terms of medicines that present a real therapeutic benefit and which satisfy real needs. If we use this as our definition, there have been very few breakthroughs in terms of pharmaceutical innovation in the past 10 to 20 years. Of the 20 or 30 new medicines brought onto the market every year, only three may be truly new, with the rest offering only marginal benefits.[17] A study published in the magazine *Prescrire* claims that of the 1 345 new medicines placed on the market between 2000 and 2013, 51% provided nothing new and only 2% presented a real benefit.

32. There are several reasons for this, including the pharmaceutical sector's business model. Fundamentally, this model used to be dominated by a "blockbuster"[18] culture, ensuring high profitability while enabling R&D costs to be recouped through high sales levels. Thus the main aim of R&D was to perfect blockbusters. As the patent on many blockbusters expired, the industry was subjected to competition from generics, while at the same time facing the problem of bringing new blockbusters to the market, *inter alia* because of the rapid growth of a more personalised medicine, more targeted at a group of persons who respond better to the molecule offered.[19] In order to maintain high profit levels,[20] the industry had to adapt and review its business model. Critics say that today this is based on aggressive promotion and meagre innovation.[21]

16. It is a process which lasts an average of between 10 and 15 years. It starts with the research stage to determine a "potential medicine". Then follows the development stage, comprising pre-clinical trials and clinical trials on human beings, divided into several phases.
17. "Pharmaceuticals industry facing fundamental change", *BBC News*, online version, 7 November 2014.
18. Molecules with a turnover exceeding US$1 billion.
19. "R&D des compagnies pharmaceutiques: Ruptures et mutations", a study by the French Ministry for the Economy, Industry and Employment, January 2008.

33. In practice, in terms of R&D, the industry has started to take fewer risks, outsourcing in some cases and purchasing from biotechnology companies[22] molecules which have reached more advanced stages, so are more expensive but have greater chances of success. Furthermore, it has placed onto the market a large number of second-generation medicines, which are new variants of old molecules whose patent has expired, released in a slightly modified form ("me-too drugs").[23] Critics claim that this enables the industry to file new patents and in this way protect themselves against competition from generic medicines.[24] In terms of promotion, the industry has invested on a massive scale in order to boost its sales, with the large pharmaceuticals' advertising expenditure now accounting for up to twice what they are spending on R&D for new treatments.

3.2. Prohibitive prices of medicines

34. For several years now, there has been an upsurge in the price of medicines. Between 2000 and 2009, public expenditure on medicines rose on average by 76% in the European Union and the increase in expenditure on patented medicines exceeded the savings made through the promotion of generic use.

35. Cancer drugs are among the medicines whose price is increasing at an untenable rate, thereby threatening not only access by cancer patients to these treatments, but also the sustainability of health systems in general on account of the costs they generate.[25] However, the most telling example is that of Sovaldi, a treatment for Hepatitis C. In 2014, the US company Gilead introduced this treatment costing 60 000 Swiss francs for a 12-week course of treatment, equivalent to almost 1 000 francs per tablet. Switzerland placed it on the list of specialities for which costs are met by compulsory health insurance, but with restrictions on its use. Consequently, only those patients who already have cirrhosis of the liver – so barely 2% of patients – may claim reimbursement, the others having to negotiate with their doctors and health insurance funds about meeting the costs.[26] In France, the Economic Committee on Healthcare Products (CEPS) has set the price of Sovaldi at €13 667 before tax for a packet of 28 pills (namely €488.10 per pill). That brings the cost of a three-month course of treatment to €41 000 before tax, with the reimbursement rate paid by the health insurance scheme set at 100%.

36. The system of patents is a decisive factor in the high price of medicines, because of the monopoly position it confers on pharmaceutical companies, which gives them a very large amount of influence over the setting of the prices of medicines.[27] The main argument put forward by these companies to justify the high prices of their new medicines is the cost of R&D, a very risky business, given that out of ten thousand or so molecules tested, only one will reach the stage of actually being placed on the market.[28] However, the cost of R&D is somewhat controversial, not only because it is never revealed in detail and it is impossible to verify the accuracy of the figures given,[29] but also because often it does not take into account public-sector funding and also includes opportunity costs, that is what the company could have hoped to obtain by investing elsewhere than in R&D, for example on the stock market.

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20. Pharmaceutical firms' profits remain the highest in any economic sector, with a profit margin close to 20%, and in some cases more, with the American firm Pfizer achieving the colossal figure of 42% (figures dating from 2013). "Pharmaceutical industry gets high on fat profits", *BBC News*, online version, 6 November 2014.

21. "Corporate influence over clinical research: considering the alternatives", *Prescrire*, April 2012.

22. These companies explore the most credible hypotheses and conduct the first trials on humans, both to prove the molecule's safety and to confirm its potential. Then they sell them on for more detailed and larger-scale research on human beings.

23. The reworking of an existing medicine may be a means of improving the molecule in various ways, for example by improving its benefit/risk ratio compared with the reference compound. The industry calls this process "incremental innovation", but detractors claim that these molecules offer little or no therapeutic advances and are expensive.

24. S. Rader and M. Rivasi, "Trop chers, trop prescrits, les médicaments tuent la sécurité sociale", *Libération*, 5 August 2014.

25. In 2013, more than a hundred cancer specialists from all over the world criticised the "astronomical" cost of medicines to treat leukaemia and called on the pharmaceutical industry to reduce their cost to a level that was "morally justifiable".

26. "It seems easier for the authorities to filter patients than to attack prices", NGO Berne Declaration, Solidaire 236, November 2014.

27. Each state negotiates with the industry the cost to be reimbursed under social insurance of each medicine under framework agreements, and the negotiation process is generally somewhat opaque.

28. The cost of failure is therefore also factored in, along with the cost of regulation-related delays. Companies also claim that the medicine helps generate substantial savings in health costs. For example, in the case of Hepatitis C, the treatment will result in a reduction in the number of liver transplants.

29. According to a 2014 study by the Tufts Center for the Study of Drug Development, in Boston – largely financed by the pharmaceutical industry – the R&D cost of each new medicine brought to the market is US$2.6 billion. That figure has been widely challenged. A representative of Médecins sans Frontières went so far as to state publicly that "if you believe this figure, you probably also believe that the Earth is flat".

37. As for public-sector research, this was traditionally limited to basic research, namely clarifying the mechanisms underpinning diseases and identifying promising intervention points. Today it also plays an ever growing role in "applied" research, which leads to the discovery of medicines to treat diseases. A study published in the United States in 2011 found that in the last 40 years, a total of 153 new drugs, vaccines or new indications for existing drugs had been discovered through research carried out by public-sector research institutes. More than half of these drugs had been used in the treatment or prevention of cancer or infectious diseases.[30] Similarly, in the European Union, 44% of innovative medicines recommended for marketing authorisation between 2010 and 2012 originated from small or medium-sized enterprises, academia, public bodies and public-private partnerships.[31]

3.3. Moving towards reform of the system?

38. In the light of the considerations briefly outlined above, more and more voices are now being heard arguing that the patent-based innovation model is not the optimal approach in public health matters. Admittedly it produces the highest return on investment, but not necessarily the medicines that society needs the most. In addition, it leads to high prices for certain new medicines, whereas there are few higher quality medicines in clinical terms. It is becoming increasingly more difficult for the public authorities to cope with high prices, bearing in mind that expenditure on medicine is set to rise considerably in the years to come, while resources are being reduced.

39. This raises a number of questions. For example, with regard to me-too drugs, it is quite legitimate to wonder what the point is of paying for R&D for medicines which present no therapeutic benefit and which do not satisfy an unmet priority health need. What will be the consequences of me-too drugs for the sustainability of social security systems given their potential costs? What will be the impact of the lack of innovation in areas such as the new classes of antibiotics,[32] on rare diseases, paediatric diseases and those, such as Ebola, prevalent in developing countries?

40. And what about public money invested in research? As indicated above, a large proportion of the public budget is invested in R&D for new medicines, without a fair return on investment. This system is not profitable for governments and does not make for the equitable recovery of the public funds invested. With regard to those medicines which have a real therapeutic value but which are sold at prohibitive prices, how will governments finance these products and ensure their accessibility? As such, and in market economy terms, commercial interests are hard to criticise. But I would like to ask the following question: can there be any justification for selling to national governments medicines at prices that are totally out of sync with their overall costs, including research costs, and in so doing making inordinately high profits at the expense of the national health systems?

41. In order to ensure the sustainability of health-care systems and the accessibility of affordable and innovative medicines in the long term, I believe it will be essential to reform the current innovation model, despite the fact that a 2009 report published by the European Commission[33] acknowledges the importance for the pharmaceutical sector of strong intellectual property protection. Nonetheless, it should be pointed out that this report confirms that there is a decline in the number of innovative medicines coming onto the market and notes certain industry practices aimed at delaying the entry of generic medicines into the market, including by means of agreements/settlements with generic companies.[34] However, making proposals in this regard does not fall within the terms of reference of the Parliamentary Assembly, but rather those of the WHO. Still, even under the current system, it is possible to propose measures to protect public health interests more effectively.

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30. "The role of public-sector research in the discovery of drugs and vaccines", *New England Journal of Medicine*, 364; 6, 10 February 2011.
31. Lincker H. et al, "Regulatory Watch: Where do new medicines originate from in the EU", *Nature Reviews Drug Discovery*, 31 January 2014.
32. The proliferation of infections by bacteria which do not respond to antibiotics poses a very significant health risk. The WHO has described this as a threat to public health worldwide, bringing with it the risk that treatment for very contagious diseases, such as pneumonia, may be rendered ineffective. Over the past 15 years, the antibiotics market has been regarded by the pharmaceutical industry as less attractive than other pathologies, *inter alia* for economic reasons. Indeed, the period of treatment by antibiotics is short, and the new treatments, often reserved for severe infections, are intended for only a small proportion of the population. As for the price of antibiotics – a therapeutic class very much dominated by generics – it stands well below the prices of treatments for cancer or diabetes.
33. Executive Summary of the Pharmaceutical Sector Inquiry Report, European Commission.
34. See also, "Zombie patents*", The Economist*, 21 June 2014.

3.4. Identifying the best solutions to protect public health interests more effectively

42. First of all, it is essential for there to be transparency about the real costs of R&D to enable the public authorities to take reasoned decisions regarding medicine prices. We must therefore demand greater transparency about R&D costs, particularly with regard to public-sector funding in R&D for new medicines. Furthermore, without seeking total harmonisation, there has to be greater transparency regarding the setting of prices in each member State, bearing in mind that there are significant differences between them.

43. It would also be necessary to adopt a stricter marketing authorisation policy at national and European level, while leaving enough margin for second-generation medicines. Regulators could introduce a criterion such as added therapeutic value (in relation to existing treatments) or a "need clause", which implies that a drug is assessed not only from a technical and scientific viewpoint but also in relation to medical need, making it possible to take health priorities into account.[35] The possibility might also be considered of restricting reimbursement by the social security system to only those medicines which satisfy such criteria.

44. However, it will be necessary to ensure not only that genuinely new medicines come onto the market, but also that effective medicines already on the market remain there. In point of fact, the industry may sometimes withdraw a medicine from the market, for ostensibly economic reasons.[36] While a country cannot place an obligation on a manufacturer to produce a medicine or keep it on the market, it could easily opt for a compulsory licence approach, a flexibility system provided for in the Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS). Governments can issue compulsory licences authorising third parties to manufacture the patented product without the consent of the patent holder. Compulsory licences may be issued only subject to certain conditions designed to protect the interests of the patent holder, in particular the payment of royalties. Member States are free to specify the grounds on which a compulsory licence may be granted, and these include the public interest and public health.

45. Lastly, there should be a public fund to finance R&D geared to unmet health needs. This fund could be financed by taxes, the levies on the pharmaceutical industry proposed in paragraph 25 as well as fines imposed on pharmaceutical companies for illegal practices which, moreover, should be much harsher than they currently are. In this connection, I would point out that in 2014, the Italian Competition Authority fined the pharmaceutical groups Novartis and Roche €182.5 million for having attempted to prevent the use of the cancer drug Avastin to treat a serious eye disease. The Italian regulator claimed that the two Basel-based groups had reached an agreement to prevent the distribution of Avastin (a Roche product) as a treatment for age-related macular degeneration in favour of Lucentis (a Novartis product), a medicine costing up to 30 times more. An investigation has been initiated in France by the French Competition Authority against the two companies for similar practices. In the same vein, agreements/settlements between the industry and generic manufacturers to delay the entry of generics onto the market should be banned, as such practices are directly detrimental to patients, national health systems and taxpayers.

4. Conclusion

46. Health policies should be decided in line with patients' needs and public health and safety considerations. In the medicines field, a responsible balance must be struck between the industry's private interests and public health interests, while at the same time promoting a climate conducive to innovation and taking into account future health needs. In these times of budgetary constraints, this is all the more important in order to ensure the sustainability of public health systems. In addition, it is essential to make sure that decisions which have an impact on individual and public health are free from any conflict of interest.

47. The proposals in this report seek to strike the aforementioned balance and ensure that conflicts of interest are handled more effectively. It is not a question of treating the pharmaceutical family as though it were the black sheep, but to highlight systemic problems and to come up with solutions. Clearly, the pharmaceutical industry should foster greater awareness of its social responsibility to respect human rights with regard to the major public health issues and act with greater transparency. For, while it has a responsibility to its shareholders, it also has a moral obligation to provide the best possible assistance to patients, even if that means not going down the most profitable route.

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35. The need clause was applied in Norway until its marketing authorisation legislation was harmonised with European regulations.

36. The industry is also criticised for resorting to this technique to put pressure on governments in order to obtain the prices they demand for their medicines.

48. Before concluding, I would like to return to an issue very close to my heart: clinical trials. At the beginning of my work on this report, I took a brief look at this question, but decided against dealing with it in detail. Not because it is less relevant, but simply because I believe it warrants a report to itself. Clinical trials lie at the very heart of the medicines approval process insofar as the health authorities responsible for deciding on the effectiveness and risks of the drug that has been tested – and granting, where appropriate, marketing authorisation – do so on the basis of the results of those trials, which are financed, conducted and analysed by the pharmaceutical industry itself.

49. In this context, the pharmaceutical industry is criticised for concealing and/or manipulating the results of clinical trials so as to systematically promote the drug that has been tested, and for failing to act transparently by refusing to publish details of their trials. The failure to publish negative results can have serious adverse health consequences, such as the prescribing of an ineffective or dangerous medicine, as well as financial consequences.[37] While the new European Regulation on clinical trials (Regulation (EU) No. 536/2014) is likely to constitute a major step forward in terms of transparency – as it provides that a summary of results must be made publicly available in a European database within one year of the end of the clinical trial in all the member states concerned – the limitations on publication on the grounds of commercial confidentiality and intellectual property rights could significantly weaken the impact of the regulation. Furthermore, the EMA's policy on access to clinical data has been criticised for its very broad definition of "commercial confidentiality", which would limit access to these data, and which therefore runs counter to the spirit of the European regulation.

50. Moreover, the way certain trials are conducted by pharmaceutical companies also gives rise to strong criticism concerning, amongst other things, failure to comply with ethical principles.[38] In this regard, in my view, particular attention should be focused on the outsourcing of trials to the developing and emerging countries – some of which are members of the Council of Europe – insofar as there are significant shortcomings in terms of supervision and consequently the risks of breaches are high. I count on the members of the Parliamentary Assembly, and in particular the members of our committee, to keep a close watch on this issue.

37. "Spilling the beans", *The Economist*, 25 June 2015.

38. According to the NGO Berne Declaration, the most frequent ethical violations include the exploitation of the health and socio-economic vulnerability of a population, the lack of free and informed consent, inadequate or no financial compensation for damage and no access to treatment at the end of the trial.