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PHARMACEUTICAL INDUSTRY: A STRATEGIC SECTOR FOR THE EUROPEAN ECONOMY

PHARMACEUTICAL INDUSTRY: A STRATEGIC SECTOR FOR THE EUROPEAN ECONOMY[1]

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[1] Important notice: this paper is mainly focusing on non-legislative actions and is without prejudice to Commission activities related to the pharmaceutical legislative framework.

1. WHY DOES EUROPE NEED AN ACTIVE STANCE TOWARDS THE PHARMACEUTICAL INDUSTRY?

Traditionally the European pharmaceutical sector has played a major role in the world and established a track record in scientific breakthrough in medicines. It has also been one of the gems of European industry with regard to economic growth. A viable European pharmaceutical industry is important for European public health, economic growth, trade and science.

The presence of a viable pharmaceutical industry contributes to the health and the quality of life of our citizens by providing remedies to an increasing number of patients, through a more timely, widespread and equal access to pharmaceuticals.

The healthcare sector and in particular the pharmaceutical industry is of economic significance: the EU pharmaceutical industry produced an output of € 220 billion and employed approximately 800,000 people in 2012. It accounts for around 1.8% of the total manufacturing workforce and is one of the industries with the highest labour productivity[2]. It is a major source of growth and economic performance as reflected by its average annual growth rate. The production index increase amounts to 2.5% (between 2006-2011) and the growth in labour productivity per person employed is 3.6% over the same period[3].The European pharmaceutical industry serves as a major contributor to the EU's trading power. The EU was the world's major trader in medicinal and pharmaceutical products in 2013, with total trade amounting to € 156.9 billion (EU28) and the value of exports reaching more than € 107.4 billion[4].

The world market for medical products is expected to reach $ 1 trillion in 2014. Global spending on medicines is expected to grow to nearly $ 1.17 trillion by 2017[5]. Demand is expected to continue to grow over time. The fact that it is relatively price inelastic[6] compared with the demand for other goods which are subject to more discretionary purchasing decisions for instance automobiles, leisure activities etc. was demonstrated in economic downturns.

The pharmaceutical industry is one of the cornerstones of a knowledge-based economy given the complexity of productions processes and development as well as the nature of many new medicines, i.e. the increasing numbers of biotech products entering the European market[7]. Industry figures show a high R&D intensity (ratio of R&D investment to net sales) when

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2 Eurostat (estimates), European Commission, 2014

3 European Competitiveness Report 2012: Reaping the benefits of globalization http://ec.europa.eu/enterprise/newsroom/cf/_getdocument.cfm?doc_id=7657

4 COMEXT Database, Eurostat, European Commission, 2014

5 The Global Use of Medicines: Outlook Through 2017, IMS Institute for Healthcare Informatics, July 2012

6 M. Simonsen, L. Skipper, N. Skipper, Price Sensitivity of Demand for Prescription Drugs: Exploiting a Regression Kink Design, http://mit.econ.au.dk/vip_htm/msimonsen/drugprices_in_progress.pdf

7 European Medicines Agency, Annual Report 2012

compared with other industrial sectors[8]. It is therefore essential for the EU to maintain its competitive edge. In its Communication of 10 October 2012[9], the Commission announced its intention to "*launch a policy strategy agenda to strengthen the competitiveness of the pharmaceuticals industry*". It recalled Europe's role as a world leader in several strategic sectors amongst which pharmaceuticals[10]. However, Europe's pharmaceutical sector suffers from a lack of confidence, market uncertainty and budgetary problems which are currently preventing it from developing its full potential.

This Staff Working Document takes stock of the current situation of the sector and particularly focuses on the developments of the last years as a first step in preparing a strategic agenda.

2. WHAT ARE THE MAJOR DRIVERS AND CHALLENGES IN THIS SECTOR?

2.1. Demographic Change

Demographic change is one of the key challenges the EU is facing. The number of EU residents aged 65 and over is expected to increase dramatically over the next 50 years, from 92 million in 2013 to 148 million in 2060[11]. As health-related spending generally increases with the age of a person and the prevalence of chronic diseases like diabetes or dementia will rise with an ageing population, demographic transition is considered a major challenge for the financial sustainability of health and care systems. Public spending on health already accounts for more than 7% of GDP in the EU .By 2060 public expenditure on acute health care and long-term care measured as a percentage of GDP is expected to increase significantly (between 8.5 and 9.1% of GDP), although not equally pronounced across all member States[12]. The urgency of the issue is also underlined in the Ageing Report 2012[13] and the 2012 Fiscal Sustainability Report[14] which conclude that the sustainability of public health expenditure is largely related to its projected increases. Based on research findings, it is not only demographic change that is driving up healthcare costs, but also non-demographic determinants of care, such as medical innovations[15]. Adequate framework

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8 The 2013 EU Industrial R&D Scoreboard, http://iri.jrc.ec.europa.eu/scoreboard13.html

9 COM(2012) 0582 final; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52012DC0582:EN:NOT

10 The importance of the pharmaceutical industry was also highlighted in the recent report "Industrial Changes in the European Pharmaceutical Sector" adopted on 29 April 2014 by the Economic and Social Committee; http://www.eesc.europa.eu/?i=portal.en.ccmi-opinions.29626

11 Eurostat, European Commission, 2014

12 7.1% of GDP in the EU in 2010 according to the Ageing Report, European Commission, 2012, http://ec.europa.eu/economy_finance/publications/european_economy/2012/pdf/ee-2012-2_en.pdf

13 http://ec.europa.eu/economy_finance/publications/european_economy/2012/2012-ageing-report_en.htm

14 http://ec.europa.eu/economy_finance/publications/european_economy/2012/fiscal-sustainabiUty-report_en.htm

15 Excerpt from the Ageing Report 2012 (Box 3 "Cost growth in health care expenditures - a short literature survey", p. 165): "In the Ageing Report 2012 the impact of non-demographic drivers on health care expenditure is used in some scenarios. Non-demographic drivers are also sometimes referred to as "excess cost growth" (Smith et al. 2009). The literature on "excess cost growth" estimates the excess of growth in per capita health expenditures to exceed the growth in per capita GDP after controlling for the effect of demographic change. "Innovations in medical technology are generally believed to be the primary driver of health care spending. Recent estimates suggests that medical technology explains 27 to 48% of health care spending growth since 1960 (Smith *et al*, 2009). Earlier studies found that technology explained a somewhat larger fraction of the increase, 50 to 75%. See e.g. Newhouse (1992); Cutler (1995); Okunade and Murthy (2002) as well as Oliveira Martins and de la Maisonneuve (2005)."; http://ec.europa.eu/economy_finance/publications/european_economy/2012/pdf/ee-2012-2_en.pdf

conditions for the role pharmaceutical products can play in medical therapy could contribute to containing health-related societal costs[16].

2.2. New and Old Health Threats

New diseases and old ones believed to be already defeated pose public health challenges. These challenges have also been clearly identified in the recent WHO "Priority Medicines for Europe and the World" Report[17] to which the Commission has contributed.

The higher degree of urbanisation and mobility increase the risk of epidemics. Severe acute respiratory syndrome (SARS) and H5N1 avian flu are reminders of potential dangers. These developments have been a vivid reminder of the need for a reliable supplier in times of urgency in order to ensure the availability of medicines in times of crisis[18] and sparked in response at EU level, the elaboration of a "Joint Procurement Agreement of medical countermeasures"[19].

Global warming is likely to be another challenge. As a consequence of rising temperatures a wide range of public health threats is to be expected. The challenges range from increasing risk of injuries and illnesses due to extreme weather events, increasing respiratory and cardiovascular illness and deaths caused by heat waves and drought as well as rising levels of ozone, and increasing numbers of allergies brought about by elevated levels of pollens. These potentially detrimental effects of climate and climate change have been acknowledged by the international community[20] and recognized as a key challenge in the European Commission's Health Strategy[21].

Furthermore, antimicrobial resistance[22] has become a global challenge. The European Centre for Disease Prevention and Control estimates that antimicrobial resistance (AMR) results each year in 25 000 deaths and related costs of over € 1.5 billion in healthcare expenses and productivity losses. The situation is all the more serious because antimicrobials have become an essential tool for modern medicine[23].

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16 The Global Use of Medicines, July 2012 (2012), IMS Health (2012) http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/Responsible%20Use%20of%20Medicines/IHII_Advancing_Responsible_Use_of_Meds_Report.pdf

17 http://www.who.int/medicines/areas/priority_medicines/MasterDocJune28_FINAL_Web.pdf

18 WHO: Global Action Plan for Influenza Vaccines (GAP), 2006; http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.13_eng.pdf?ua=1

19 The agreement states that "*the institutions of the Union and any Member States may engage, on a voluntary basis, in a joint procurement with a view to an advance purchase of medical countermeasures for serious cross-border threats to health"*, pursuant to Article 5 of the Decision 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health

20 Atlas of health and climate, WHO/WMO, http://www.who.int/globalchange/publications/atlas/report/en/

21 See http://ec.europa.eu/health-eu/doc/whitepaper_en.pdf

22 http://www.who.int/mediacentre/factsheets/fs194/en/

23 Communication from the Commission to the European Parliament and the Council - Action plan against the rising threats from Antimicrobial Resistance,, 17 November 2011, COM (2011) 748, http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf and AMR Road Map European Commission, http://ec.europa.eu/dgs/health_consumer/docs/road-map-amr_en.pdf

Changing life styles are expected to be a further driver in defining public health needs. Chronic diseases like coronary heart disease and diabetes are becoming more widespread and increasingly affect not only the older part of the population[24].

2.3. Investment in Pharmaceutical Research and Development

Developing medicinal products is increasingly complex, expensive and risky. The reasons for this phenomenon are many. R&D expenditures in the pharmaceutical sector have grown dramatically. It is furthermore widely acknowledged that industry's R&D productivity has declined[25]. This is largely due to the increased costs associated with developing a new medicine. R&D costs in the pharmaceutical industry are estimated to amount to approximately € 1 billion for each new medicinal product entering the market. According to some sources, while in 1975 development costs amounted only to € 149 million (in 2000 prices), in 2000 development costs had increased already to € 868 million[26]. From 2010 to 2012 alone the cost of bringing an active ingredient asset from discovery to launch increased by 18%, rising from $ 1.1 billion in 2010 to $ 1.3 billion in 2013[27].

The increasing focus on more complex diseases leads to increasing R&D costs[28] and R&D projects targeting more complex diseases have a lower average probability of successful development[29].

Another reason relates to regulatory factors which have led to: higher demand by the marketing authorization agencies with regard to the quality, scope and scale of data submitted as a consequence of legitimate public health objectives[30].

2.4. European Intellectual Property Regime

Intellectual property (IP) rights are of critical value in a knowledge-based society. This aspect is of particular relevance to the pharmaceutical industry since the nature and development of pharmaceutical products make companies highly dependent on proper IP

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[24] A. Dans et al. Lancet (2011), The rise of chronic non-communicable diseases in southeast Asia: time for action, 377(9766), 680-689

[25] Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg and Aaron L. Schacht; How to improve R&D productivity: the pharmaceutical industry's grand challenge

[26] ECORYS Research and Consulting Competitiveness of the EU Market and Industry for Pharmaceuticals Volume II: Markets, Innovation & Regulation (Released December 2009); http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/vol_2_markets_innovation_regulation_en.pdf and Di Masi JA, Hansen RW, and Grabowski HG, 2003, The Price of Innovation: New Estimates of Drug Development Costs, *Journal of Health Economics*, *22*, 151-185; and Goozner M, 2004, The $800 million pill. Berkeley: University of California Press; however, considerable variation exists with regard to estimating the exact costs of pharmaceutical R&D, see http://moglen.law.columbia.edu/twiki/pub/LawNetSoc/BahradSokhansanjFirstPaper/100HealthPoly4_cost_of_drug_development_2010.pdf

[27] Measuring the return from Pharmaceutical innovation 2013 Deloitte report;http://www.deloitte.com/assets/Dcom-UnitedKingdom/Local%20Assets/Documents/Industries/Manufacturing/uk-manufacturing-measuring-the-return-from-pharmaceutical-innovation-2013v1.pdf

[28] This fact has been confirmed by Pammolli and Ricaboni (2007) based on an analysis of R&D portfolios of pharmaceutical companies in two periods

[29] Diagnosing the decline in pharmaceutical R&D efficiency; Jack W. Scannell, Alex Blanckley, Helen Boldon1 & Brian Warrington2; http://www.nature.com/nrd/journal/v11/n3/abs/nrd3681.html

[30] Diagnosing the decline in pharmaceutical R&D efficiency; Jack W. Scannell, Alex Blanckley, Helen Boldon1 & Brian Warrington2; http://www.nature.com/nrd/journal/v11/n3/abs/nrd3681.html

protection and enforcement. This is particularly true for patents. Equally, effective competition between innovative medicines and between innovative and generic medicines generates incentives for innovative pharmaceutical companies to continue investing in R&D.

In the case of a pharmaceutical product the actual manufacturing process is often easy to replicate. It can be copied with a fraction of the investment that is required for research and development. These research and development costs are incurred in order to comply with the requirements of marketing authorities, i.e. before putting the medicinal product on the market. During this long period, normally after the patent application, the product must complete a rigorous testing process to establish that it is safe, efficacious and of high quality before a decision on pricing and reimbursement is normally taken. This business model contrasts with industries where a product can enter the market soon after a patent application is made.

The importance of a modern intellectual property regime, including its enforcement and complementing activities in other policy areas (e.g. competition), has been recognised as pivotal. This because R&D-intensive industries make a substantial contribution to the EU's economic performance and employment[31]. The Commission's Pharmaceutical Sector Inquiry of 2009[32] identified a truly European patent scheme as a significant stimulator for innovation and effective competition. The creation of a European patent with unitary effect[33] is a step forward particularly relevant to R&D-intensive industries like the pharmaceutical one.

However, an effective intellectual property regime for medicinal products goes beyond patents. Other IP instruments also play a significant role in this industry: these include copyright in supporting materials, trademark, brands, and sui generis provisions like the Supplementary Protection Certificates (SPC)[34] and data exclusivity[35]. These instruments address the specifics of medicinal products which have been referred to above. The SPC aims at compensating at least partially for this loss in the commercially relevant time elapsed between the patenting and the actual marketing of a medicinal product which is likely to occur several years later.

Generating the data which corroborates the claim that the medicine is safe, efficacious, and of high quality is a response to the requirements for obtaining marketing approval constitutes a major investment. Therefore the EU data exclusivity regime protects pre-clinical and

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[31] Study: "Intellectual Property Rights intensive industries: Contribution to economic performance and employment in Europe" – Industry-Level Analysis Report, September 2013, A joint project between the European Patent Office and the Office for Harmonization in the Internal Market, 30 September 2013, http://ec.europa.eu/internal_market/intellectual-property/docs/joint-report-epo-ohim-final-version_en.pdf

[32] COM(2009) 351; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2009:0351:FIN:EN:PDF

[33] Regulation (EU) No 1257/2012; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:361:0001:0008:EN:PDF

[34] Council Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products (Codified version) [2009] OJ L 152/1. The SPC amounts to an extension of the patent right for a maximum of five years. This extension is in accordance with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement)

[35] Medicinal products for human use which have been authorised in accordance with the provisions of Directive 2001/83/EC and Regulation (EC) 726/2004 benefit from eight years of data exclusivity and ten years of marketing protection. The latter period shall be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which are held to bring a significant clinical benefit in comparison with existing therapies

clinical data submitted by private economic operators for the purpose of obtaining a marketing authorisation for a medicinal product.

Intellectual property rights related to pharmaceuticals have gained prominence in debates about intellectual property rights policy. They have been at the forefront in discussions about the impact of intellectual property rights in terms of the access to medicines, particularly in developing countries. In the light of these divergent views, European companies are often faced with significantly lower levels of intellectual property protection in third countries, particularly in emerging economies. The challenges range from a lack of or non-enforcement of patents to the disclosure or reliance on data submitted by the original manufacturer for obtaining a marketing authorisation by regulatory authorities, thus depriving companies of the economic benefits of their investments.

2.5. Constraints in Public Budgets

In 2010 total pharmaceutical expenditure reached more than EUR 190 billion in the European Union[36]. The economic crisis in many European countries has had a significant effect on pharmaceutical spending. Between 2000 and 2009, pharmaceutical spending increased on average in EU Member States by 3.2% per year in real terms, while constant average growth in pharmaceutical spending came to a halt in 2010 (0.0%)[37]. Due to a combined effect of the so-called "patent cliff" (as a large number of key small molecules brands reach generic status) and the current economic crisis, most OECD countries have in recent years even experienced a consolidation or decrease in pharmaceutical expenditure as a share of total healthcare expenditure[38;39]. Manufacturers, prescribers and the distribution chain are under growing pressure to cut costs so as to ensure the sustainability of public health expenditure.

On the other hand, given trends like demographic ageing and progress in medical science, combined with the fact that in European welfare systems there are relatively low out-of-pocket costs, it is reasonable to assume that these drivers will lead to higher demand for medicinal products. Consequently the global economic downturn is not likely to impede[40] the growth in pharmaceutical expenditure in the long-run, at least until 2016[41].

The challenge during the years to come consists in finding a balance between the emergences of new and often more costly pharmaceutical therapies and the legitimate expectation of patients to get access to innovative and effective medicines, on the one hand,

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[36] OECD (2012), *Health at a Glance: Europe 2012*, OECD Publishing; http://dx.doi.org/10.1787/9789264183896-en

[37] OECD (2012), Health at a Glance: Europe 2012, OECD Publishing; http://dx.doi.org/10.1787/9789264183896-en

[38] Executive Agency for Health and Consumers-EAHC-European Commission, EU Pharmaceutical expenditure forecast, Final report, 26 November 2012, http://ec.europa.eu/health/healthcare/docs/creativ_ceutical_eu_pharmaceutical_expenditure_forecast.pdf

[39] ECORYS Research and Consulting Competitiveness of the EU Market and Industry for Pharmaceuticals Volume II: Markets, Innovation & Regulation (Released December 2009); http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/vol_2_markets_innovation_regulation_en.pdf

[40] The future of healthcare in Europe; A report from the Economist Intelligence Unit; The Economist Intelligence Unit Limited 2011

[41] 3095th Employment, Social Policy, Health and Consumers Affairs Council meeting conclusions (6 June 2011); http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/122395.pdf; The Global Use of Medicines: Outlook Through 2016, IMS Institute for Healthcare Informatics (2012

and the need to ensure sustainable public healthcare budgets on the other hand. Revenues of the pharmaceutical industry will be subject to the utmost scrutiny. Pharmaceuticals undergo price reductions, which is the most frequent cost-containment measure, and changes in co-payments[42;43]. Furthermore changes affecting reimbursement lists and procedures (e.g. de-listings, introduction of a positive and/or negative lists) and the reference price system (i.e. changes in the methodology allowing lower reference prices, broader clusters of similar medicines etc.) and/or the pricing of generics in a cluster ("generic price link") are being made. Generic promotion measures (e.g. making indicative INN[44] prescribing mandatory, public awareness-raising campaigns) were frequently applied as well. Pharmaceutical expenditure accounts for a considerable percentage of total healthcare spending in Europe with percentages ranging from 6.8% in Denmark to 33.4% in Hungary followed by Greece (28.5%) and the Slovak Republic (27.4%) in 2011[45], Member States' governments will need to continue their efforts to contain future growth in medical expenditures, notably for medicines.

In addition, governments and other major purchasers increasingly require proof of medical and economic added value while the use of generic and biosimilar medicines is expected to be promoted by public and private payers.

Historically, the so-called "blockbusters" have been commonly used to treat common medical problems like high cholesterol, diabetes, high blood pressure, asthma. They are defined as medicinal products generating annual sales of at least $ 1 billion for the company that creates it. Traditionally, the pharmaceutical industry has been looking at maintaining the high profitability by incremental innovation focusing on maintaining existing brand franchises or discovering the next blockbuster. Given the scientific progress, however, and a deeper understanding of the pathology and causes of diseases, this so-called "blockbuster drug model" seems to become less relevant while more focused medicine based on advances in the knowledge of the human genome will find more widespread use. This "personalised medicine"[46] is a medical model based on the customisation of healthcare using molecular analysis - with medical decisions, practices, and/or products being more specifically tailored to the individual patient. In this model, diagnostic testing is often employed for selecting appropriate and optimal therapies based on the context of a patient's genetic characteristics[47].

The less prominent uses of "one-fits-all" products may also have implications for national healthcare budgets. More individualised medicines tend to be superior in their therapeutic

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[42] S. Vogler et al. South Med Rev (2011) 4(2), 69-79

[43] 3095th Employment, Social Policy, Health and Consumers Affairs Council meeting conclusions (6 June 2011); http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/122395.pdf

[44] INN (International non-proprietary name) prescribing refers to physicians prescribing medicines by its INN, i.e. the active ingredient name instead of the brand name. INN prescribing may be allowed (indicative INN prescribing) or required (mandatory INN prescribing)

[45] OECD (2013), "Pharmaceutical expenditure", *Health: Key Tables from OECD*, No. 7. http://www.oecd-ilibrary.org/social-issues-migration-health/pharmaceutical-expenditure-2013-1_pharmexp-table-2013-1-en

[46] http://personalizedmedicinecoalition.org/Resources/The_Case_for_Personalized_Medicine

[47] Most prominent examples are e.g. trastuzumab, a monoclonal antibody drug that interferes with the HER2/neu receptor to treat certain breast cancers or the use of tyrosine kinase inhibitors such as imatinib to treat chronic myeloid leukaemia in presence of the BCR-ABL fusion gene

properties but, at the same time, they are often more expensive, at least in view of the more elaborated diagnostics which are needed before prescribing them[48;49].

Public authorities face the challenge to accommodate different objectives with constrained resources, i.e. striking a balance between guaranteeing patients' access to state-of-the-art medical treatment and ensuring that incentives are provided for the industry to continue to invest in pharmaceutical R&D. Fair payment mechanisms and sustainable and predictable expenditures are required to guarantee access while effective competition among pharmaceutical companies and sufficient rewards for innovation are crucial to foster innovation. Hence issues related to pharmaceutical expenditure require a comprehensive approach design[50].

Assessing pharmaceutical expenditure also requires taking into account the effects on other health-related costs (like hospitalisation, sick leave, pensions, etc.) as well as the overall implications for industrial competitiveness and external trade. This idea of a more integrated approach aiming at overcoming the traditional compartmentalised way to deal with issues related to pharmaceuticals is already reflected at Member State's level, Indeed life sciences initiatives with a focus on the pharmaceutical industry have been launched in Member States, i.e. involving relevant stakeholders and public bodies[51].

2.6. Policy Consistency regarding the Pharmaceutical Sector

The rules affecting pharmaceutical are set at both EU and national level.

The framework concerning the placing of a pharmaceutical product on the market in the EU and other related subject matters (e.g. the supervision of products after authorisation, the manufacturing, wholesaling or advertising of medicinal products for human use, clinical trials, and specific rules addressing the particularities of certain types of medicinal products and promoting research in areas like orphan medicinal products) fall under the competences of the EU.

The definition of health policies and relevant allocation of resources are national competences[52]. This includes decisions on pricing and reimbursement of medicinal products. However, the EU has also competences in this field as confirmed by the so-called

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[48] A new pharma launch paradigm: From one size fits all to a tailored product, by Michael Kunst, Rafael Natanek, Loic Plantevin and George Eliades Copyright © 2013 Bain & Company, Inc, http://www.bain.com/Images/BAIN_BRIEF_A_new_pharma_launch_paradigm.pdf

[49] At this point in time hard data is scant since personalised medicine is still in its infancy. However, there are claims it can lower costs, and on what seem to be reasonable grounds – that savings in e.g. cancer care can result from pinpointing treatments that will or will not be beneficial 2008 Congressional Budget Office study http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/89xx/doc8947/01-31-techhealth.pdf

[50] This approach has already been considered helpful in the High Level Group on Innovation and Provision of Medicines G10 Medicines whose recommendations led to the Communication, "A stronger European-based pharmaceutical industry for the benefit of the patient - a call for action adopted on 1 July 2003 which outlines the Commission's proposals for advancing the G10 recommendations. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2003:0383:FIN:EN:PDF [please clean & clarify this footnote; a COM Communication should btw not be presented as driven by outside processes]

[51] https://www.gov.uk/government/organisations/office-for-life-sciences

[52] Art.168(7) TFEU; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:083:0047:0200:en:PDF

"Transparency Directive"[53], which requires Member States to respect minimum procedural requirements when taking decisions concerning these subject matters. Shortcomings in the coordination between the policy objectives and subsequent effects of national decisions in other Member States can have detrimental effects by creating market distortions and endangering the predictability of the business environment for industry. Short-term considerations often motivated by healthcare budgetary needs may lead to national ad hoc measures with effects on businesses in other Members States or even beyond[54].

In this context the issue of external reference pricing mechanism (ERP) which is used by a number of national pricing authorities has gained significant attention. Intra-EU ERP describes a specific price setting method which is applied by public authorities. Official prices of medicinal products in predefined Member States (or the cheapest official price in the EU) are used by other Member States to determine their official domestic price. In light of the economic crisis, some countries have taken emergency measures which led to a significant drop in reimbursement prices for medicinal products. While the ERP mechanism may provide useful benchmarks for price negotiations between governments and producers, some stakeholders have voiced concerns about ERP being applied without taking into consideration the socioeconomic features of each country and in particular over the fact that reference prices affected by such emergency measures may influence the price level in other Members States or in third countries.

These often unintended consequences led to an intense discussion among stakeholders and public authorities on how to avoid shortages and guarantee continued access to medicines in Member States The need for improved co-operation and better coordination to minimise any unintended effects that current pricing systems[55] may have in terms of accessibility throughout the EU was acknowledged in the recent Communication of the Commission on effective, accessible and resilient health systems.

Under another form of reference pricing, the so-called extra-EU ERP, medicinal products in certain Member State form the basis for setting prices in non-European countries. This means that the price setting in a national context has implications on the terms of trade since non-EU countries, particular high income emerging economies like Korea and Taiwan, make extensive use of ERP with European countries serving as benchmarks[56]. As a significant share of EU exports is made up by pharmaceuticals while other international trading partners rely mostly on non-pharmaceutical products (like electronics, motor vehicles, etc.) which are not subject to pricing and/or reimbursement decisions taken by public bodies, attention should be paid to the implications in non-EU markets for our pharmaceutical industry.

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[53] Council Directive 89/105/EEC; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1989:040:0008:0011:EN:PDF

[54] Vogler S, Zimmermann N, Leopold C, Joncheere KD. Pharmaceutical policies in European countries in response to the global financial crisis. Southern Med Review (2011)

[55] COM(2014)215final of 4/4/2014: http://ec.europa.eu/health/healthcare/docs/com2014_215_final_en.pdf

[56] http://www.ecipe.org/publications/price-tagging-priceless-international-reference-pricing-medicines-theory-and-practice

2.7. Ethical Behaviour

Public attention with regard to the social and ethical performance of enterprises is increasing and the sector has to respond to this. Citizens expect the industry to go beyond a purely economic role and make a growing contribution to society as a whole, particularly in times of crisis. This increased interest of the public in the ethical conduct by all parties concerned, i.e. industry, healthcare professions, the distribution chain, hospitals, and public authorities, has also been reflected in the Commission's activities[57;58].

The pharmaceutical industry is subject to increased public scrutiny since a major part of its revenues is paid by public bodies, particularly in European welfare states. The level of interest and national practises vary between Member States. As a result, certain Member States (for example the Netherlands and France) have introduced legislative provisions aimed at increasing transparency, i.e. disclosing links between the different parties affected in the marketing of medicines and potential conflicts of interest as well as restricting promotional activities[59]. Such measures have also been taken in third countries[60].

Trade associations have provided some responses to the societal needs through revising or establishing Codes of Conduct and by raising awareness among their members and other organisations[61]. These initiatives were partly related to the Commissions' initiative related to corporate responsibility in the field of pharmaceuticals[62].

2.8. New Challenges and Competitors in the Global Market

Due to the relatively weak economic growth in advanced economies in the aftermath of the economic crisis since 2008, in particular in the EU, the demand for medicines in mature markets is likely to be outpaced by the growth in sales in emerging and developing countries[63].

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[57] Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions A renewed EU strategy 2011-14 for Corporate Social Responsibility (COM (2011) 681 final); and the "List of Guiding Principles promoting good governance in the pharmaceutical sector" of the Process on Corporate Responsibility in the Field of Pharmaceuticals (http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/outcomes_et_en.pdf

[58] The general aspects related to social responsibility of the pharmaceutical industry in relation to its employees are covered by the European Sectoral Social Dialogue Committee (SSDC) for the chemical industry which meets four times per year; issues related to the pharmaceutical industry are also addressed in this forum. It and is attended by representatives of European employers' organisations and trade unions from the industry. At its plenary meeting on 9 April 2013 in Dublin, the SSDC for the chemical industry was enlarged to include representatives of the pharmaceutical industry

[59] http://www.transparantieregister.nl/en-GB/Home; http://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000025053440&categorieLien=id

[60] For instance so-called "gift laws" requiring all pharmaceutical companies to disclose how much they give doctors, hospitals and pharmacists each year have been passed by U.S. States while the U.S. federal government has introduced the Sunshine Act law which requires pharmaceutical companies to report most of the payments and gifts they give to doctors and teaching hospitals and, in addition, to disclose to the competent authority on an annual basis, any ownership held by doctors or their immediate family members, in their establishments

[61] http://transparency.efpia.eu/ (EFPIA code); http://198.170.119.137/ega-code.htm (EGA code)

[62] http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

[63] Pharma 2020: The vision (2007) PricewaterhouseCoopers, http://www.pwc.de/de/gesundheitswesen-und-pharma/pharma-2020-the-vision-which-path-will-you-take.jhtml

Improved benefits available under social insurance systems, a growing number of supplementary private insurance schemes, the ability of patients to pay pharmaceutical costs out-of-pocket due to rising levels of prosperity as well as ageing societies are drivers for pharmaceutical and healthcare products not only in general but even more in emerging economies. Europe's pharmaceutical sector benefits in particular from these trends. The European industry accounted for half of the pharmaceutical imports of the world's fast growing markets[64].

However, globalisation does not only mean new market opportunities; it also means increased competition. Trade competition in the pharmaceutical sector is no longer confined to the traditional competitors like the U.S. or Japan. Several emerging countries, particularly in Asia, target life sciences as future engines of economic growth and are investing in biomedical R&D innovation[65]. The objective of these countries is two-fold: on the one hand they intend to reduce their dependence on imported drugs, and on the other hand they encourage international firms to expand their local presence in manufacturing and/or R&D activities in order to climb up the value chain.

China's current Five Year Plan earmarks $ 300 billion in biomedical R&D innovation funding[66] to foster international competitiveness in medicinal products. Factors such as integrated research networks, geographic/cultural proximity to new Asian markets and active public support might also explain why countries like Singapore have emerged as a biomedical location of choice attracting European companies to establish international or regional headquarters. Emerging economies are climbing up the value chain. They are, therefore, likely to become exporters of high-value medicinal products destined for Europe and the US in the foreseeable future[67]. Countries like China, India, Singapore, and Israel have already emerged as major manufacturers and markets for pharmaceuticals in recent years with expanding manufacturing capacities[68].

Asia's strength as a supplier of active pharmaceutical ingredients (APIs) may also be indicative of future developments. While in the 1980s more than 80% of APIs destined for the European market were of European origin, the proportion had decreased to 20% in 2008[69]. The increased dependency on non-European sources has already led to concerns with regard to maintaining security and quality of supply in Europe.

Today the EU is still a world leader in the trade of pharmaceutical products. It has traditionally been the biggest exporter of pharmaceuticals in the world, with more than a

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64 ECORYS (2009), 'Competitiveness of the EU Market and Industry for Pharmaceuticals – Volume II: Markets, Innovation & Regulation' (2009) - http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/vol_2_markets_innovation_regulation_en.pdf

65 Pharma 2020: From vision to decision (2011) PricewaterhouseCoopers, www.pwc.com/pharma2020

66 Pharma 2020: From vision to decision (2011) PricewaterhouseCoopers, www.pwc.com/pharma2020

67 The relative demise of the European pharmaceutical industry is a well-established fact and has been the focus of exchanges of views, e.g. already in the High Level Group on Innovation and the Provision of Medicines, then called G-10 Medicines in detail – This process lea to a report, http://ec.europa.eu/health/files/phabiocom/docs/g10-medicines_en.pdf

68 Kiriyama, N. (2011), "Trade and Innovation: Pharmaceuticals", *OECD Trade Policy Papers*, No. 113, OECD Publishing; http://dx.doi.org/10.1787/5kgdscrcv7jg-en

69 A 25-Year Landslide in the Manufacture and Business of Active Pharmaceutical Ingredients (APIs) in Europe between 1983-2008, T. Scott, C. Oldenhof European Fine Chemicals Group/CEFIC

quarter of Europe's total high-tech exports. While the US is clearly the most important export destination, the EU exports significant amounts to other countries as well, including many of the emerging countries that experience high growth in pharmaceutical sales.

Given this dependence on markets outside the developed world, a fair trade regime is of the outmost importance for the long-term viability of the pharmaceutical industry. The numerous trade barriers (like opaque pricing/reimbursement mechanisms and medicine-specific requirements e.g. local clinical trials, administrative market entry delays, etc.) as well as the lack of IP rules and their enforcement which the industry faces in third countries can constitute trade impediments and thus negatively affect the future of the Europe-based pharmaceutical industry.

Medicinal products are particularly vulnerable to trade barriers in non-EU countries, as they are subject to many rules and decisions taken by public bodies. Given the importance of medicinal products in EU exports and the prominent role of the EU as a world trader, discriminatory action or unjustified barriers against imported products in third countries have considerable effects on the EU's terms of trade. A level playing field and fair competition are essential prerequisites to create a win-win situation for all parties concerned.

3. WHAT HAS THE EUROPEAN UNION DONE SO FAR?

Apart from non-sector specific polices which equally affect the pharmaceutical industry (e.g. competition policy and the guidance in improving Member States' governance and fiscal sustainability), several legislative and non-legislative actions have been taken at EU-level to tackle certain aspects related to the challenges identified above.

With regard to legislative actions the Commission has accelerated the delivery of safe and effective medicines, protected public health and strengthened the competitiveness of the European industry. Over the years, several mechanisms such as a centralised procedure for the authorisation of medicines, rules facilitating the approval of generics, support to SMEs, and regulatory data protection incentives were built into the legislation to facilitate innovation and timely access of patients to innovative medicines. Additional incentives were also introduced by specific legislation in order to promote research and development and marketing of paediatric and orphan medicinal products. These incentives in particular the market exclusivity period for orphan medicinal products, are important and have provided incentives to invest in this area.

The most recent legislative actions cover a wide range of topics. The new clinical trials regulation[70] is expected to foster more clinical research in Europe by simplifying current rules, featuring a 'one-stop' portal and database for submitting applications, a flexible assessment procedure, simplified reporting systems and increased transparency on the

[70] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158/1 of 27.05.2014)

conduct and results of clinical trials. The EU pharmacovigilance legislation[71] strengthens the safety monitoring of pharmaceuticals. It makes roles and responsibilities clear, minimises duplication of effort, frees up resources by rationalising and simplifying periodic safety update reports (PSURs) and adverse-drug-reaction (ADR) reporting and establishes a clear legal framework for post-authorisation monitoring.

The ongoing review of the "Transparency Directive"[72] aims at creating a more predictable, stable and effective legal and administrative framework for national pricing and reimbursement decisions for medicines.

Non-regulatory instruments of general nature and financing programmes have also been put in place recently. These include actions aimed at fostering cooperation to tackle major and chronic diseases, public health threats and health information needs[73] and the Commission staff working document on the use of '-omics' technologies which takes stock of the progress in personalised medicine[74]; the Communication from the Commission on effective, accessible and resilient health systems[75]; the European Innovation Platform on Active and Healthy Ageing; specific financing initiatives in health thought the Health Programme, the European research programme Horizon 2020 and the Structural Funds 2014-2020.

The results of the Process on Corporate Responsibility in the Field of Pharmaceuticals[76], which was concluded in October 2013, also fit into this framework. It established a dialogue between public and private stakeholders throughout the whole value chain which addressed specific topics relevant to the pharmaceutical sector, including innovation responsive to public health needs, the specific needs and problems of smaller populations and markets, and the potential of an increased uptake of biosimilars for public health and sustainable healthcare budgets and non-prescription medicines. Other relevant topics are new forms of public-private cooperation to facilitate access to medicines notably through managed entry agreements, coordinated access to orphan drugs, as well as ethical and transparent behaviour shared by all stakeholders.

Several different factors affect and determine whether a medicinal product is therapeutically and economically viable before finally being put on the market. Decisions taken by public authorities determine the viability of a medicinal product starting from the development and research phase, which has to comply with the requirements to obtain a marketing

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[71] Directive 2012/26/EU; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:299:0001:0004:EN:PDF; Regulation (EU) No 1027/2012; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:316:0038:0040:EN:PDF; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0001:0016:EN:PDF; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0074:0099:EN:PDF

[72] Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems [1989] OJ L40/08; http://new.eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31989L0105&qid=1393338053296&from=FR and http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/pricing-reimbursement/transparency/index_en.htm

[73] http://ec.europa.eu/eahc/health/actions.html

[74] SWD(2013) 436 final, see http://ec.europa.eu/health/files/latest_news/2013-10_personalised_medicine_en.pdf

[75] COM(2014) 215, see http://ec.europa.eu/health/healthcare/docs/com2014_215_final_en.pdf

[76] http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

authorisation. This is followed by varying forms of health technology assessment and finally subjected to national pricing and reimbursement decisions. While the decisions related to the marketing authorisation tend to be rather uniform in the EU due to the European legislative framework, the two latter areas are prone to a wide diversity of approaches and administrative practices.

In the following chapter a more detailed overview of the numerous non-regulatory measures and actions recently undertaken by the Commission in order to face the abovementioned challenges at different steps of the cycle for medicinal products is provided.

3.1. Ensuring long-term Sustainability of the Pharmaceutical Sector

The issue of sustainability of public finances is a key challenge relating to pharmaceutical expenditure and has gained increased the attention of European institutions. In the 2014 Annual Growth Survey the European Commission has identified an improved efficiency of healthcare systems as a key lever to ensure sustainability of national budgets whilst underlining the importance of ensuring broad access to affordable and high-quality health services[77]. The Council has also recognised the need to make health systems financially sustainable[78] since a significant share of healthcare costs in the EU is borne by public means.

3.1.1 Identifying Priorities with regard to the Development of Medicines

Supported by the European Commission, the WHO in 2003 delivered a report on Priority Medicines for Europe and the World, taking into account Europe's ageing population, the increasing burden of non-communicable illnesses in developing countries and diseases which persist in spite of the availability of effective treatments. The report looked at the gaps in research and innovation for these medicines and provides specific policy recommendations on creating incentives and closing those gaps.

In view of budgetary constraints and multiple public health challenges prioritising development of certain medicines has gained renewed attention. The Commission took the initiative of updating the 2004 priority medicines report, in cooperation with World Health Organization (WHO) experts.[79] This work was done in the framework of the already ongoing Process on Corporate Responsibility in the Field of Pharmaceuticals.

In the 2013 "Priority Medicines for Europe and the World" Report[80] the World Health Organization elaborated a public health-based medicines development agenda which notably puts forward 24 diseases and disease groups as priorities for new or improved

[77] COM(2013) 800, p.7

[78] Council Conclusions on the sustainability of public finances in the light of ageing populations (3167th ECOFIN Council meeting, 15 May 2012): data/docs/pressdata/en/ecofin/130261Ēpdf

[79] See conclusions of the 3053rd meeting of the Employment, Social Policy, Health and Consumer Affairs Council (December 2010)" take the initiative of updating the 2004 priority medicines report, in cooperation with World Health Organization (WHO) experts, (…) continue to encourage the strengthening of coordination and prioritisation in the allocation of resources for pharmaceutical research to increase the probability of valuable innovations that meet unmet health needs, where appropriate through the development of partnerships, (…) and to foster the dialogue with stakeholders on access to medicines in Europe", http://register.consilium.europa.eu/doc/srv?l=EN&f=ST%2016586%202010%20REV%201

[80] http://www.who.int/medicines/areas/priority_medicines/MasterDocJune28_FINAL_Web.pdf

pharmacological approaches, including prevention approaches through vaccination. While the report primarily looks into identifying priorities for medical research, it is equally important for raising awareness among competent authorities responsible for pricing and reimbursement. The results of the report, if taken into account in the European and Member States' research and development programmes, could help to influence public and private R&D investment.

Given limited resources, it is necessary to exploit synergies between the European, national, regional, public and private levels. Key initiatives have been put in place to foster pharmaceuticals related research and development at the European level. Horizon 2020[81] is tailored to deal with health, demographic change and well-being societal challenges and will address the needs identified in the WHO report in the coming years.

In the framework of Horizon 2020 the public-private partnership "Innovative Medicines Initiative 2's (IMI2)[82] overall goal is to speed up the development of new medicines. The Strategic Research Agenda[83] of this public-private partnership will also take into account the priorities identified in the "Priority Medicines for Europe and the World" Report.

Another initiative is the European Innovation Partnership for Active and Healthy Ageing whose objective are numerous, namely improving the health and quality of life of Europeans with a focus on older people, supporting the long-term sustainability and efficiency of health and social care systems, and enhancing the competitiveness of EU industry through business and expansion in new markets[84].

Developing a favourable EU framework for small and medium sized enterprises (SMEs) in order to stimulate innovation and growth is also a key component of Horizon 2020. Supporting the innovation capacity of SMEs through company-focused and market-driven approaches which aim at increasing the economic impact of research and innovation results[85] have been on the Commission's agenda. Nurturing a vibrant European health-related industrial sector will also be through the Programme for the Competitiveness of Enterprises and small and medium-sized enterprises (COSME)[86].

3.1.2 Health technology Assessment (HTA)

In the context of sustainable healthcare systems and in view of maximising patient benefits, the enhanced cooperation between EU Member States to find economies of scale and

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[81] Regulation of the European Parliament and of the Council establishing Horizon 2020 - The Framework Programme for Research and Innovation (2014-2020) (COM (2011) 809 final) OJ L 347, 20.12.2013, http://ec.europa.eu/research/horizon2020/pdf/proposals/com(2011)_809_final.pdf

[82] Proposal for a Council Regulation on the Innovative Medicines Initiative 2 Joint Undertaking (COM (2013) 495 final). The proposed estimated budget of IMI2 is €3.45 billion. The EU will contribute up to €1.725 billion from Horizon 2020, the EU research and innovation programme. This will match the in-kind EFPIA commitment of up to €1.5 billion and an additional amount of up to €225 million if other life science industries decide to join and contribute to IMI2 as members or associated partners in individual projects. http://www.ipex.eu/IPEXL-WEB/dossier/document/COM20130495.do

[83] http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_SRA_March2014.pdf

[84] http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing

[85] Nat Rev Drug Discov. 2014 Feb;13(2):92-3. doi: 10.1038/nrd4232. Regulatory watch: Where do new medicines originate from in the EU? Lincker H, Ziogas C, Carr M, Porta N, Eichler HG,http://www.nature.com/nrd/journal/v13/n2/full/nrd4232.html

[86] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R1287&from=EN

pooling of resources in the implementation of systematic Health Technology Assessment (HTA) is crucial.

HTA is a multi-disciplinary approach analysing the medical, social, ethical, and economic implications of development, diffusion, and use of medicines. HTA is applied by Member States to assess the "value for money" of medicines and it means that pricing authorities put methodologies in place to determine the price that aims at reflecting the added therapeutic value of innovative medicines, i.e. providing financial rewards according to the actual therapeutic value added. Although HTA has been proven to be a valid tool for addressing cost-effectiveness issues, approaches to HTA across Member States differ considerably. Diverging requirements between Member States can lead to shortcomings in the efficient allocation of resources, thus possibly to higher costs for competent authorities and industry and even to delays in access to new medicines for patients.

To address this situation and facilitate more consistent approaches in HTA throughout Europe, the Commission has been supporting cooperation on scientific issues between national and regional agencies since the late 1990's. The Joint Action EUnetHTA[87] has developed and is implementing practical tools to support national HTA Agencies in providing reliable, timely, transparent and transferable information to contribute to HTAs in Members States.

With the objective of strengthening further the cooperation also on strategic issues, the Cross Border Care Directive[88] has established the HTA Network. The Network gathers competent authorities responsible for HTA in all Member States and Norway. It builds on the results of the scientific cooperation and is expected to adopt its strategic vision paper in October 2014.

The Commission has supported the cooperation between competent authorities on the cost effective use of medicines and how their pricing and reimbursement policies for pharmaceuticals could better contribute to the sustainability of their health systems. In this context the European Commission has funded two studies[89]. The first on "External reference pricing of medicinal products: simulation based considerations for cross country coordination", in order to identify and asses further cross country coordination issues relating to external reference pricing while acknowledging the need for sustainable public finances and the delivery of high quality healthcare. The second on the "Policy mix for the reimbursement of medicinal products: proposal for a best practice – based approach based on stakeholder assessment", that explored which policy mix related to the reimbursement of medicines is considered best suited by a variety of interviewed stakeholders, based on the need to reconcile a variety of policy objectives, such as patient access and equity, cost-containment, sustainable funding and innovation.

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87 www.eunetHTA.eu. EUnetHTA gathers over 35 national and regional HTA Agencies and is co-funded by the Health Programme 2012-2015

88 Directive 2011/24/EU on the application of patients' rights in cross-border healthcare (Article 15) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:EN:PDF

89 http://ec.europa.eu/health/healthcare/docs/policymix_final_report_excl_annexes_cleared.pdf and http://ec.europa.eu/health/healthcare/docs/erp_reimbursement_medicinal_products_en.pdf

already existing interactions between parties (e.g. early stage dialogue between pharmaceutical companies and public authorities) have been identified as valuable instruments[90] as they might provide a forum to discuss, on a voluntary basis and whenever feasible, regulatory, HTA and pricing & reimbursement aspects.

As a concrete follow-up to the WG "Orphan Drugs" established under the Process of Corporate Responsibility interested Member States have engaged in establishing a network, the so-called mechanism of Coordinated Access (MoCA). This platform fosters coordination between volunteering Member States parties (e.g. manufactures and social security representatives as well as relevant parts of the executive) so as to evaluate the value of an orphan drug while speeding up overall access by bringing together the decision makers in the area of pricing/reimbursement at an earlier stage[91].

More generally possibilities to foster synergies amongst public and private stakeholders through regulatory, HTA and pricing & reimbursement dialogues, at an early stage and during the development phase, not confined to orphan medicinal products, have been identified in the Process on Corporate Responsibility as areas worth exploring in order to help to accelerate market access[92].

Another form of enhanced public-private cooperation can be found in innovative pricing and reimbursement mechanisms going beyond niche products like orphan drugs. Due to stretched health care budgets national authorities request from manufacturers who seek inclusion in reimbursement lists, proof of value for money and additional benefit compared with available therapies. Alternative pricing and reimbursement mechanisms have been developed in order to ensure earlier access to medicines for patients while mitigating associated risks. For instance, payers and manufacturers conclude formal arrangements with the aim of sharing the financial risk due to uncertainty surrounding the introduction of new technologies. The Commission has collected quantitative information on Managed Entry Agreements (MEA)[93] (e.g. the number of agreements by therapeutic area and the types of agreements implemented). Managed Entry Agreements constitute a special kind of contract which is concluded between the marketing authorisation holders of an innovative medicinal product and the health insurance system in order to be included in the scope of pharmaceuticals whose costs are covered. Through these arrangements it is possible to speed up the market entry of new products while guaranteeing a close monitoring of their

[90] See results of Process of Corporate Responsibility in the Field of Pharmaceuticals http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

[91] Working Group on Mechanism of Coordinated Access to Orphan Medicinal Products, final report (http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/orphans_report_en.pdf)

[92] See results of Process of Corporate Responsibility in the Field of Pharmaceuticals http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

[93] A Managed Entry Agreement (MEA) is an arrangement between a manufacturer and payer/provider that enables access to, coverage or reimbursement of a health technology (e.g. a medicine) subject to specified conditions. These arrangements can use a variety of mechanisms to (i) address uncertainty about the performance of technologies or (ii) manage the adoption of technologies in order to maximize their effective use, or limit their budget impact (Klemp, M et al. What principles should govern the use of Managed Entry Agreements? International Journal of Technology Assessment in Health Care (2011), 27:1, 77-83)

therapeutic benefits as well as of the monitoring of their effectiveness and/or relative efficacy. The analysis[94] of the information obtained made it possible to draw conclusions on the kind of uncertainty that payers are trying to address (related to budget impact, clinical and cost-effectiveness or both), and develop a taxonomy for MEAs to classify the identified agreements while trying to assess the role MEAs could play in Member States.

The possibility of exchanging experience related to MEA schemes and other price-setting mechanisms in order to facilitate earlier access to medicines for patients, based on increased collaboration between Member States has been identified as worth exploring. It would allow gathering and exchanging clinical data regarding the relative effectiveness of a medicinal product so as to support pricing and reimbursement decisions[95]. In particular, the initial work carried out has prepared the ground for further European cooperation. This could be for instance in those fields where limited data is available, i.e. in markets of small population such as those relating to orphan medicinal products[96], personalised medicines or smaller national markets.

3.1.4 Facilitating the Availability of and Access to Specific Medicinal Products

Orphan medicinal products (OMPs) are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU[97]. Despite a number of EU incentives (e.g. concerning the regulatory framework for the development and marketing of OMPs, support for research and development as well as for health information and education) discrepancies in patient access to authorised orphan medicinal products persist between EU Member States. A major obstacle is the lack of information sharing between Member States as regards pricing, reimbursement and related assessments. This fragmentation increases the costs for companies while slowing down the market entry and consequently patients' access. First steps to agree on criteria on which the value could be assessed have already been proposed[98], notably concerning more predictable market conditions.

Further discussions could also be facilitated to assess the potential benefits of multi-country managed entry agreements (MEAs), differentiated pricing or joint medicines purchasing in order to overcome issues related to constraints in available clinical data and address the needs of smaller populations (e.g. orphan medicinal products, personalised medicines).

The sustainable delivery of medicines for the smallest EU markets should not only ensure a high level of public health, but also address the issue of economic viability of the actions to

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94 http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/mea_report_en.pdf

95 See results of Process of Corporate Responsibility in the Field of Pharmaceuticals http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

96 Working Group on Mechanism of Coordinated Access to Orphan Medicinal Products, final report http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/orphans_report_en.pdf

97 Regulation (EC) No 141/2000 of the European Parliament and of the Council and the Implementing Commission Regulation (EC) No 847/2000

98 The Transparent Value Framework (TVF) developed by the working group "Mechanism of Coordinated Access to OMPs" should help to coordinate the assessment of value of orphan medicinal products in EU Member States by providing a simple and consistent terminology and methodology

be undertaken by interested stakeholders. Although availability is often influenced by country-specific variables, ensuring patients' timely access to medicines is a general objective in all Member States, irrespective of market size[99]. Exchanging information on the reasons for non-availability in a more structured way has been identified as a means to improve co-operation among stakeholders and public authorities in the smallest national markets during the Process on Corporate Responsibility[100].

Biosimilars[101] can also play a major role in improving public health since they address the need of a responsible allocation of public funds while opening up promising treatment options for patients by increasing their affordability. The overall experience to date suggests that the most important conditions for market uptake of biosimilar medicines are driven by factors such as (i) physician perception, (ii) patient acceptance, (iii) local pricing and reimbursement regulations and (iv) procurement policies and terms. It is recognised that realising the potential benefits[102] which biosimilar medicinal products offer requires not only a robust regulatory framework such as the one in place in the EU and effective risk management[103].

Fostering the informed uptake and improving early access to high-quality biosimilars on the basis of the EU's regulatory framework **(**i.e. through access to unbiased information and education of patients, healthcare professionals and payers), while closely monitoring the EU's market penetration of biosimilar medicinal products may contribute to the objectives of improving overall public health and the sustainability of Member States' healthcare systems.

As regards non-prescription medicines, stakeholders have recognised that their use reduces public expenditure and thus contributes to the stability of the national healthcare systems[104].

In order to further explore the possible advantages of self-care initiatives within a healthcare system, the European Parliament granted for the 2013 budget year 1 million EUR for a Pilot Project on the 'promotion of self-care systems in the European Union' (general reference). On this basis the European Commission launched two actions: (1) setting up a cost/benefit analysis of patient self-care oriented health systems in the European Union and the current frameworks in place to enhance self-care oriented heath care systems and patients' empowerment[105] and (2) a platform of experts in self-care and healthcare[106]. Both actions

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[99] A study on the availability of medicinal products for human use in EE/EAA countries was commissioned in 2012 by the Commission to assess the impact of the existing regulatory framework on availability

[100] For the purpose of this exercise the following countries were considered small markets: Slovenia, Malta, Cyprus, Latvia, Lithuania, Estonia, and Iceland

[101] A biosimilar is a biological medicinal product similar to another biological medicine that has already been authorised for use, the "reference medicinal product"; Consensus Information Document "What you need to know about biosimilar medicinal products", http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf

[102] According to the updated market data published by IMS Health, although biosimilars are a small segment in the total pharmaceutical market (ca. 1%), they have an exceptional growth (38% in 2012). Biosimilars' share of the accessible European market has grown steadily from their launch and is now at 18%. Biosimilars have a 13% of growth hormone market, 19% share of Erythropoietin market and 49% of Granulocyte colony-stimulating factor market. The per capita uptake of biosimilars and the size of the accessible market however differ between European markets. See: http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_imsstudy_en.pdf

[103] See: http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf, (p.15-17)

[104] http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/otc_report_en.pdf

[105] Open call for tender SANCO/2013/D2/027

will focus on self-limiting conditions in health care. The launch of this project will offer cross-functional stakeholders with expertise in self-care and healthcare the opportunity to co-operate further in related work areas.

3.2. Fostering Transparency and Ethical Behaviour

The Commission launched the Platform on Ethics and Transparency in the framework of the Process on Corporate Responsibility in order to encourage the exchange of views and experiences for ethical behaviour in the pharmaceutical sector between European industries, competent authorities responsible for pricing and reimbursement, patient and health professional associations and other interested stakeholders. The intensive and fruitful discussions are reflected in the consensus document "List of Guiding Principles promoting good governance in the pharmaceutical sector[107]". It sets up a "Decalogue" in this area and minimum standards endorsed by all participating stakeholders. These minimum standards concern public disclosure of relationships and potential conflicts of interest, ensuring all stakeholders responsible behaviour, benefits or inducements in relation to prescribing medicines and others like the meaningful involvement of patients in clinical research and honest representation of the outcomes of all clinical trials.

To increase transparency and trust further, setting up a European registry, i.e. public and private signatories of these "Guiding Principles – promoting good governance in the pharmaceutical sector", would represent the natural way forward along the same lines. This registry could also be used to publicly reference initiatives taken by authorities and private stakeholders to implement the Guiding Principles.

3.3. Improving Access to Medicines Worldwide

Better access to medicines is a challenge which is not limited to Europe but which extends to developing countries. This issue is at the heart of the global health debate. A wide range of recent and ongoing Commission actions and policies exists in order to facilitate the political dialogue with EU Member States, third countries and public-private Stakeholder organisations including industry (e.g. Process on Corporate Responsibility in the Field of Pharmaceuticals – Platform Access to Medicines in Developing Countries with a focus on Africa). General agreement exists that access to medicines is not a mono-causal issue; it rather depends on multiple factors determining to what extent medicines are accessible and affordable to the populations of developing countries.

Access challenges occur along the value chain from discovery of a medicine to the use by the patient. Apart from potential access barriers related to research and development and intellectual property rights access to medicine is constrained by barriers that affect quality, adequate use, availability and affordability. Large segments of the population in low and

[106] Request for specific services EAHC/2013/Health/26

[107] http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/outcomes_et_en.pdf

middle income countries face major difficulties with regard to affordability in treating non-communicable diseases and infectious diseases.

Numerous important factors come to play to determine the prices of medicines (e.g. local taxes and import tariffs, distribution mark-ups, but also the lack of competition, insufficient or ineffective policies promoting the use of generic medicines, etc.).The EU has played a lead role in helping developing countries access medicines through its development policies. The EU is a major provider of funds and technical assistance to support comprehensive health policies in developing countries[108]. However, the EU's efforts are not confined to the instruments traditionally associated with development policy as they go beyond and include a wide spectrum of activities.

The EU complements its comprehensive support to health systems with a major contribution to the EC/African, Caribbean and Pacific Island (ACP)/WHO Partnership on Pharmaceutical Policies with the aim to develop national health policies to improve access to essential medicines for the ACP countries. The EU is also engaged in programmes with global partners such as the WHO, UNICEF and United Nations Population Fund (UNFPA) to provide developing countries with quality medical products. Moreover, the EU and its Member States are a major contributor to the Global Fund to Fight AIDS, Tuberculosis and Malaria and to the Global Alliance for Vaccines and Immunisation (GAVI Alliance) supporting immunisation for all. Furthermore, the EU supports the development of medicines for the three main poverty-related diseases (HIV/AIDS, Tuberculosis and Malaria) through the Europe and Developing Countries Clinical Trial Partnership in sub-Saharan Africa (EDCTP), the EU 7th Research Framework Programme (FP7) as well as Horizon 2020.

In addition, the EU has been one of the main supporters of the Doha Declaration on the TRIPS Agreement and Public Health so that developing countries which lack sufficient production capabilities can effectively get access to medicines. The EU has, in 2006, adopted legislation on compulsory licensing of patents for the production of medicines for export to countries facing public health problems (Regulation EC No 816/2006[109]).

In its bilateral trade agreement the EU systematically refers to the provisions of the Doha Declaration as an overarching principle (see for example the agreements with Korea, Colombia and Peru, and Central America). It also adopted legislation in 2003 to encourage pharmaceutical companies to sell their medicines at lower prices in developing countries and simplify such processes (Regulation EC No 953/2003)[110].

With regard to the quality of medicines, the EU has been a defender of high quality standards since low quality and falsified medicines can endanger the health or even life of people across the globe[111]. Given the frequent lack of adequate market surveillance,

[108] COM(2011) 840 final 2011/0406 (COD); Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL establishing a financing instrument for development cooperation; http://ec.europa.eu/europeaid/how/finance/documents/prop_reg_instrument_dev_coop_en.pdf

[109] http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2006:157:TOC

[110] http://trade.ec.europa.eu/antitradediversion_html/en.pdf

[111] COM(2008) 666 final; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0666:FIN:EN:PDF

populations in developing countries suffer disproportionately. It is of the utmost importance to prevent the sales of falsified medicines which constitute threats to public health.

A consensus with regard to the importance of public-private co-operation and the role economic operators can play has materialised, in particular with regard to the pressing needs in developing countries as regards administrative capacity and quality in the field of pharmaceuticals. This notion seems to be increasingly shared by authorities in developing countries, the EU and economic operators engaged in manufacturing and distributing medicinal products in developing countries[112]. Hence increased cooperation could create a win-win situation for all parties involved. This could be achieved e.g. by enhanced collaboration between governments, international organisations, pharmaceutical companies and civil society in particular with a priority on improving access to quality medicines in developing countries.

3.4. Global Markets

Free and fair trade creates a win-win situation for all trading partners. It generates economic growth and employment, and gives consumers a wider choice in products. Due to the EU's industry dependence on markets outside the developed world, a free and fair trade regime is pivotal to preserve the EU's competitive advantage and the long-term viability of a European-based pharmaceutical industry. Europe is able and willing to face fair competition in global markets[113]. EU trade policy pays particular attention to removing non-tariff (TBT) barriers to exports of pharmaceutical products and promoting regulatory convergence with trade partners. Issues related to requirements in quality, clinical trials, IPR, pricing and reimbursement can also have serious ramifications for European medicines.

The increasing internationalisation of the value chain which is a consequence of the international division of labour may lead to the efficient factor allocation in manufacturing and distributing goods. The growing reliance of European manufacturers on non-European sources for Active Pharmaceutical Ingredients (APIs) raises concerns with regard to the security of supplies and the quality of finished pharmaceuticals which are still manufactured in Europe. In case of supply disruptions, difficulties in accessing sufficient quantities of essential finished medicines such as antibiotics could be faced. Quality-related concerns have notably led to the Falsified Medicines Directive[114] which aims at improving the quality of medicinal products in the legitimate supply chain. Global convergence towards high-level standards for safety, quality and efficacy, the conclusion of Free Trade Agreements (FTAs) and a fair and efficient IPR regime can play an important role in this context.

The EU and its Member States are actively engaged in multilateral organisations that are catalysing international collaboration on medicinal products. This is notably the case through

[112] Communication: A Stronger Role of the Private Sector in Achieving Inclusive and Sustainable Growth in Developing Countries: http://ec.europa.eu/europeaid/what/economic-support/private-sector/documents/psd-communication-2014_en.pdf; This was also one of the key outcomes of the Seventh Joint African Union (AU) Conference of Ministers of Economy and Finance and the Economic Commission for Africa (ECA) Conference of African Ministers of Finance, Planning and Economic Development held in Abuja, Nigeria, from 25 to 30 March, 2014

[113] COM(2010) 612 final; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2010:0612:FIN:EN:PDF

[114] Directive 2011/62/EU; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF

WHO, the International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S). These organisations will continue to play a major role for strengthening international co-operation and promote global adoption of high-level standards.

The EU has engaged in bilateral trade agreements with important trading partners, including emerging economies representing an increasing share of world trade, as well as established industrial countries. Free Trade Agreements have been concluded with South Korea, Singapore, Central America, Peru and Colombia, Ukraine, Moldova, Georgia and Canada, and negotiations proceed with US, Japan, other Eastern Partnership countries, Southern Mediterranean neighbours (Morocco is the more advanced, while Tunisia and Jordan are at the initial or pre-negotiation stages), other ASEAN countries (Thailand, Malaysia and Vietnam are under way), India, and others.

Trade negotiations, including Free Trade Agreements (FTAs), usually seek to harmonize and reciprocate – or at least to obtain a more level playing field – market access, transparency, foreign direct investment, and other areas of mutual and long-term benefit to the EU and its trading partners. These new trade agreements aim at covering all issues relevant to pharmaceuticals, i.e. they tend to go beyond tariffs by addressing matters of critical importance to pharmaceuticals, like regulatory barriers, intellectual property or pricing and reimbursement by public authorities. FTA negotiations have proven to be an instrument to further improve regulatory co-operation and alignment, establishing bilateral commitments and eventually fostering harmonization of technical requirements, often by formalising and deepening already existing co-operation. Trade agreements take into account the specific legal, economic and social situation of the Union's trading partners. With regard to developing countries the EU takes into account the respective development status and the specific public health concerns of our trading partners.

The EU’s ability to defend and guarantee effective protection and enforcement of intellectual property (IP) in third countries deserves particular attention due to the importance of the different forms of IPR for the competitiveness of the EU pharmaceutical industry. In this respect, it is also worth recalling that the EU has been a staunch defender of the flexibilities foreseen in the Doha Declaration and taking an active role in clarifying the obligations and rights stemming from the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), i.e. to address the needs and concerns of developing countries when seeking to promote access to affordable medicines. Progress towards ensuring effective intellectual property protection and, at the same time, its implications for the viability of the European industrial manufacturing base and the competitiveness of our industry with third country producers, particularly with regard to high income emerging economies, will require constant review and continued attention.

4. NEXT STEPS

The Commission has engaged in a variety of activities affecting the pharmaceutical industry on wide range of subject matters. These include synergising and monitoring the

implementation of European and national innovation policies to create incentives/rewards for a sustainable and competitive pharmaceutical sector to improve patients' access to medicines, by exploring interactions between regulatory, HTA and pricing/reimbursement dialogues at an early stage. Other relevant activities deal with innovative pricing and reimbursement models (e.g. managed entry agreements) in order to find ways to improve the availability and affordability of medicines for smaller EU markets and populations, and reaping the potential of biosimilars and vaccines for public health. In addition, issues related to the external dimension including trade and development policy have been on the agenda of the EU. These activities have aimed at improving access to medicine in developing countries while creating a level playing field in the international marketplace for European pharmaceutical companies.

Based on previous, as well as ongoing Commission activities and taking on board the broad spectrum of policies which are at stake when defining and creating conditions conducive to innovation and pharmaceutical industrial competitiveness, a comprehensive approach helping to streamline the policy formulation process at European and Member States level[115] could facilitate future decisions.

Against this backdrop, Commission services will organise an event bringing together relevant EU and national public and private stakeholders: decision-makers from public bodies in charge of industrial competitiveness, health, pricing and reimbursement, research and innovation at Member States level, and their Commission counterparts, patients, healthcare professionals, trade unions and industry representatives.

This event could provide an important contribution to an extensive debate on the European pharmaceutical industry.

[115] See experiences of previous Commission initiatives addressing the wider scope of issue affecting the pharmaceutical industry like the High Level Group on Innovation and Provision of Medicines G10 Medicines whose recommendations led to the Communication, "A stronger European-based pharmaceutical industry for the benefit of the patient - a call for action adopted on 1 July outlines the Commission's proposals for advancing the G10 recommendation.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2003:0383:FIN:EN:PDF
and the Pharmaceutical Forum
http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/pharmaforum_final_conclusions_brochure_en.pdf