ECIPE OCCASIONAL PAPER ▪ 02/2022

Strategic Autonomy and Long-term Innovation Competitiveness:

On the Importance of Intellectual Property Rights for the Production of High-value Medicines in the EU

By **Matthias Bauer, Senior Economist at ECIPE**[1]

[1] ECIPE gratefully acknowledges the support of AbbVie to this study. The paper was completed in December 2021.

ECIPE | EUROPEAN CENTRE FOR INTERNATIONAL POLITICAL ECONOMY

EXECUTIVE SUMMARY

Europe's political leaders have in recent months called for "European industrial autonomy". Notions of dependency, sovereignty and resilience are now also referred to in policy proposals targeted at pharmaceutical companies, with "strategic autonomy" being the ultimate political ambition. The precise meaning of strategic autonomy in biopharmaceutical industries remains yet to be defined, although the current Pharmaceutical Strategy only refers to "open strategic autonomy" in the context of dependencies and supply chains. This is regrettable, as it does not take into account the importance of strategic research and innovation autonomy, allowing the EU to ensure a high degree of autonomy in innovative medicines and therapies. Current policy conceptions fail to account for businesses' long-term international innovation competitiveness and Europe's capability to attract investments in pharmaceutical research and cutting-edge production technologies.

Present conceptions of strategic autonomy of Europe's pharmaceutical industry disregard the fact that the EU is substantially lagging the USA and, increasingly, other parts of the word in pharmaceutical innovation. Clinical trials' pipeline data shows that, in the future, EU Member States will very likely become increasingly dependent on innovative medicines that are temporarily protected by patents and market exclusivity rights held by non-EU rights holders in many therapeutic areas. This gives some urgency to Commission President von der Leyen ensuring that the European industry remains an "innovator" and "world leader" (Mission Letter by Commission President von der Leyen to Commissioner Kyriakides).

The European Commission's current understanding of sovereignty in pharmaceutical industries centres around one core theme: the reduction of dependencies from pharmaceutical suppliers outside the EU. At the same time, in an effort to achieve equitable access to affordable medicines and to foster research into unmet medical needs, it considers changes in the incentive structure for research in medicines for children and rare diseases, and new obligations for companies to achieve a more equitable access to medicines across Member States.

While these objectives are generally merited, the Commission has established a narrow perspective about a concept that is aiming for ambitious long-term achievements for Europe's pharmaceutical industry. The industry's future innovation competitiveness and the capacity to develop and produce high value-added medicines, which should be at the core of any concept of long-term autonomy, have largely been ignored.

Therefore, we argue that strategic or long-term autonomy in the domain of pharmaceuticals should focus on the following items, which are all worth being pursued in their own right, but which – as the analysis will show – are highly interrelated:

- An industrial set-up that avoids supply dependencies or vulnerabilities when it comes to critical medicines or active pharmaceutical ingredients (APIs), through secured global supply chains and/or local production capacities.

- A legal framework that is conducive to investments into research and development (R&D) in those areas that are essential to Europe's health needs, allowing it to respond to both emergency situations and chronic diseases linked to the population, and to be the source of medical innovation.

In this study, we argue that EU policymakers need to account for the critical link between the strength of intellectual property rights (IPRs) and the effective incentives for investments in the development and production of innovative high value-added medicines in the EU. A narrow policy focus on temporary and sometimes negligible supply chain dependencies and affordability considerations would not help European companies to remain or become global leaders in pharmaceutical innovation and high value production. An erosion of pharmaceutical IPRs in the EU would reduce the level of skilled employment in pharmaceutical industries and impede knowledge creation by European companies.

Considering the above, we argue that the core of the concept of long-term autonomy needs to account for European companies' future capacity to compete with pharmaceutical innovation and the production of high value-added medicines. As such, achieving strategic autonomy in Europe's pharmaceutical industry requires a public policy framework that rewards risk taking and investment.

For the EU, we show that the geographical location of production of high value-added medicines is closely linked to the geographical location in which R&D activities take place and investments in production capacities are made. We therefore argue that internationally strong IPRs are not only an important prerequisite for high innovation performance in the EU; strong IPRs are also fundamental for the future production of high value-added medicines in the EU and a skilled and well-compensated pharmaceutical labour force.

We highlight two critical functions of IPRs with respect to investments and the production of innovative and high value-added medicines:

1. Pharmaceutical IPRs provide the most effective incentive for private-sector investments in pharmaceutical R&D and clinical trials, and are thus fundamental to any future production of novel and high value-added medicines in the EU. Pharmaceutical IPRs allow successful innovators to earn sufficient revenues to reinvest in innovation, which is why strong IPRs are key for a self-sustaining innovation system in the EU.

2. Pharmaceutical IPRs allow innovators and producers, including EU and third-country entities, to enter into licence agreements through which rights holders can manage the exchange of know-how and the transfer of technology, as well as production and distribution rights.

Recognising these mechanisms, EU policymakers should strive for an internationally competitive IPR incentive regime that allows for a high level of EU and international investments in pharmaceutical innovation and production capacities in the future. By contrast, an erosion of pharmaceutical exclusivity rights in the EU, e.g. reductions of patent terms and patent term extensions, risks reducing investments in research and innovation in the EU. A drop in innovation and the licensing of technologies and manufacturing rights would translate to lower production levels, less employment, and lower wages and salaries in the industry. Less investment in innovation and production in the EU would increase medicinal dependencies from non-EU suppliers over time, contradicting political ambitions for long-term autonomy.

The main body of this study is composed of four sections.

Following the introductory remarks on the concept of strategic autonomy in the light of long-term innovation competitiveness, Section 2 recaps the European debate about autonomy and sovereignty in the pharmaceutical industry and discusses the EU's latest policy priorities, including those outlined in the "Pharmaceutical Strategy for Europe". It is argued that:

- Blanket claims regarding shortages in supply and dependencies on third countries are misleading. The overall level of EU dependencies from only a small number of non-EU suppliers is rather low, both for APIs and finished pharmaceuticals, questioning political efforts to intervene through potentially far-reaching regulation.

- Political efforts to reduce IPR-based rewards for investments in pharmaceutical research stand in opposition with the objective to improve Europe's pharmaceutical innovation track record. Less innovation would result in lower levels of high value-added production and less skilled employment in the EU.

- Measures towards more equitable access to medicines in the EU would require Member States to further harmonise market access conditions, such as health technology assessments and national reimbursement practices. The impact of intellectual property-related reforms for paediatrics and orphan drugs on access to medicines in the EU is largely negligible, while an erosion of universal research incentives in the EU would likely reduce innovation efforts and thus impede European citizen's access to innovative treatments in the future.

- The current policy priorities are unfit for achieving "EU leadership" in global pharmaceutical innovation.

Section 3 discusses the role of IPRs in the production of high value-added medicines. The focus is on intellectual property as the prime incentive for investment in pharmaceutical R&D and a prerequisite for sharing technical knowledge through the transfer of production and distribution rights globally. The section outlines key industry indicators, including investment in intangibles and R&D spending in the EU, patterns in high value-added production and employment in the EU, and the investment intensities of EU production.

Section 4 provides a discussion of the concept of strategic autonomy in the light of increasing international competition of research-intensive pharmaceutical companies. It is shown that EU pharmaceutical innovators are still strong and internationally competitive in producing and exporting innovative and high-value medicines. On current trend, the EU's pharmaceutical industry is only surpassed by US innovators, which, on aggregate, generate more innovation and a significantly higher value-added than EU companies for a broad spectrum of medicines. It is also shown that pharmaceutical innovators from Asia are rapidly catching up. Based on the assessment of innovation data, it is outlined that EU producers and healthcare systems in the Member States could, in the future, become increasingly dependent on innovative medicines that are originating from companies outside the EU. It is concluded that strong and internationally competitive IPRs granted by EU law would, in the medium to long term, help mitigate future dependencies from non-EU suppliers. It is also argued that internationally competitive pharmaceutical IPRs would contribute to direct investment and in-licensing of production from non-EU innovators, of which many already have a large manufacturing footprint in EU Member States.

Section 5 outlines potential economic impacts of a loss of long-term autonomy with respect to output losses of innovative and high value-added medicines in the EU. We provide a comparative static analysis of three hypothetical scenarios in which the EU's overall pharmaceutical research and production mix is assumed to "degenerate" towards less innovation-intensive activities relative to the status quo. Quantitative estimates are provided for lost pharmaceutical production, forgone investments in intangibles, drops in R&D spending and changes in employment in the EU's pharmaceutical sector. The estimates indicate that a degeneration of Europe's innovation-driven pharmaceutical sector towards a more generics-driven (off-patent) industry would result in substantial losses of high value-added production in the EU, less investments in intangibles, less R&D spending and less employment in pharmaceutical companies in the EU. The largest losses would be experienced in Western European countries.

It is concluded that a viable innovation-enabling regulatory framework will be key for any political ambition that is aiming at a high degree of long-term autonomy of Europe's pharmaceutical sector. Political efforts to support the future autonomy of the EU's pharmaceutical industry should focus on promoting high innovation capabilities, universal IPR-based research incentives, and advanced and internationally connected manufacture capacities.

TABLE OF CONTENTS

1.	Strategic autonomy in the light of long-term innovation competitiveness	9
2.	Strategic autonomy for Europe's pharmaceutical industry: political ambitions and misconceptions	11
2.1.	Reduction of dependencies from suppliers outside the EU	11
2.2.	Revision of the EU's incentive regime for paediatrics and medicines for rare diseases	14
2.3.	IPR reforms to improve affordable access to medicines in the EU	17
3.	The role of IPRs for producing high value-added medicines	20
3.1.	IPRs as incentive for innovation and collaboration in the pharmaceutical industry	20
3.2.	Patterns in high value-added production and investment spending	25
3.2.1.	Production of high value-added medicines in the EU	25
3.2.2.	Investment-intensity of the pharmaceutical industry in the EU	27
3.2.3.	Patterns in value-added and the compensation of labour in the pharmaceutical industry in the EU	29
3.2.4.	Differences in EU Member States' pharmaceutical industry performance	31
3.2.5.	Correlations between investment-intensity, production, employment and the compensation of labour in EU Member States	32
4.	Strategic autonomy in an environment of increasing international competition in the innovative pharmaceutical industry	36
4.1.	Patterns and trends in global pharmaceutical innovation	36
4.2.	Patterns in the value-added of EU pharmaceutical exports and imports	39
4.3.	The EU's pharmaceutical innovation gap	40
4.4.	Trends in drug development costs	42
4.5.	Implications for the conception of strategic autonomy of Europe's innovative pharmaceutical industry	45
5.	Scenario analysis of the economic impact of a decline in the value-added of EU pharmaceutical production	47
5.1.	Methodological considerations	47
5.2.	Estimated changes in production, investment, R&D spending and employment	53
6.	Conclusions	60

References 61

Annex 67

I. Pharmaceutical products list by category and combined nomenclature 67

II. Production, employment and investment in the EU's pharmaceutical industry 68

III. Value-added of EU27 pharmaceutical exports and imports, top-10 by average trade value for the period 2016 to 2020 73

IV. EU pharmaceutical manufacturing 77

V. Market size of pharmaceutical products 80

VI. Patents as technology innovation indicators 82

a. Overall patenting activity across industries 82

b. Patent grants and publications by technology 84

VII. Scenario analysis 86

1. STRATEGIC AUTONOMY IN THE LIGHT OF LONG-TERM INNOVATION COMPETITIVENESS

The EU's political leaders have in recent months called for "European industrial autonomy", along with calls for securing the EU's future "industrial sovereignty". These demands are now formally flanked by political concepts of "open strategic autonomy" and an industrial policy ambition to build a "more resilient economic and industrial model" in the EU. The EU's latest industrial strategy aims explicitly at addressing dependencies in "areas of strategic importance" and supports industry efforts to reduce supply dependencies, including the supply of medicines and pharmaceutical ingredients (European Commission 2021a). In trade policymaking, policymakers strive for an EU that charts its "own course on the global stage […] making the best possible use of the opportunities of our openness and global engagement" (European Commission 2021b).

Notions of strategic autonomy and dependency are now also referred to in political speeches and legislative proposals targeted at pharmaceutical companies. The precise meaning of "strategic autonomy in pharmaceutical industries" remains yet to be defined. However, early policy documents, such as the EU's Pharmaceutical Strategy (European Commission 2020b) and the recent legislative initiative on medicines for children and rare diseases (European Commission 2020d), demonstrate that the European Commission established a rather narrow discourse about the long-term autonomy of Europe's pharmaceutical industry.

The current debate is to a large extent coined by ambitions to repatriate the production of a small number of medicines to Europe. The debate is also about more affordable access to medicines. Even though policymakers still express the ambition for Europe's pharmaceutical industry to remain a global leader in innovation, the policies proposed so far neglect the need for a legal framework that encourages investments in pharmaceutical research and innovation by EU and non-EU companies. In addition, the current discussion in Brussels is largely ignorant to the EU's distinct innovation gap vis-à-vis the USA and, increasingly, aspiring innovators from Asia and other emerging market economies.

Therefore, we argue that strategic autonomy in the domain of pharmaceuticals should focus on the following items, which are all worth being pursued in their own right, but which – as the analysis will show – are highly interrelated:

- An industrial set-up that avoids supply dependencies or vulnerabilities when it comes to critical medicines or APIs, through secured global supply chains and/or local production capacities.

- A legal framework that is conducive to investments into R&D in those areas that are essential to Europe's health needs, allowing it to respond to both emergency situations and chronic diseases linked to the population, and to be the source of medical innovation.

Below we argue that any concept of long-term autonomy of the EU's pharmaceutical sector needs to account for the critical link between innovation incentives and high value-added production. Rather than emphasising the temporary dependencies of a small number of medicinal products and affordable access considerations, we understand the need for a strategic or long-term autonomy for European companies to internationally compete with pharmaceutical innovation and the production of high value-added medicines. As such, achieving strategic autonomy in Europe's pharmaceutical industry requires a public policy framework that rewards risk taking and investments in research and innovation.

It will be outlined that Europe's pharmaceutical industry will only thrive in the future if EU Member States remain attractive to research-intensive companies – from the EU and abroad – that have the financial, technological and scientific capacities to innovate and manufacture in the EU. To achieve long-term autonomy of the sector, EU policymakers should strive for a universal and internationally competitive incentive regime that allows for a high level of future investments in innovation and modern production facilities. Recognising that intellectual property rights (IPRs) are the most effective policy tool for incentivising research, innovation and advanced production, pharmaceutical patents and universal market exclusivity rights are key for achieving long-term autonomy of the EU's pharmaceutical industry.

The remainder of this study is structured as follows: Section 2 recaps the European debate about strategic autonomy in the pharmaceutical industry. It provides a critical discussion on the current policy objectives and legislative initiatives, including the Pharmaceutical Strategy for Europe. Section 3 discusses the role of pharmaceutical IPRs for the production of high value-added medicines in the EU. Section 4 elaborates on the concept of strategic autonomy in the light of rising international competition in the biopharmaceutical industry. Section 5 provides an analysis of three hypothetical scenarios in which the EU's overall pharmaceutical research and production mix is assumed to "degenerate" towards less knowledge and innovation-intensive activities relative to the status quo. Section 6 concludes.

2. STRATEGIC AUTONOMY FOR EUROPE'S PHARMACEUTICAL INDUSTRY: POLITICAL AMBITIONS AND MISCONCEPTIONS

When presenting the EU's latest Pharmaceutical Strategy in November 2020, Ursula von der Leyen, the serving President of the European Commission, stated that "[t]he coronavirus pandemic has highlighted the vital need to strengthen our health systems. This includes access to safe, effective and high-quality medicines at an affordable price". (European Commission (2020a) Stella Kyriakides, serving Commissioner for Health and Food Safety, emphasised the EU's prime ambition to "help ensure Europe has the supply of affordable medicines to meet its needs". At the same time, Commissioner Kyriakides stressed that public support for Europe's pharmaceutical companies may be needed to "ensure that [the EU] remains an innovator and world leader". (European Commission (2020a)

These thoughts are reflected in the policies outlined in the Pharmaceutical Strategy and a recently proposed action to revise the incentive regime for paediatrics and orphan drugs. It appears that the Commission wants to achieve strategic autonomy in the EU's pharmaceutical industry by increasing the production of medicines in EU Member States in order to reduce dependencies from suppliers outside the EU. At the same time, to achieve more equitable access to medicines and to foster research in unmet medical needs, it is considering a revision of the legal incentive regime for paediatrics and orphan drugs so as to stimulate their development by European companies, and a revision of the legal incentive regime for paediatrics and orphan drugs to ensure that Europeans benefit from more affordable access.

While these priorities are generally merited, a deeper analysis of policymakers' motives and the proposed policy measures reveals that the Commission and some national governments have established a short-sighted and potentially counter-productive discourse about how to achieve ambitious long-term objectives. With reference to the understanding of the concept of long-term (strategic) autonomy in this study, we discuss the extent to which current policy priorities could improve companies' innovation competitiveness and their future capacity to develop and produce high value-added medicines in the EU.

2.1. Reduction of dependencies from suppliers outside the EU

Political concerns over shortages in the supply of certain medicines are reflected by the EU's latest Pharmaceutical Strategy, which calls for legal action to diversify production and supply chains and the introduction of strategic stockpiling. The Pharmaceutical Strategy was preceded by a joint initiative of France and Germany in 2020 calling for "strategic health sovereignty" of the EU (Health Strategy 2020). In May 2020, the German government started to campaign for a joint EU undertaking to push pharmaceutical production on the

continent, with Germany's Minister for the Economy arguing "[i]t is not a good idea to turn back globalisation, but it is the right idea to minimise one-sided dependencies and to assert or regain national sovereignty in sensitive areas". (RND 2020)

In the subsequent Health Strategy from May 2020, the repatriation of production became an official political ambition. The Franco-German strategy sought to "increase EU sovereignty on pharmaceutical products" by reducing import dependencies for medicines and active pharmaceutical ingredients from non-EU countries. Echoing the Franco-German initiative, the European Commission's Pharmaceutical Strategy stresses the need for new EU law to diversify supply chains and the introduction of strategic stockpiling.[2]

Are such measures merited and to what extent could these measures contribute to long-term autonomy of Europe's pharmaceutical industry?

First of all, trade and production data reveal that Brussels and national policymakers overstate EU dependencies from third-country suppliers in the case of pharmaceutical products, both for APIs and finished medicines.

Concerning pharmaceutical ingredients, the EU and the USA are still major production hubs for APIs.[3] A recent survey from the European Federation of Pharmaceutical Industries and Associations (EFPIA 2020) of research-intensive member companies indicates that 77% of APIs consumed in the EU27 are actually sourced from within the EU. As outlined by Guinea and Espés (2021), EU Prodcom data for 2019 show that the share of APIs produced in the EU27 was 57.8% of EU27 domestic consumption and exports; 17.5% was imported from other European countries and 24.7% was imported from outside Europe, mainly the USA, China and India.[4] As regards chemical APIs, suppliers in India and China together provided 29% of the raw materials, while at the same time 59% of the raw materials and intermediates for chemical APIs originated and were manufactured in Europe, qualifying blanket political statements about strategic dependencies in ingredients' markets.

For finished pharmaceuticals, Guinea (2020) shows that suppliers from more than 127 countries supplied the EU27 with medicines in 2019. The top 5 jurisdictions supplied

[2] France and Germany also called on establishing a common strategic stock of medicines and medical products, such as protective equipment and testing kits, encouraging the production capacity of these products in the EU.

[3] For APIs, industry intelligence indicates that the global API market size was valued at USD 162 billion in 2018 and is expected to grow at a compound annual rate of 5.7% by 2027 (Vision Research Reports 2020). Together, the USA and the EU account for the majority of API manufacturing facilities, with each hosting approximately 26% of global facilities. The remaining facilities are divided between India (19%), China (13%) and the rest of the world (14%).

[4] The largest producer countries for APIs were Ireland (EUR 13.5 bn), Germany (EUR 9.1 bn) and Italy (EUR 5.0 bn). Importantly, with regard to imports, 53.4% of EU27 API imports (in value terms) originate from the EU27 itself (72.7% from Europe as a whole), followed by 8.4% from the USA, 7.2% from China and 3.4% from India. When looking at imports in absolute quantities (tonnes), the numbers are different, but still do not support the claim of dependency. In volume terms, the main source of APIs imported from outside Europe was China (22.6%), followed by the USA (5.7%) and India (3.1%). Accordingly, the highest level of dependency for non-EU API imports is found for China, with 23% of all intra- and extra-EU imports in volume terms.

96.1%. In 2019, 86.2% of EU27 imports of finished pharmaceuticals came from Europe (68.1% from intra-EU27, 13.3% from Switzerland and 4.8% from the UK); 8.3% of EU27 imports of finished medicines originated in the USA.[5]

As outlined by Guinea and Espés (2021), from a list of 163 pharmaceutical products that includes finished and semi-finished pharmaceutical products (see Annex I), antibiotics, vaccines and APIs, 91 products passed the threshold of more than 50% of total imports coming from outside the EU (extra-EU imports). Of these 91 products 84 are APIs, which, most of the time, are basic easy-to-manufacture components. The 91 products that passed the threshold of more than 50% of total imports coming from outside the EU represent only 17% of the value of the 163 selected pharmaceutical products imported into the EU.[6] Moreover, international supply chains for many products are quite diverse. For example, in 2019, 95% of insulin[7] was sourced from outside the EU. However, for this substance, Europe has a diversified source of supply from 13 different countries including the USA and China.

In the innovative pharmaceutical industry, certain dependencies may exist for raw materials, for which the data, including those mined by the European Commission for APIs and related supply chain vulnerabilities (such as the location of contract manufactures), is largely missing. However, as recognised in the European Commission's recent staff working paper "Strategic dependencies and capacities" (European Commission (2021c, p. 103), "[a]ny measures to address strategic dependencies would need to be tailored and proportionate based on a policy mix that considers the potential of both external and internal actions".

Summing up the above, bold assertions about extensive shortages in supply are misleading. According to the analysis of Guinea and Espés (2021), only 0.8% (in volume terms) and 6.1% (in value terms) of EU27 pharmaceutical products' imports could be classified as "vulnerable".[8] Given strong global supply chain performance in 2020 and 2021, including for the vulnerable 1%-6%, political calls for new and potentially far-reaching EU regulation of supply chains should be addressed with caution.

Shortages in supply may temporarily exist for certain compounds and finished medicines. For such cases, the EU could improve market-monitoring facilities, e.g. access points for

[5] At the same time, 181 countries are supplied by suppliers from the EU27 with finished medicines. The top 5 export destinations constituted 78.4% of EU27 exports in 2019; 57.5% of EU27 exports of finished pharmaceuticals went to Europe (46.2% to intra-EU27, 6.6% to Switzerland, 4.8% to the United Kingdom). In 2019, 17.5% of EU27 exports of finished medicines went to the USA. China and India received 3.4% and 0.2% of EU exports of finished medicines respectively.

[6] Including imports from outside the EU and imports from within the EU.

[7] CN 8 Product code: 29371200. Product description: Insulin and its salts, used primarily as hormones.

[8] Whereby vulnerability is defined as "high import dependency (export vulnerability) and high supplier county (destination country) concentration". See Guinea and Espés (2021), p. 55.

companies, pharmacies and hospitals to report such shortages. Policymakers could then take action on a case-by-case basis, following solid investigations of the extent and root causes of supply chain disruptions.

With regard to long-term autonomy of the industry, potential production localisation requirements, local content requirements and stockpiling obligations would not have a positive effect on European companies' innovation competitiveness and their future capacity to develop and produce high value-added medicines in the EU. Such policies would undermine the freedom of choice and production efficiency of pharmaceutical companies that are based in the EU, increase their input costs and likely reduce their international competitiveness. At the same time, government-imposed production localisation requirements would offer protection from competition for inward-oriented EU suppliers, while EU exporters could be exposed to retaliatory measures by governments of third countries, with negative effects on EU export revenues and R&D budgets. Equally, legislative measures such as those proposed in the Pharmaceutical Strategy, such as "stronger obligations on industry to ensure the supply of medicines, earlier notification of shortages and withdrawals, enhanced transparency of stocks across the supply chain, and a stronger coordinating role for the EMA in monitoring and managing shortages", while less invasive than a blanket localisation-mandate, would present a very high burden for companies – especially smaller European small and medium-sized enterprises (SMEs) – which may not be justified by the small amount of molecules that are actually vulnerable.

Alternative and less-distortive remedies for temporary supply chain disruptions include the full elimination of EU import tariffs on APIs (and medical goods) and simplified trade facilitation procedures. At the same time, none of these measures would have a significant positive impact on future pharmaceutical innovation and high value-added production in the EU. In other words, none of these measures is fir for conserving or advancing EU leadership in global pharmaceutical innovation.

2.2. Revision of the EU's incentive regime for paediatrics and medicines for rare diseases

With the Pharmaceutical Strategy, the European Commission is also seeking for "more balanced and fair incentives" for investment in pharmaceutical research, aiming to protect innovation and create the right conditions for competitiveness. In addition, the strategy underlines that "research priorities should be aligned to the needs of patients and health systems". To achieve this goal, the Commission is considering a revision of the EU's IPR incentives regime with the aim to stimulate more innovation in areas of unmet medical needs, such as neurodegenerative and rare diseases.

It is stated that incentive policies for pharmaceutical innovators in the EU need to be rethought to stimulate native EU innovation in areas where companies' investment has not been focused in the past due to an absence of commercial interest (European Commission 2020b).[9] The Commission is considering new rules for innovation incentives that would allow designated governmental agencies to direct companies' innovation activities to areas of accepted unmet medical needs.

According to the European Commission's problem description intended to justify this revision, the existing EU Orphan Drug and Paediatric Regulation has indeed stimulated research and development of medicines to treat rare diseases and of medicines for children. At the same time, it is noted that existing regulation failed to "stimulate development of medicines in areas of unmet needs (e.g. 95% of rare diseases still have no treatment option) and to better ensure that European patients actually get the medicine, independently from which country they live". (European Commission 2020d)

According to the latest proposals, the European Commission aims to establish a new legal relationship between unmet medical needs, which are yet to be defined, and future incentives for innovation in the EU.[10] Several legal options were presented regarding the eligibility of a new drug to be granted market exclusivity in the EU. For example, the Commission is considering a reduction in the number of medicines that would qualify for special market exclusivity awards, reductions in the lifespan of supplementary protection certificates (SPCs) and making potential rewards conditional on an innovator's commitment to market a new medicine in all EU Member States (European Commission 2020d).

Are limitations of universal R&D incentives merited and to what extent could the proposed measures contribute to long-term autonomy of Europe's pharmaceutical industry?

Even though the options presented so far are only vaguely circumscribed, the Commission essentially considers granting additional market exclusivity only for a limited number of politically defined medical needs, while limiting market exclusivity in all other areas. Industry representatives argued that the options outlined in the ongoing impact assessment would produce legal uncertainties and weaken universal research incentives designed to

[9] In its "Pharmaceutical Strategy for Europe" from November 2020, the European Commission outlines three overarching objectives and policy priorities respectively: 1) "delivering for patients: fulfilling unmet medical needs and ensuring accessibility and affordability of medicines"; 2) "supporting a competitive and innovative European pharmaceutical industry"; and 3) "enhancing resilience: Diversified and secure supply chains; environmentally sustainable pharmaceuticals; crisis preparedness and response mechanisms" (see European Commission 2020a). These objectives are reflected in the planned revision of EU legislation on medicines for children and rare diseases, which is based on three key assumptions: 1) insufficient development in areas of greatest unmet medical needs for patients; 2) the considerable differences in availability and accessibility across Member States; and 3) the inability to fully exploit scientific and technological developments.

[10] In the EU, "orphan medicines" benefit from 10 years of market exclusivity once they receive a marketing authorisation in the EU. This right is intended to encourage the development of medicines for rare diseases, by protecting them from competition from similar medicines with similar indications, which cannot be marketed during the exclusivity period. In the USA, with orphan designation, the Food and Drug Administration (FDA) grants a 7-year market exclusivity that applies specifically to the designated orphan use. It should be noted that this exclusivity does not preclude generic competition for other non-orphan approved uses of that drug.

support innovation in multiple areas, including rare diseases and medicines for children. An industry response by the EFPIA (2021) challenges the adequacy of the Commission's ambiguous claim that 95% of rare diseases still do not have a treatment option. The EFPIA clarifies that the actual "burden of a disease is unevenly distributed across the 7-8,000 rare diseases". Indeed, 10.9% of the most prevalent rare diseases account for 98.6% of the rare disease patients (and hence the aggregate burden; see Wakap et al. 2019). 79.2% of rare diseases affect a single patient or family. Dedicating research efforts to a small share of rare diseases allows the pharmaceuticals sector to address a large proportion of rare disease patients' unmet needs and is proportional to the distribution of the disease burden." The EFPIA generally argues that "any assessment of the costs and benefits of incentives should be supported by a holistic comprehension of the dynamics of biopharmaceutical innovation. Understanding the interplay of incentives and investment decisions is elemental to evaluating the innovation that accrued from the Orphan Regulation."

The European Commission's evaluation of existing incentive regimes for the development of medicines for rare diseases and for children concludes that both laws have indeed incentivised the drug development in these areas. However, it is also argued that the incentive regimes were not able to "sufficiently" stimulate the development of medicines in areas of unmet needs. Previously, the Commission's 2020 impact assessment of the orphan drug regulation (European Commission 2020e) found that since the adoption of the regulation in 2000, the number of marketing authorisations for orphan medicines has not only increased over time, but actually grew substantially faster than the number of authorisations of non-orphan medicines.[11] In this assessment, market exclusivity rights are considered the main incentive that EU regulation provides, citing that for 73% of orphan medicines the market exclusivity reward has helped to increase the profitability of these products, incentivising investment in research. It should be noted that the assessment also found that authorisation and development processes remained slow in the EU. In this regard, the EU was found to lag the USA and Japan.

A study by Dolon (2020) also evaluated the impact of the orphan medicinal products (OMPs) regulation on innovation, using a risk-adjusted return on investment approach to reflect how research incentives directed investment and impacted innovation. The assessment finds that more than half of the 142 studied drugs that were developed and approved between 2000 and 2017 would not have been economically viable in the absence of research grants and orphan medicines' marketing exclusivity. It is concluded that "maintaining a positive incentive framework is essential to advancing therapeutic innovation towards effective

[11] The Commission estimates that between 18 and 24 orphan medicines are direct results of existing EU legislation. Also, orphan medicines analysed were available on average 9 months earlier and to more people across the EU than would have been the case without the regulation. According to the assessment, data from the efficiency analysis suggest that the market for orphan medicines has become more commercially attractive than it was before 2000, enabling new companies to attract venture capital.

preventative medicines and treatments for rare diseases, and for fostering a productive biopharmaceutical industry in Europe".

Summing up the above, the Commission recognises the critical importance of IPRs for investments in pharmaceutical research and innovation. At the same time, the Commission is taking into consideration an erosion of universal research incentives to effectively steer companies' investments towards certain R&D activities. Regarding the long-term autonomy of the EU's pharmaceutical industry, increased uncertainty over market exclusivity status and an effective reduction of universal market exclusivity rights would not help to improve Europe's overall pharmaceutical innovation track record, with negative implications for the number of high value-added medicines produced in the EU in the future. As recently outlined by a study of Gaessler and Wagner (2019), reducing expected exclusivity leads to greater abandonment of development projects. A de facto reduction of market exclusivity will thus likely reduce R&D projects, with adverse impacts on patients and the objective of achieving high levels of innovation. Following the introduction of the SPC manufacturing waiver in 2019, a further reduction of universal market exclusivity rights and government interference in corporate research programmes could have a deterrent effect on companies willing to invest in a broad spectrum of biopharmaceutical R&D in EU Member States, especially in therapeutic areas that fall out of the scope of designated medicines for children and rare diseases. An erosion of universal exclusivities would thus likely contradict the European Commission's overarching objective to achieve leadership in global pharmaceutical innovation.

2.3. IPR reforms to improve affordable access to medicines in the EU

In its initial impact assessment from November 2020, the European Commission argues that the availability and patients' accessibility of orphan medicines and paediatrics vary considerably across EU Member States. It is argued that in some Member States, "market entry is delayed or not happening at all". As there is currently "no legal nexus between research and development incentives for medicines for rare diseases and paediatrics" on the one hand, and "incentives for placing them on the market in most or all Member States" on the other, the Commission is now aiming to condition market exclusivity rights in the EU on a company's legally binding commitment to make available new medicines equally across the EU.

Are market access conditions merited to improve access to medicines in the EU, and to what extent could such conditions contribute to long-term autonomy of Europe's pharmaceutical industry?

The literature on market access restrictions for pharmaceuticals in the EU identifies several challenges that have been left unaddressed in the Commission's inception impact assessment. As outlined by Musazzi et al. (2020), "[i]n Europe, the capability of the Regulatory Authorities and other subjects involved in the pharmaceutical distribution chain and the healthcare assistance services in defining suitable problem-solving strategies has been limited by the fragmentation of the regulatory framework" (see also Bochenek et al. 2018, De Weerdt et al. 2015). Different national approaches for national health technology assessments as well as reimbursement and price policies contribute significantly to access problems within the EU. Concerning potential shortages, it was only in 2019 when the European Medicines Agency (EMA) together with the Heads of European Medicines Agencies (HMA) released the first harmonised "shortage of medicines" definition and corresponding guidelines to address shortages and availability problems, which are a national EU competence (EMA-HMA 2019).

An industry analysis by the EFPIA (2020) on the "root causes of unavailability and delay to innovative medicines" in EU Member States points to the length of time it takes for medicines to be made available in individual EU countries. It is shown that the length of time has increased in recent years, rooted in national medicine access systems and procedural differences between EU Member States. The analysis identifies five broad factors underlying uneven access to multiple medicines within the EU: 1) the time prior to market authorisation; 2) national pricing decisions and reimbursement procedures; 3) national differences in value assessment criteria (Health Technology Assessments); 4) differences in Member States' health system readiness, and 5) delays due to national and regional approval procedures and decisions respectively.[12]

One salient example highlighted by EFPIA (2021) is international (or external) reference pricing (IRP), which is known to create significant disincentives to launch medicines in less wealthy countries. A large body of scientific research confirms the negative impact of IRP. It is further stressed by EFPIA that companies (especially SMEs) do not have the capacity to investigate and undertake very time-consuming pricing and reimbursement processes simultaneously across the EU27 as companies must balance the commercial opportunity offered by a country with the investment of required resources when deciding to engage in a

[12] In terms of the time prior to market authorisation, the granting of market authorisation by the European Medicines Agency (EMA) covering all EU Member States takes away the requirement to seek authorisation from individual states. This centralised process is slow when compared to regulatory processes elsewhere, such as in the USA. Secondly, once a medicine has market authorisation, there can still be a delay before the start of the reimbursement process. The length of time taken from application for reimbursement to approval for reimbursement varies significantly across the EU. In some markets, there is immediate access to medicines that are dispensed in hospitals; in other cases there are different channels for different types of medicine. With regard to the third factor, misalignment on evidence is reported as one of the most prominent and complex delaying factors of the value assessment process, and can be found in all assessment criteria including patient population, comparators, trial design, end points and statistical analysis. Even once there is agreement on evidence, there can be a significant debate on whether this justifies the price of the medicine. As with previous factors, approaches to class competition and value of choice vary between Member States. The fourth factor identified by the EFPIA relates to funding, infrastructure and the overall readiness of health systems, which relates to insufficient budgets to implement decisions and the infrastructure for diagnosis. The final, fifth factor relates to delays from national to regional approval in contexts where there are multiple layers of decision-making processes, which ultimately prolong the time before patients can access treatments.

national process. The problem is amplified for orphan and paediatric medicines due to more limited commercial opportunities because of small patient populations. The EFPIA (2020) thus proposes novel policy solutions other than reforms, targeting pharmaceutical patents and market exclusivity rights, including proposals to speed up national regulatory processes, reforms aiming to increase transparency of information, proposals to facilitate a process that allows prices to align with value and the ability to pay, and reforms targeting improvement in efficiency and the quality of value assessments.

Summing up the above, affordable access to medicines is an important policy objective. However, a more complete understanding of the major root causes of unavailability and delays in patient access is fundamental to achieve noticeable improvements in access to medicines across the EU. Bold reforms would be needed to harmonise and/or coordinate Member State regulation on market access conditions, including Health Technology Assessments and national reimbursement practices. Granting market exclusivity awards only on the basis of universal availability in all EU Member States ignores much more profound legal and procedural obstacles to drug market entry and pricing determinants in individual EU Member States. Making conditional certain IPRs to regional sales obligations would not improve affordability of medicines if the major barriers to market access in the Member States would remain in place. Interferences in sales practices may even have a deterrent effect on companies' marketing strategies with the ultimate effect of keeping their products out of the market. Conditional market exclusivity rights would undermine universal incentives for innovation in the EU and may ultimately discourage future innovation and the production of high value-added medicines by EU companies.

3. THE ROLE OF IPRS FOR PRODUCING HIGH VALUE-ADDED MEDICINES

In this Chapter, we begin with a discussion of the "strategic" link (long-term causal relationship) between intellectual property rights and pharmaceutical production. We outline two major links: intellectual property as an incentive for investment in pharmaceutical R&D and IPRs as a prerequisite for sharing technical knowledge and the transfer of production and distribution rights globally, allowing collaboration between EU and non-EU pharmaceutical innovators and producers (and distributors). The Chapter proceeds with an outline of key industry indicators for the EU, including investment and R&D spending, patterns in high value-added production and employment, and investment intensities of EU production. It is concluded by a discussion of how a relative decline in the strength of pharmaceutical IPRs in the EU would, over the medium to long term, impact on innovation and the production of high value-added medicines by European companies.

3.1. IPRs as incentive for innovation and collaboration in the pharmaceutical industry

Establishing empirically the causal (long-term) relationship between intellectual property rights and the location and value-added of pharmaceutical production is not an easy task. The causal relationship between IPRs, the precise location of production capacities for medicines, production values and volumes as well as licensing-based production generally lacks empirical investigation. The lack of research can be attributed to several empirical challenges:

- Information about the volume and location of production of IP-protected medicines, on the one hand, and generics on the other is generally scarce and typically not publicly available. The same applies for licensing arrangements for joint R&D and contract manufacturing, which are usually not disclosed by businesses and whose underlying determinants and contractual details vary from company to company.

- There are no clear-cut boundaries between originators and companies manufacturing generics/biosimilars. For example, the European Commission (2018) assesses that many originators have branches devoted to generics, referring to Novartis/Sandoz, Pfizer and Merck KGaA as the top sellers of unbranded products in the EU. This includes non-EU companies and their subsidiaries of which many maintain production facilities and sales operations in EU Member States and, accordingly, hold numerous patents and additional market exclusivity rights in the EU.

- As regards detailed production statistics, sector concordance tables linking industry classifications of trade and production data with patent data (e.g. the international patent classification system IPC) are only available at a very aggregate level (see, for example, Eurostat 2015 and FDZ 2017). For generic products, information is only available for sales and market penetration on a country-by-country basis, while detailed production data is generally unavailable on a country-by-country basis.

- The degree of vertical integration and the use of contractual manufacturing agreements vary across smaller companies and larger conglomerates. Results Healthcare (2020), for example, reports a strong correlation between the size of a company and its likelihood to outsource certain production activities. In 2017, according to their report, the manufacturing of 20% of newly approved drugs was outsourced by large pharmaceutical companies, while approximately 80% of all manufacturing was contracted out by small pharmaceutical and biotechnology companies.[13]

- Very little data is available that can be used to derive the extent to which a strengthening of pharmaceutical IPRs will lead to increased inflows in foreign direct investment (FDI) focusing on the biopharmaceutical activities.

Despite shortages of empirical data, a vast body of literature exists on the role of intellectual property for stimulating pharmaceutical innovation and facilitating contract research and licence-based production collaborations. Following on from this literature, there are two major links between the strength of IPRs granted and the level of production of high value-added medicines (see, e.g., WIPO 2009):

1. Pharmaceutical IPRs provide the most effective incentive for investments in pharmaceutical R&D and clinical trials, and are thus fundamental for any future production of novel and typically high value-added medicines. Pharmaceutical IPRs allow successful innovators to earn sufficient revenues to reinvest in innovation, which is why strong IPRs are important for a self-sustaining innovation system in the EU.

2. Pharmaceutical IPRs allow innovators and producers, including EU and third-country entities, to enter licence agreements in which rights holders can manage the exchange of know-how and the transfer of technology, as well as production and distribution rights.

[13] It should be noted that pharmaceutical SMEs generally form the greatest number of customers for contract manufacturers but do not necessarily represent the majority share of contractual manufacturers' revenues.

New medical treatments are the backbone of the research-intensive pharmaceutical industry, in which private sector companies and not-for-profit research organisations play an important role. Innovation in the pharmaceutical industry is, however, complex, risky and costly. The development, production and distribution of medicines are subject to heavy government regulation. The process of generating value-added involves many actors: innovators, marketing authorisation bodies, like the European Medicines Agency (EMA), but also doctors, pharmacies and patients. All of these actors contribute to generating value-added through basic research, clinical trials, regulatory approval and, finally, production operations.

To protect their financial investments, pharmaceutical companies critically rely on the market exclusivity granted by IPRs, such as patents, data exclusivity periods and supplementary protection certificates. Effective international protection and the enforcement of IPRs for medicinal products is thus a key concern in EU trade and economic policymaking. In the EU, as in most developed and many developing countries, the term of a patent is generally 20 years from the date on which the application for the patent is filed. In addition, innovators can typically rely on data exclusivity and patent term extensions to be compensated for costly data generation and lengthy marketing approval procedures. Through the granting of IPRs, EU policymakers aim to support investments in innovation in the EU and prevent unauthorised exploitation of innovative creations. Beyond the internal market, EU economic diplomacy, i.e. cooperation through trade and investment agreements and multilateral fora like the World Trade Organisation (WTO), also aims to strengthen IP protection and enforcement in third countries.

The long continuity in the EU's IP policymaking suggests that policymakers generally recognise that innovation in knowledge-intensive industries, including Europe's pharmaceutical sector, is key for creating an internationally competitive economy. This is also confirmed by a joint report from the European Patent Office and the European Union Intellectual Property Office (EUIPO 2019, p. 2) that achieving competitiveness and a high level of employment "depends on several different factors, but an efficient system of intellectual property rights undoubtedly ranks among the most important, given IP's capacity to encourage creativity and innovation throughout the economy". Moreover, the extensive stakeholder consultation conducted for the Pharmaceutical Strategy demonstrates that academia, civil society and industry consider IPRs key incentives for pharmaceutical innovation. Both the Synopsis Report and the Final Report by the European Commission (2020f, 2020g) lay out stakeholders' views relating to the access, availability and affordability of medicines in the context of promoting sustainable innovation and support of EU industry to remain an innovator and world leader. It is outlined that IPRs are considered key for a)

incentivising the future innovation and production of APIs in the EU, b) the effectiveness of alternative incentives for pharmaceutical R&D and innovation in the EU, and c) R&D and innovation in areas of unmet needs.[14]

The innovation impact of pharmaceutical IPRs tends to be higher in economically more developed countries. Generally, the innovation impact of IPRs critically depends on a broad spectrum of socio-economic determinants such as economic freedoms, the quality of education, access to technology and skilled labour, the strength of the rule of law, and the quality of governmental institutions (see, e.g., Neves et al. 2021 and de Beer 2016). The impact of IPRs on the innovation performance and production in developing countries is generally weaker than their impact on innovation and production in more economically developed countries, including many EU Member States. Accordingly, the value-added of pharmaceutical production in countries with a relatively high level of economic development, such as OECD countries and many EU Member States, is generally more dependent on IPRs compared to production in countries with lower levels of economic development. For economically more developed countries, the positive impact of IPRs on investments in research-intensive industries is therefore well documented in the literature.

In developed countries that have a long tradition of encouraging private-sector innovation, including many EU Member States (see EUIPO 2019 for IPR-intensive industries in the EU), internationally competitive IPRs are critically important for maintaining an ecosystem in which research activities, innovation successes and high value-added production can be sustained in the long term. This is particularly true for the pharmaceutical sector, which is characterised by high investment costs, high development risks and increasing international competition.

Research also shows that countries with higher levels of pharmaceutical IP protection and enforcement tend to show a higher level of clinical trial activity by multinational research-driven companies (see, e.g., Pugatch and Chu 2011). This, in turn, indicates that strong IPRs, when embedded in good governmental institutions, can have a positive impact on investment in and technology transfer to less developed countries.[15] However, as found by an analysis of UNCTAD-ICTSD (2003), the economic gains of IPRs on developing

[14] In addition, other actions considered by stakeholders to be the most effective to support innovative research and development of medicines were to foster research collaboration between universities, research centres and industry (50%), making legislative framework more adaptive to new technologies and advances in science (48%) and providing more public funding for research (35%). Across all stakeholder groups there was broad consensus surrounding the urgent need for a simplified, harmonised and competitive legislative and regulatory framework, including predictable IPR protection in the EU, which is regarded as crucial in order to incentivise pharmaceutical R&D to ensure European companies remain internationally competitive in the future. Stakeholders had the opportunity to provide their feedback on the Commission roadmap between 2 June and 7 July 2020. There were 242 responses from stakeholders in 22 Member States and from outside the EU. There were 20 responses from citizens and the rest from organisations. Relevant points from this Synopsis Report are summarised as follows: generally, civil society organisations underlined the importance of improving affordability and accessibility of treatments to address unmet medical need while industry stakeholders focused more on ensuring supply and improving research and production infrastructure in the EU.

[15] Pugatch and Chu (2011, p. 308) argue that "by choosing to improve their level of protection of pharmaceutical IPRs (together with other factors), developing countries may also be exposed to higher levels of biomedical FDI, not least in the field of clinical trials".

countries mainly accrue through increased investments and technological inflows, but are likely to be mainly realised only over the long term.[16]

While IP-based incentives are critically important to incentivise innovation in the pharmaceutical industry, the licensing of IPRs is an important driver of technology transfer, global innovation chains (GIC), risk diversification and value-chain efficiency (see, e.g., Lee and Kim 2019; Thomas and Chugan 2019; Barnett 2017). Consistently enforced IPRs are a precondition for reliable licensing contracts that allow firms to engage in the in- and out-licensing of technology as well as production and distribution rights. As a high-tech industry, the pharmaceutical industry requires multiple combinations of in-depth knowledge from various technical and organisational areas. IPRs constitute the basis of a reliable legal infrastructure that encourages not only innovation but incentivises collaborations between biopharmaceutical companies, which are supplying financial resources and exchanging technical, regulatory, production and organisational knowhow. As outlined by Lee and Kim (2019), IP licensing has become an important precondition for open innovation strategies, allowing firms to increase R&D productivity through several dynamic capabilities to improve their internal and external resource management.

Due to lacking data, it is generally difficult to provide quantitative estimates for the level of EU production that can be attributed to IPRs. Detailed production statistics are neither available for IP-protected medicines, nor for generic drugs. As regards licensing agreements, publicly available data on the volume or value of license-related production is not available either. At the same time, there are numerous direct and indirect determinants underlying licensing agreements for which data is not publicly available, preventing statistical analysis.[17]

While the lack of data does not allow for a bottom-up analysis of the level of EU production that can be attributed to IPRs (neither for their innovation-incentive, nor for their licensing incentive function, high-level production indicators for the EU reveal that the location of production of high value-added medicines very closely correlates with high investment intensities (see discussion below). The data also reveal that the level of high value-added production is highest in EU Member States that have a long track record of providing strong IPR protection and high investments in R&D and intangible assets, mainly Western European market economies.

[16] The authors state that there might be short-term costs for the domestic industry, resulting from a strengthening of IPRs in least-developed countries (in terms of increased difficulties to copy or reverse-engineer foreign technology), as these impacts would accrue immediately.

[17] Direct determinants are attributable to the molecule, e.g. indications, type of molecule, effectiveness, safety dose, presentation, shelf-life, treatment cost, target clinicians, availability, owner, stage of development, patent life, product differentiation, number of competitors offering similar product, or the probability of regulatory and technical success. Indirect determinants include the management, type of organisation, size of organisation, location of the company, quality of scientific publications, scientific advisory board, the current reputation in a certain therapeutic area, stage of the deal, the type of licence sought, valuation approach, or any advances sought (see Thomas and Chugan 2019).

Below, we analyse relevant industry data from different sources to arrive at a ballpark picture of the level and nature of EU pharmaceutical production that can be attributed to pharmaceutical IPRs in the EU. Data is provided for production and trade, R&D, investment and employment in the industry.

3.2. Patterns in high value-added production and investment spending

The EU's legal framework of the past was generally supportive of growth in the sector. According to Eurostat, the pharmaceutical industry was the sector with the highest average annual growth rate (6.8%) of production between 2008 and 2018. Eurostat data also demonstrates that the IPR-intensive pharmaceutical sector is Europe's largest high-tech sector.[18] In 2018, the largest category in production of "high-tech products" was pharmaceuticals with an annual production of EUR 78.3 billion, representing 14% of the total production of the EU's high-tech manufacturing sectors.

3.2.1. Production of high value-added medicines in the EU

The EU's pharmaceutical industry accounts for a high level of high value-added production and a large number of well-paid employees, particularly in Western European countries, which are economically more developed than Member States in Central and Eastern Europe (CEE). Data on innovation performance (see Section 4.1) indicates that many European pharmaceutical companies are still strong innovators, highly involved in international research and production chains, and successful high value-added exporters. Industry data also shows that EU-based pharmaceutical companies are very active in serving domestic and international markets, especially with high value-added products.

In 2018, according to the most recent Eurostat industry data, the pharmaceutical sector in the EU27 comprised of a total of around 4,000 enterprises.[19] The overall industry accounted for EUR 222 billion in production value, which represents 22% of the total value of production in (non-financial) knowledge-intensive activities and about one quarter of output in the EU's prominent motor vehicle sector. EU production statistics indicate that pharmaceutical production[20] in the EU amounted to EUR 183 billion in 2019, exports amounted to EUR 205 billon, imports amounted to EUR 101 billion, leaving the EU27 with an aggregate trade surplus of EUR 104 billion in 2019 (see Figure 1).

[18] Eurostat "Statistics on high-tech industry and knowledge-intensive services" (sometimes referred to as simply "high-tech statistics") comprise economic, employment and science, technology and innovation (STI) data describing manufacturing and services activities, products traded, and patents applied selected on the basis of their technological intensity. Sold production of high-tech products increased from EUR 288 billion in 2008 to EUR 337 billion in 2018. This was equivalent to an average annual increase of 1.6%. See Eurostat (Prodcom database DS-045339).

[19] Excluding companies from Ireland, for which Eurostat does not report data.

[20] Sold pharmaceutical production across all 52 registered pharmaceutical product categories.

EU production is, on aggregate, characterised by a relatively high share of high value-added medicines. At the same time, there are no clear-cut boundaries between originators and companies manufacturing generics/biosimilars. Data from Medicines for Europe (2016), an association representing European generics manufacturers, indicate that only a small fraction of the total number of pharmaceutical companies in the EU is engaged in the development, manufacturing and distribution of generics, whereby considerably higher shares are reported for the number of employees in the generics industry in the EU. Medicines for Europe states that some "350 manufacturing and research & development sites across Europe produce your essential medicines, employ over 160,000 employees and invest up to 17% of their turnover into R&D activities". More recent information by Medicines for Europe (2021) indicates that "over 400 manufacturing and research & development sites across Europe produce essential medicines, employ over 190,000 employees and invest up to 17% of their turnover into R&D activities". The 2016 numbers stated by Medicines for Europe (350 generics companies) are confirmed by a report from the European Commission (2018), which further states that the EU's pharmaceuticals manufacturing sector is generally composed of a relatively small number of large and capital-intensive enterprises, while SMEs are also active in manufacturing, in particular in generics production.[21] It is also reported by the European Commission that the largest share of EU manufacturing is controlled by patent-holding companies. However, the Commission does not report shares for the production of original and innovative drugs and generic medicines respectively.

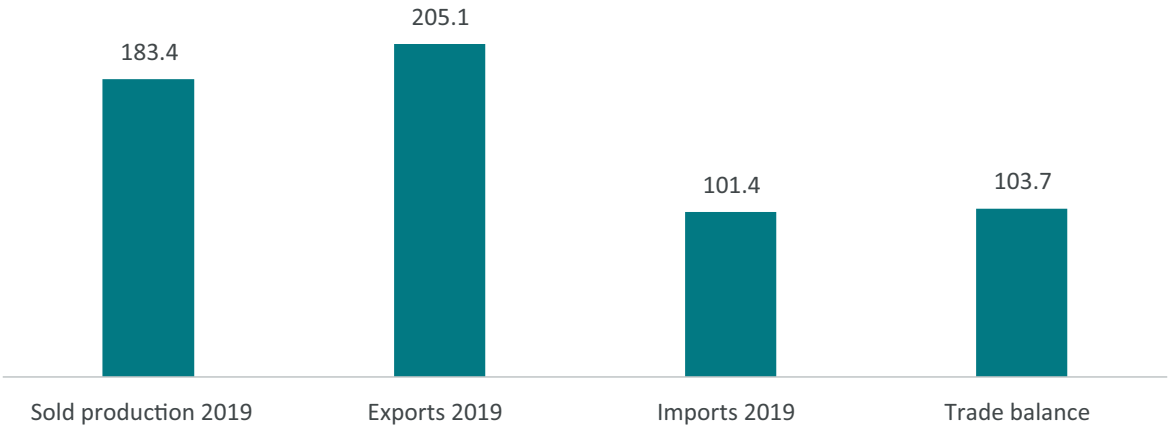
The numbers provided by Medicines for Europe should be interpreted with care. Many companies including contract manufacturers engage in the production of both original and generic medicines. At the same time, numbers do not allow conclusions to be drawn about differences in enterprise size, production volumes, the commercial value of produced or sold production, and the level and distribution of the number of employees across generics companies. At the same time, the numbers indicate that generics manufacturing currently accounts for only small shares of total pharmaceutical manufacturing in the EU. The numbers provided by Medicines for Europe indicate that generics manufacturing companies account for only about 10% of all pharmaceutical companies in the EU, while employment in generic medicine production is found to account for roughly one third of the total number of employees directly employed in the EU pharmaceutical industry. A verification of the discrepancy in these data would require additional information.

In this context, it should be noted that a 2014 study from Vicente and Simoes (2014, p. 39), which estimated the employment effects of an SPC production waiver in the EU, solely relied

[21] It is reported that 60% of European production is generated by global firms that are active in several EU Member States. Manufacturing includes innovative drugs, biological/biosimilars, as well as high-end APIs and value-added generic medicines.

on "anecdotal data collected from players in the pharmaceutical industry". These data were used to estimate the changes in the number of employees resulting from a manufacturing provision and the export provision (the EU's SPC waiver).[22]

FIGURE 1: EU PRODUCTION, EXPORTS AND IMPORTS OF PHARMACEUTICAL PRODUCTS IN 2019, IN BILLION EUR



Source: EU's Prodcom database. Sold production is the value of production sold during the survey period (2019). The trade balance reflects an EU trade surplus vis-à-vis the rest of the world. Trade and production data comes from two distinct surveys: the data on sold production comes from Eurostat Prodcom and the data on trade from Eurostat's Comext. The production data is collected from producing enterprises and the survey is mandatory for enterprises with 20 employees or more. International trade data, on the other hand, is recorded in the EU Member States where the goods are placed under the customs procedures. Each time a product crosses a border it is registered as a "trade", and if the same product crosses borders several times, it is recorded as several trades. These specificities should be considered when comparing the production and external trade data.[23]

3.2.2. Investment-intensity of the pharmaceutical industry in the EU

The EU's pharmaceutical industry is an investment-intensive industry, which is reflected by high levels of investments in tangibles and high levels of R&D spending.[24] For example, in 2018, investment in tangible goods amounted to almost EUR 10 billion, which corresponds to about one quarter of the EU's motor vehicle industry (39.8 billion EUR). At the same time, corporate investment in intangibles per employed person is higher in the pharmaceutical

[22] It was assumed that that a "typical medium-sized European pharmaceutical manufacturer employs, on average, 249 workers and holds a manufacturing capacity of 1,000,000,000 [oral solid dosage] units/year". It was concluded that "over the next 9 years, the European ratification of the manufacturing provision and of the export provision could potentially […] generate up to 8,890 new direct jobs" in the EU, which according to Eurostat data amounts to about 1.5% of total employment in the EU's pharmaceutical industry in 2018.

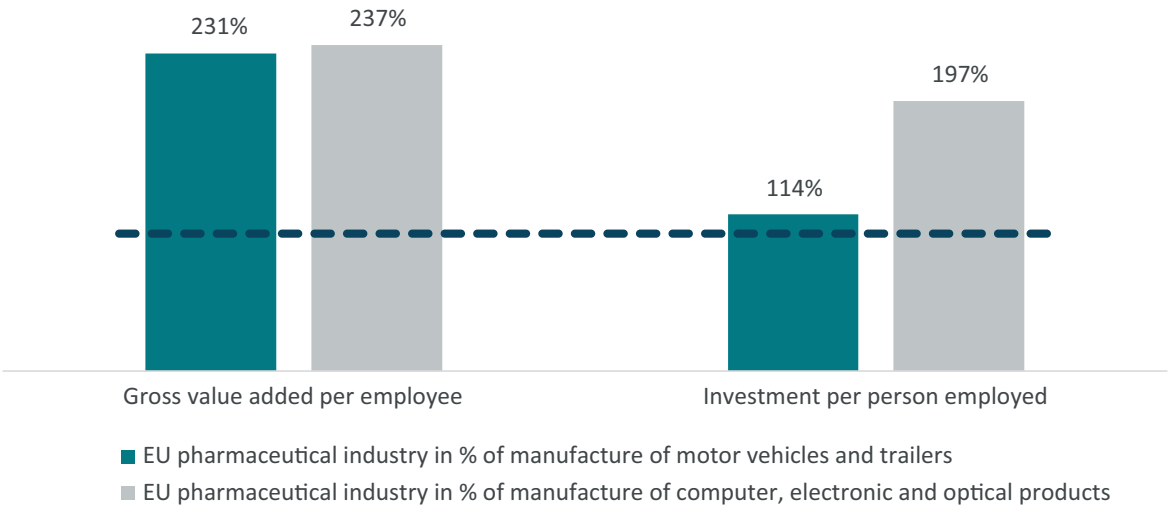
[23] Extra-EU imports and exports are reported by the Member State where the customs declaration is lodged, usually the place where the goods cross the EU external frontier (here referred to as the exit/entry Member State). This is not necessarily the Member State of actual import or export. The geographical allocation of an extra-EU flow is biased in the case where the entry/exit Member State is not the actual importing/exporting Member State. In such a case, the extra-EU trade will be allocated to the entry/exit Member State and the actual importing/exporting Member State will report only intra-EU flows with the exit/entry Member State. This issue particularly impacts the extra-EU imports of Member States having important ports for transhipment of goods like Antwerp in Belgium and Rotterdam in the Netherlands. This is why it is known as the "Rotterdam effect". See Eurostat (2021).

[24] Investment in tangible goods is defined as investment during the reference period in all tangible goods. Included are new and existing tangible capital goods, whether bought from third parties or produced for own use (i.e. capitalised production of tangible capital goods), having a useful life of more than 1 year including non-produced tangible goods such as land. Investments in intangible and financial assets are excluded.

industry, amounting to about EUR 13,300 compared to EUR 12,900 in the motor vehicles sector and EUR 8,000 in the computer, electronic and optical products manufacturing sector (Figure 2).[25]

Industry data for individual Member States with high research, manufacturing and export capacities (e.g. Germany, Denmark and Sweden) demonstrate that investment per employed person in the pharmaceutical industry, while fluctuating over time, is significantly higher in these countries compared to the EU27 average (see Figure 2 and Figure 3).[26] An outline of the development of key industry indicators for individual EU Member States for 2010 and 2018 (the most recent year for which data is available) is provided by Figure 15 to Figure 19 in Appendix II.

FIGURE 2: GROSS VALUE-ADDED AND INVESTMENT PER PERSON EMPLOYED IN THE EU'S PHARMACEUTICAL INDUSTRY COMPARED TO THE EU MANUFACTURE OF MOTOR VEHICLES AND THE MANUFACTURE OF COMPUTER, ELECTRONIC AND OPTICAL PRODUCTS, EU27 (WEIGHTED) AVERAGE, IN 2018

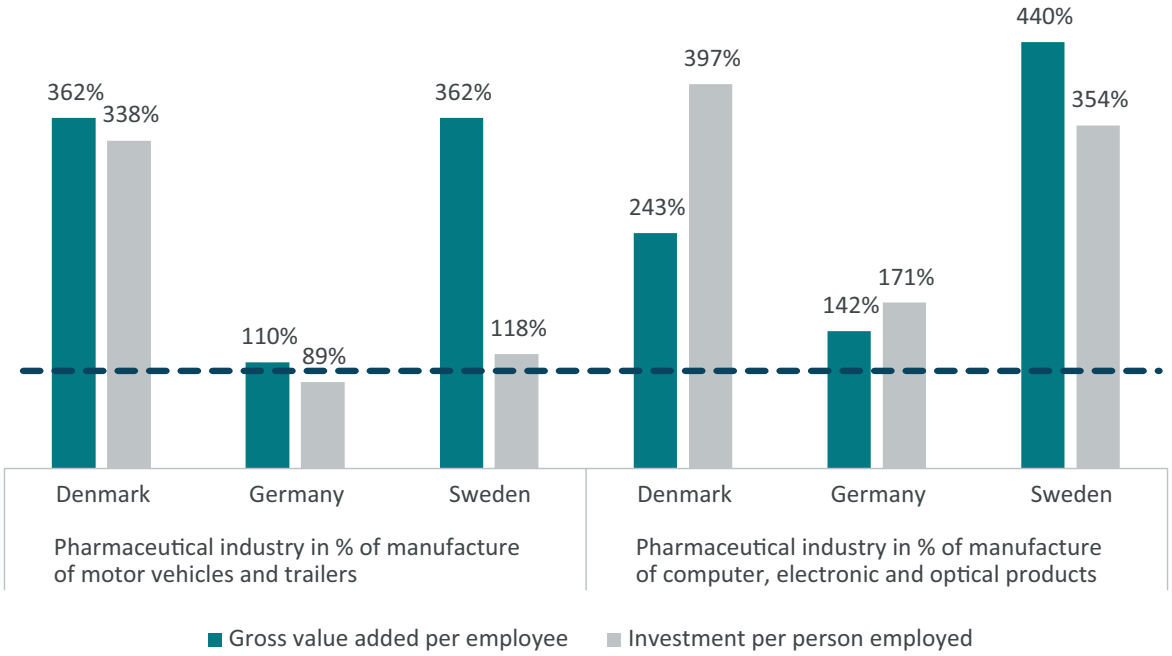


Source: Own calculations based on Eurostat SBS data.

[25] Numbers are based on the weighted average using the number of enterprises by country as weights. Due to lacking data for investment per person in the pharmaceutical sector, France, which is a major manufacturing country in the EU, has been excluded from the calculations.

[26] Due to Germany's strong footprint in the automotive industry, investment per person employed is slightly higher in the motor vehicle sector, amounting to EUR 18,600 compared to EUR 16,600 in the pharmaceutical sector.

FIGURE 3: ANNUAL INVESTMENT PER EMPLOYED PERSON IN THE EU'S PHARMACEUTICAL INDUSTRY COMPARED TO EU MANUFACTURE OF MOTOR VEHICLES AND MANUFACTURE OF COMPUTER, ELECTRONIC AND OPTICAL PRODUCTS, EU27 AVERAGE, GERMANY, DENMARK AND SWEDEN, IN 2018

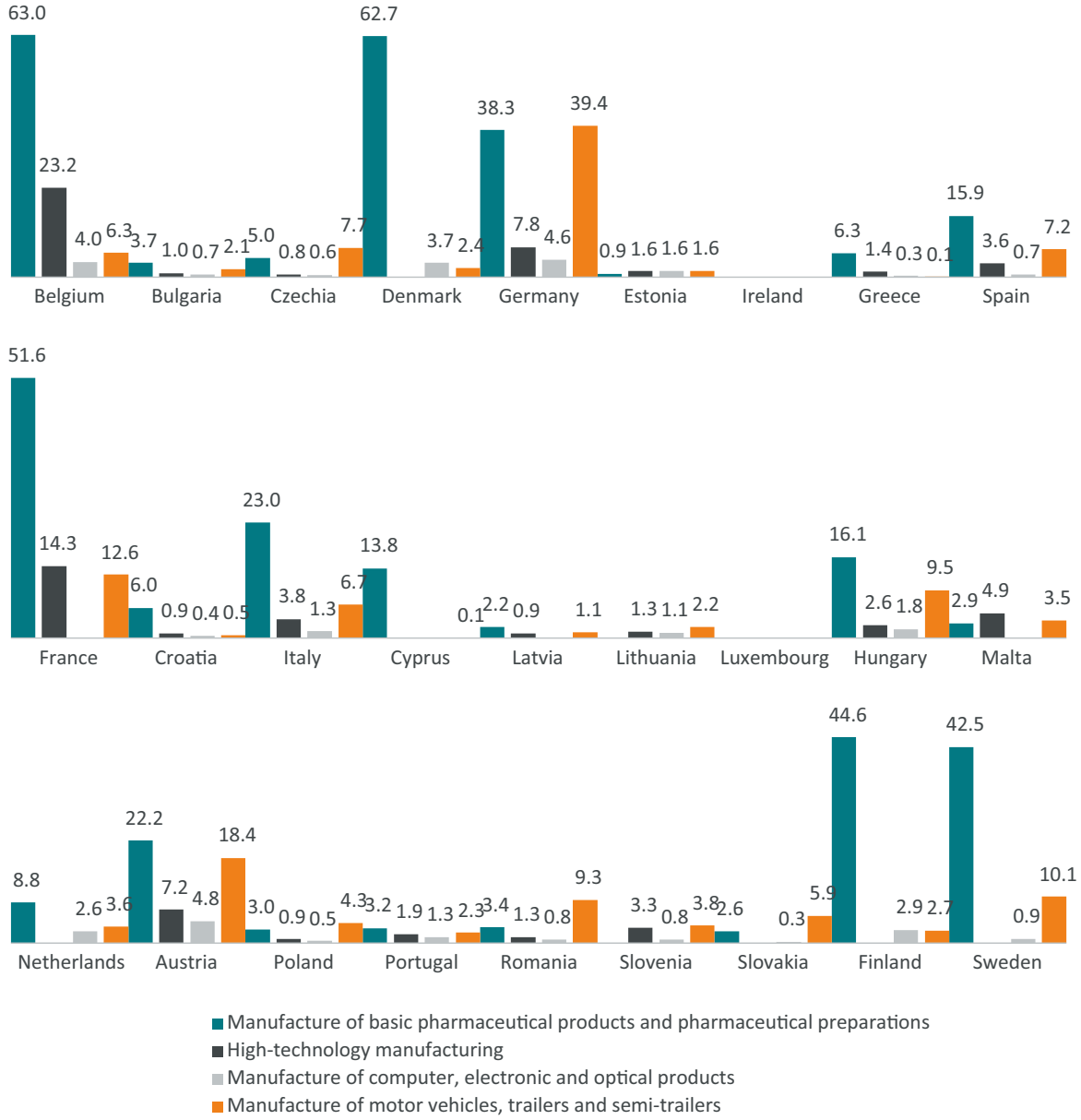


Source: Own calculations based on Eurostat SBS data.

3.2.3. Patterns in value-added and the compensation of labour in the pharmaceutical industry in the EU

The EU's pharmaceutical sector is particularly outstanding when measured against the value-added generated throughout the pharmaceutical value chain, i.e. basic research, drug development, production and distribution activities. Pharmaceutical companies in the EU show a considerably higher value-added (per enterprise and per person employed) compared to the value-added generated in other technology-driven manufacturing sectors in the EU, with a higher average value-added compared to, for example, companies manufacturing computer, electronic and optical products and companies manufacturing motor vehicles. This pattern is particularly pronounced in Member States with high pharmaceutical research and production capacities, e.g. Belgium, Denmark, Germany, France, Italy, Austria and Sweden (see Figure 4 as well as Figure 2 and Figure 3).

FIGURE 4: AVERAGE ANNUAL VALUE-ADDED BY ENTERPRISE IN 2018, PHARMACEUTICAL INDUSTRY VS. TOTAL HIGH-TECHNOLOGY MANUFACTURING; MANUFACTURE OF COMPUTER, ELECTRONIC AND OPTICAL PRODUCTS; AND MANUFACTURE OF MOTOR VEHICLES, IN MILLION EUR



Source: Own calculations based on Eurostat SBS data. Note: Value-added at factor cost is the gross income from operating activities after adjusting for operating subsidies and indirect taxes. It can be calculated as the total sum of items to be added (+) or subtracted (-): turnover (+); capitalised production (+); other operating income (+); increases (+) or decreases (-) of stocks; purchases of goods and services (-); other taxes on products which are linked to turnover but not deductible (-); duties and taxes linked to production (-).

In most EU Member States, the gross value-added per employee in the pharmaceutical sector is significantly higher than in the motor vehicle manufacturing industry and the sector manufacturing computer, electronic and optical products, amounting to EUR 130,000 in Germany, EUR 307,000 in Denmark and EUR 375,000 in Sweden. Driven by the high

value-added generated in the pharmaceutical industry, average wages and salaries per full-time equivalent (FTE) in the EU27 are significantly higher, amounting to an estimated EUR 72,000 per FTE in the pharmaceutical industry (445,000 FTEs in 2018) compared to EUR 44,000 in the motor vehicle sector (2.43 million FTEs in 2018) and EUR 46,000 in the computer, electronic and optical products manufacturing sector (933,000 FTEs in 2018).

3.2.4. Differences in EU Member States' pharmaceutical industry performance

As summarised by Table 1, EU Member States show a high degree of heterogeneity in key industry indicators. CEE countries show, on average, considerably lower values for key industry indicators compared to the EU27 average, including overall turnover per person employed, gross value added per worker, the overall production value per worker, investment in intangibles and overall R&D spending per worker. By contrast, as outlined in detail in Table 3 below, these indicators are significantly higher in most Western European countries, in which many companies and R&D clusters (including public research institutes) are characterised by a firm track record of pharmaceutical R&D and high value-added pharmaceutical production.

TABLE 1: STATISTICAL INDICATORS OF KEY INDUSTRY DATA OF EU27 PHARMACEUTICAL INDUSTRY

	Turnover per person employed in 1,000 EUR (2018)	Apparent labour productivity (gross value-added per person employed) in EUR 1,000 (2018)	Gross value-added per employee in EUR 1,000 (2018)	Investment in intangibles per person employed in EUR 1,000 (2018)	Production value per enterprise in million EUR (2018)	Production value per employee in million EUR (2018)	R&D spending per person employed in EUR 1,000 (2017)
Min.	85.5	21.3	21.5	3.8	2.8	0.1	4.2
1st quartile*	143.7	43.4	44.3	10.5	8.0	0.1	9.6
Average	298.7	118.1	119.9	15.0	49.1	0.3	34.6
2nd quartile (median)*	183.1	66.3	66.4	14.2	26.0	0.2	23.2
3rd quartile*	457.3	137.2	137.6	19.1	69.0	0.4	48.4
Max.	931.1	370.4	374.8	27.4	182.2	1.1	124.1
Average CEE countries	148.1	44.7	45.1	11.0	15	0.1	7.9
Average EU27	500.0	186.0	187.0	17.7	73.1	0.5	38.0

Source: Eurostat SBS statistics (2018), EFPIA (2019). Note: The group of CEE countries follows CA Market Monitor (2020) and includes: Bulgaria, Czechia, Hungary, Poland, Romania and Slovenia.
* indicates that statistical parameters are used for scenario analysis.

Numbers for the production value per employee reveal that CEE countries are positioned at the lower end of the EU27 scale, reflecting a relatively low value-added, generics- (or API-) driven output of pharmaceutical products in these countries. Likewise, for investments in intangibles and R&D spending per employee, CEE countries are also positioned at the lower end of the EU27 scale, reflecting, overall, a relatively low R&D-intensity of pharmaceutical production in these countries.

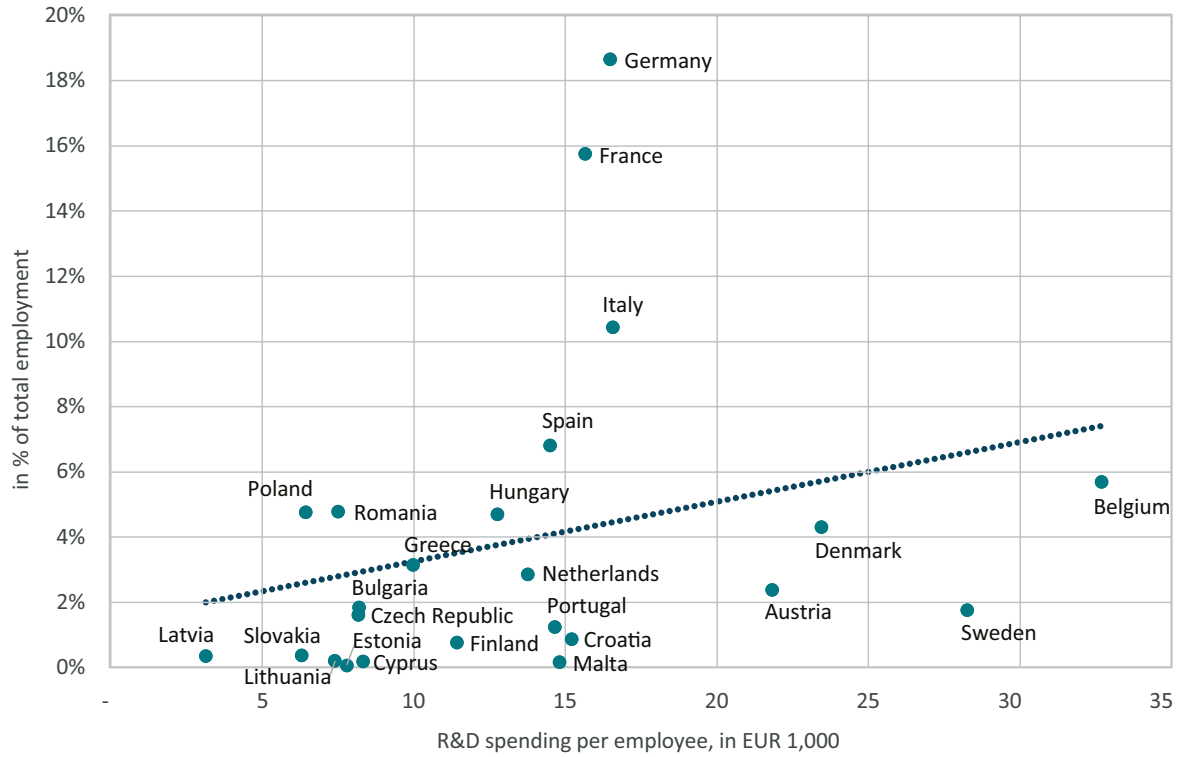
3.2.5. Correlations between investment-intensity, production, employment and the compensation of labour in EU Member States

As outlined by Figure 5, as well as Table 2 and Table 3 below, there is a relatively strong positive correlation between the level of R&D spending per employee and the share of a country's total number of employees in the pharmaceutical industry in the EU's total pharmaceutical labour force. Positive correlations are also found for the empirical relationship between R&D spending per employee and the production value of pharmaceuticals, and for investment spending per employee and the level of employment and industry output respectively. These correlations indicate that the geographical location of the production of high value-added medicines is closely linked to the geographical location in which R&D activities take place (took place) and investments in tangibles are (were) made.

Taking into account the historically high international competitiveness of pharmaceutical companies from Western Europe, strong pharmaceutical IPRs are generally more important for EU Member States whose pharmaceutical sectors are characterised by a relatively long track record of high innovation activity, as well as investment-intensive and high value-added production, compared to Member States whose pharmaceutical industry is characterised by low investment intensities and low value-added production, respectively.

As will be shown below, a relative erosion of pharmaceutical IPRs vis-à-vis third countries could in the medium to long term cause a decline in the level of investments made in the EU, with adverse effects on the output of medicines manufactured in EU Member States. An erosion of pharmaceutical IPRs could even accelerate the EU's relative decline in innovation competitiveness compared to other countries, especially the USA and rising emerging market economies.

FIGURE 5: CORRELATION BETWEEN R&D SPENDING PER EMPLOYEE AND THE PERCENTAGE SHARE OF EMPLOYMENT IN THE PHARMACEUTICAL INDUSTRY IN TOTAL EU PHARMACEUTICAL EMPLOYMENT, 2017



Source: 2017 R&D data were taken from EFPIA (2019). 2017 employment data were taken from EFPIA (2019). Ireland has been excluded from the sample because of an outlier of EUR 162,700 in R&D spending in 2017. Note: Due to missing data for R&D spending, correlations are only presented for the year 2017. The observation of longer-term averages would offer a more robust picture.

TABLE 2: TOTAL PHARMACEUTICAL R&D AND EMPLOYMENT IN THE EU27

	R&D spending in million EUR in 2017	In % of total EU R&D spending	Employment (EFPIA 2017 estimates)	In % of total EU employment in pharma-ceutical industry	Employment (Eurostat 2018 estimates)	In % of total employment
Austria	294	1.3%	14,860	2.4%	16,550	2.8%
Belgium	3,508	15.3%	35,711	5.7%	28,278	4.7%
Bulgaria			11,500	1.8%	8,814	1.5%
Croatia	40	0.2%	5,474	0.9%	4,859	0.8%
Cyprus	85	0.4%	1,140	0.2%	1,755	0.3%
Czechia	77	0.3%	10,083	1.6%	10,494	1.8%
Denmark	1,632	7.1%	26,963	4.3%	25,306	4.2%
Estonia			380	0.1%	346	0.1%
Finland	201	0.9%	4,722	0.8%	4,684	0.8%
France	4,451	19.5%	98,786	15.8%	96,985	16.3%
Germany	6,918	30.2%	117,013	18.7%	157,424	26.4%
Greece	42	0.2%	19,700	3.1%	10,095	1.7%
Hungary	176	0.8%	29,400	4.7%	19,479	3.3%
Ireland	305	1.3%	29,766	4.7%	16,125	2.7%
Italy	1,530	6.7%	65,400	10.4%	65,852	11.0%
Latvia			2,154	0.3%	2,225	0.4%
Lithuania			1,220	0.2%	659	0.1%
Luxembourg						
Malta			1,057	0.2%	1,033	0.2%
Netherlands	642	2.8%	17,900	2.9%	13,124	2.2%
Poland	340	1.5%	29,873	4.8%	25,090	4.2%
Portugal	100	0.4%	7,700	1.2%	7,856	1.3%
Romania	101	0.4%	30,000	4.8%	10,507	1.8%
Slovakia			2,287	0.4%	2,185	0.4%
Slovenia	180	0.8%	9,964	1.6%	6,514	1.1%
Spain	1,147	5.0%	42,687	6.8%	47,341	7.9%
Sweden	1,104	4.8%	11,012	1.8%	12,799	2.1%
Total EU27 ex Luxembourg	22,873	100%	626,752	100%	596,379	100%

Source: 2017 R&D data were taken from EFPIA (2019). 2017 employment data for 2017 were taken from EFPIA (2019). 2018 employment data were retrieved from Eurostat's SBS database. Eurostat employment data for Ireland are from 2014, Eurostat employment data for France are from 2017, Eurostat employment data for Lithuania are from 2015, and Eurostat employment data for Slovenia are from 2011.

TABLE 3: STATISTICAL INDICATORS OF INDUSTRY CHARACTERISTICS OF EU27 PHARMACEUTICAL INDUSTRY, BY COUNTRY

	Number of employees	Turnover per person employed in EUR 1,000 (2018)	Apparent labour productivity (Gross value added per person employed) in EUR 1,000 (2018)	Gross value added per employee in EUR 1,000 (2018)	Investment in intangibles per person employed in EUR 1,000 (2018)	Production value per enterprise in million EUR (2018)	Production value per employee in million EUR (2018)	R&D spending per person employed in EUR 1,000 (2017)	Average personnel costs in EUR (2018)
EU27	602,315	500.0	186.0	187.0	17.7	73.3	0.5	38.0	73,015
Belgium	28,278	931.1	370.4	372.0	27.4	182.2	1.1	124.1	109,190
Bulgaria	8,814	n/a	21.3	21.5	n/a	n/a	n/a	n/a	9,961
Czechia	10,494	158.5	42.8	43.9	11.4	16.0	0.1	7.3	24,252
Denmark	25,306	593.2	307.0	307.1	23.0	124.8	0.6	64.5	105,939
Germany	157,424	483.5	129.5	129.8	16.6	112.2	0.4	43.9	89,096
Estonia	346	105.4	31.7	32.0	13.1	2.8	0.1		26,300
Ireland	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Greece	10,095	233.2	61.8	61.9	9.3	18.5	0.2	4.2	37,959
Spain	47,341	308.6	110.5	110.8	16.4	43.1	0.3	24.2	57,054
France	n/a	n/a	n/a	n/a	n/a	174.6	n/a	n/a	n/a
Croatia	4,859	148.2	57.8	59.3	9.5	15.3	0.2	8.2	27,762
Italy	65,852	426.3	139.8	140.2	16.3	66.0	0.4	23.2	72,602
Cyprus	1,755	143.7	70.8	70.8	18.5	28.1	0.1	48.4	30,142
Latvia	2,225	101.1	36.2	36.4	3.8	5.5	0.1		22,112
Lithuania	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Luxembourg	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Hungary	19,479	183.1	72.4	72.5	13.5	29.6	0.1	9.0	30,099
Malta	1,033	152.4	56.6	56.6	14.8	8.0	0.2		33,785
Netherlands	13,124	457.3	153.2	153.3	n/a	23.9	0.4	48.9	73,163
Austria	16,550	330.0	128.2	128.7	21.0	46.7	0.3	17.8	79,776
Poland	25,090	139.9	45.0	45.4	8.3	7.6	0.1	13.6	22,797
Portugal	7,856	168.4	61.3	61.9	23.1	8.3	0.2	12.7	32,662
Romania	10,507	110.7	41.9	42.0	10.8	6.9	0.1	9.6	16,017
Slovenia	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Slovakia	2,185	85.5	32.1	32.1	5.3	6.5	0.1	n/a	21,006
Finland	4,684	489.8	285.1	285.4	13.0	70.0	0.4	42.9	60,802
Sweden	12,799	523.7	342.0	374.8	24.1	83.1	0.7	86.3	83,561
Min.	346.0	85.5	21.3	21.5	3.8	2.8	0.1	4.2	9,961
1st quartile	4,728	143.7	43.4	44.3	10.5	8.0	0.1	9.6	24,764
Average	21,641	298.7	118.1	119.9	15.0	49.1	0.3	34.6	48,457
2nd quartile (median)	10,501	183.1	66.3	66.4	14.2	26.0	0.2	23.2	33,224
3rd quartile	23,687	457.3	137.2	137.6	19.1	69.0	0.4	48.4	73,023
Max.	157,424	931.1	370.4	374.8	27.4	182.2	1.1	124.1	109,191

Source: Own calculations based on Eurostat SBS statistics (2018) and EFPIA (2019).

4. STRATEGIC AUTONOMY IN AN ENVIRONMENT OF INCREASING INTERNATIONAL COMPETITION IN THE INNOVATIVE PHARMACEUTICAL INDUSTRY

Below, we outline patterns in international pharmaceutical R&D and general trends in the development costs of new medicines. The data generally show that many European companies are still strong innovators, highly involved in international research and production chains, and successful high value-added exporters. At the same time, the data demonstrate that Europe's overall innovation performance is substantially lacking behind the USA. Moreover, the rapid rise of research-intensive and knowledge-accumulating companies from non-European jurisdictions, especially large emerging market economies like China and India, will likely erode EU companies' relatively strong position in pharmaceutical innovation and global market penetration of innovative IP-protected medicines originating in the EU. Considering the relevance of IPRs for investments and high value-added production in the pharmaceutical industry, it will be outlined that strong IPRs granted in the EU could moderate the relative decline in competitiveness by way of protecting the EU's international attractiveness as a location for investments in R&D and its position as a production hub for high value-added medicines.

4.1. Patterns and trends in global pharmaceutical innovation

International patent data show that EU companies are exposed to increasing competition for innovation globally. Innovators from the EU27 still account for a relatively high number of patent filings across all industries globally, reflecting the relatively high state of economic development in EU Member States. The data show, however, that growth in the EU's overall innovative capacity, when measured by the total number of patent filings, is lacking behind the growth recorded for major emerging market economies.[27]

The relative decline of Europe's innovative capacities is also noticeable for pharmaceuticals. As outlined in Table 4, pharmaceutical companies and other (non-commercial) innovators from the EU27 ranked second in the total number of granted patents counted globally, accounting for approx. 8,000 patent grants in 2019, only topped by innovators from the USA (12,000 patent grants; +47% compared to the EU27), and followed by innovators from China (7,000 patent grants; -12% compared to the EU27). The numbers also reveal that average annual growth rates constantly declined for EU-originating patents over the past

[27] Between 2000 and 2019, filings made by applicants from the EU within the EU increased from approx. 138,000 to 155,000 (+13%). By contrast, the number of filings made by US applicants at their home office increased to 285,000 (+73%), filings made by Indian applicants at their home office increased to 19,000 (+782), and filings made by Chinese applicants at their home office increased to 1.24 million (+4,806%; see Figure 21 and Figure 22 in Appendix VI). Patent data also reveals that innovators from EU Member States are still highly active in filing patents abroad, i.e. in countries other than their country of origin. The number of EU patent filings abroad increased from approx. 142,000 in 2000 to 275,188 in 2019 (+93%). Over the same period, filings abroad made by applicants from the USA increased to 236,000 (+104%), filings from India to 14,600 (+2,057%), and filings from China to about 84,000 (+7,569%; see Figure 23 and Figure 24 in Appendix VI).

20 years. The annual growth rates were particularly low for the past 10 years, amounting to 0.3% for the period 2010-2015 and 0.5% for the period 2016-2019, respectively. By contrast, the number of patent grants increased at significantly higher rates for the USA and, particularly, China. The pattern is similar for patent grants in biotechnology sectors (incl. green and blue biotechnology), although less pronounced, with China already being the largest innovating jurisdiction when measured by patent grants in the sector (see Table 15 in Appendix VI).

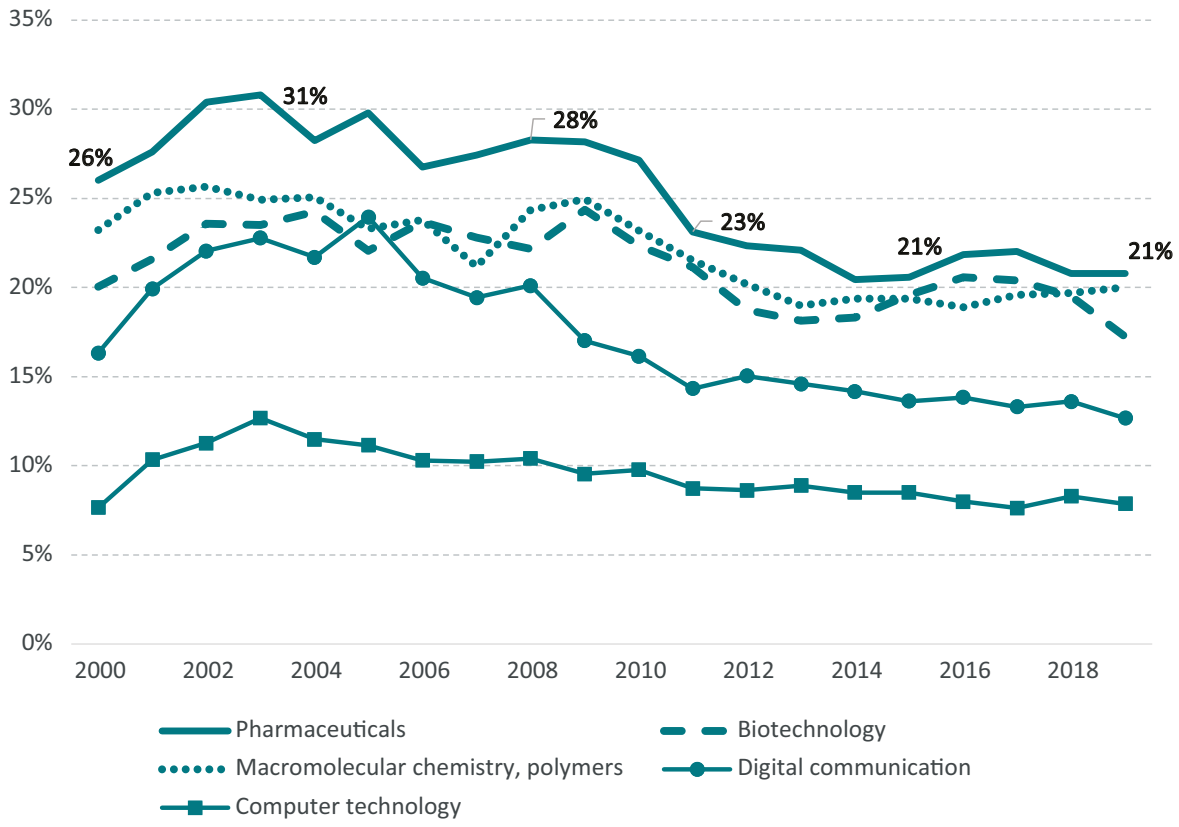
TABLE 4: PATENT GRANTS IN PHARMACEUTICAL SECTORS, ABSOLUTES AND ANNUAL GROWTH RATES, 2000-2019, TOP 20 INNOVATING COUNTRIES IN 2019

		2000	2005	2010	2015	2019	CAGR 2000-2005	CAGR 2005-2010	CAGR 2005-2010	CAGR 2010-2015	CAGR 2015-2019
1	USA	5,304	6,338	7,647	10,495	12,017	3.6%	3.6%	3.8%	6.5%	3.4%
2	China	1,221	2,165	4,762	8,800	7,165	12.1%	12.1%	17.1%	13.1%	-5.0%
3	Japan	1,483	1,540	2,631	3,132	2,538	0.8%	0.8%	11.3%	3.5%	-5.1%
4	Republic of Korea	193	1,003	716	1,789	2,324	39.0%	39.0%	-6.5%	20.1%	6.8%
5	Germany	1,205	1,970	2,290	2,298	2,187	10.3%	10.3%	3.1%	0.1%	-1.2%
6	Switzerland	386	900	1,551	1,625	1,739	18.4%	18.4%	11.5%	0.9%	1.7%
7	France	902	1,324	1,543	1,597	1,435	8.0%	8.0%	3.1%	0.7%	-2.6%
8	United Kingdom	751	935	1,093	1,132	1,386	4.5%	4.5%	3.2%	0.7%	5.2%
9	Russian Federation	747	797	958	1,334	1,185	1.3%	1.3%	3.7%	6.8%	-2.9%
10	Italy	392	458	690	713	672	3.2%	3.2%	8.5%	0.7%	-1.5%
11	Belgium	254	405	564	627	627	9.8%	9.8%	6.8%	2.1%	0.0%
12	Nether-lands	166	359	422	418	621	16.7%	16.7%	3.3%	-0.2%	10.4%
13	Sweden	258	604	542	390	517	18.5%	18.5%	-2.1%	-6.4%	7.3%
14	Canada	254	329	417	494	493	5.3%	5.3%	4.9%	3.4%	-0.1%
15	Spain	93	213	388	439	425	18.0%	18.0%	12.7%	2.5%	-0.8%
16	Denmark	136	298	351	375	424	17.0%	17.0%	3.3%	1.3%	3.1%
17	India	29	176	265	340	408	43.4%	43.4%	8.5%	5.1%	4.7%
18	Australia	96	124	201	336	342	5.3%	5.3%	10.1%	10.8%	0.4%
19	Israel	81	159	216	330	317	14.4%	14.4%	6.3%	8.8%	-1.0%
20	Ireland	65	104	203	260	297	9.9%	9.9%	14.3%	5.1%	3.4%
21	EU27	3,828	6,395	7,883	7,994	8,152	10.8%	10.8%	4.3%	0.3%	0.5%
22	Top 20	14,016	20,201	27,450	36,924	37,119	7.6%	7.6%	6.3%	6.1%	0.1%
23	Total	14,720	21,464	29,020	38,824	39,236	7.8%	7.8%	6.2%	6.0%	0.3%

Source: World Intellectual Property Organisation (WIPO). Indicators: Total count by applicant's origin (equivalent count). WIPO statistics database. Last updated: January 2021.

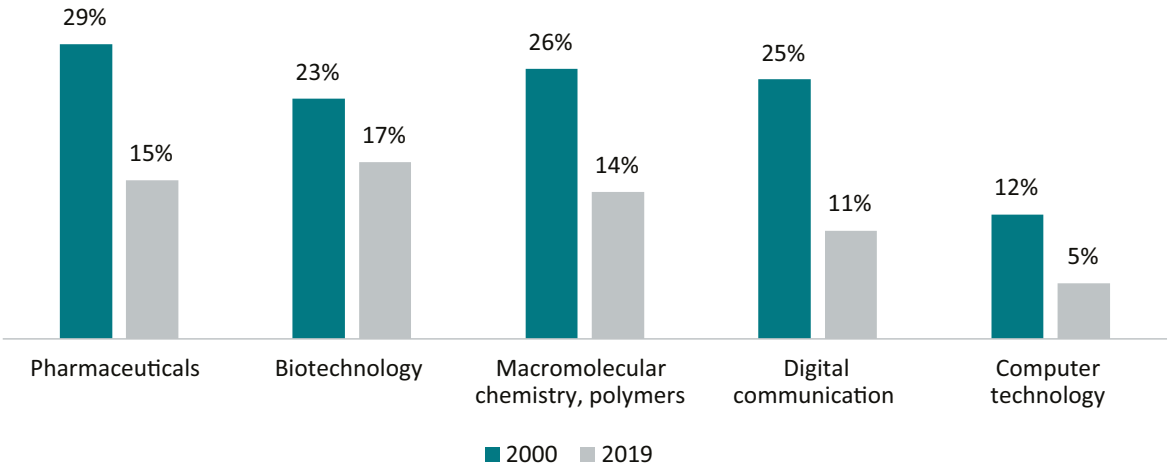
Figure 6, which outlines the development of the relative share of granted patents for the pharmaceutical industry and, for the sake of comparison, four additional technology sectors, demonstrates that the share of patent applications originating from EU innovators in total patent applications steadily decreased over the past 20 years. In 2000, patent applications in the pharmaceutical industry originating in EU27 Member States accounted for 26% of all patent applications in the sector. After reaching a peak of 31% in 2003, the share of granted applications originating from the EU gradually declined to 21% in 2019. At the same time, the data demonstrates that EU innovators still hold a relatively strong international position compared to other high technology sectors such as macromolecular chemistry and polymers (20% in 2019), biotechnology (17%), digital communication technologies (13%) and computer technologies (8%). These patterns and developments are generally confirmed by the number of actual patent publications (see Figure 7).

FIGURE 6: PATENT GRANTS BY TECHNOLOGY, SHARE OF GRANTED APPLICATIONS ORIGINATING IN THE EU27 AS A PERCENTAGE OF TOTAL APPLICATIONS GLOBALLY, 2000-2019



Source: WIPO. Indicators: total count by applicant's origin (equivalent count). WIPO statistics database. Last updated: January 2021. Note: Grants are exclusive IP rights conferred to an applicant by an IP office. For example, patents are granted to applicants (assignees) to make use of and exploit an invention for a limited period of time. The holder of the rights can prevent unauthorised use of the invention.

FIGURE 7: PATENT PUBLICATIONS BY TECHNOLOGY, SHARE PUBLICATIONS ORIGINATING FROM THE EU27 AS A PERCENTAGE OF TOTAL PUBLICATIONS, 2000 VS. 2019



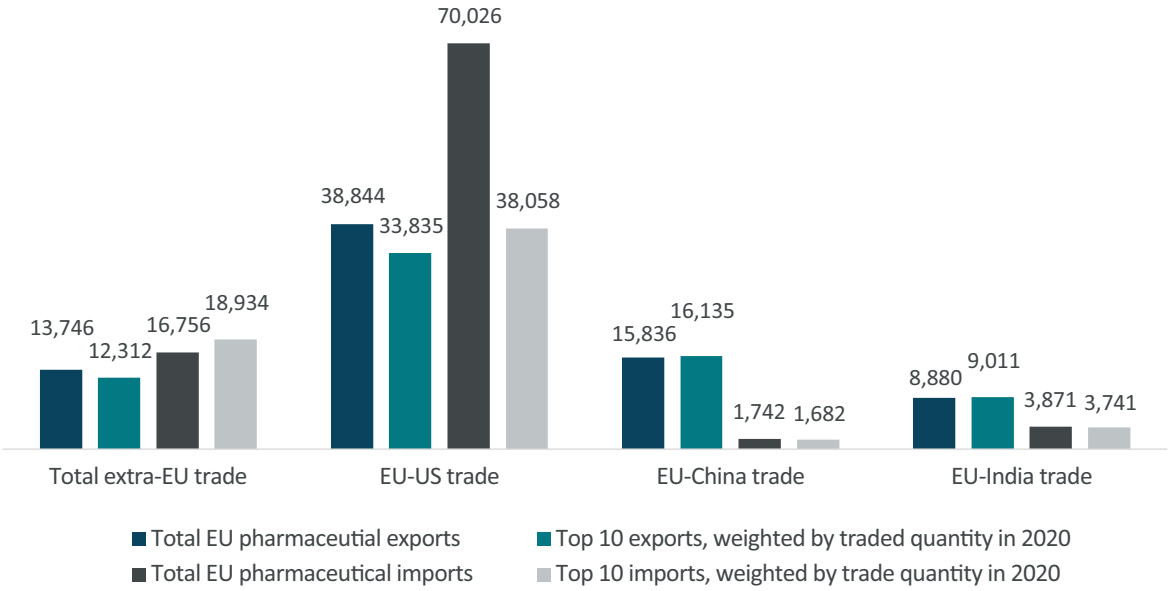
Source: WIPO. Note: In most countries, the patent application is published 18 months after the priority date, i.e. after the filing date or the priority filing. In general, a patent is also published once granted.[28]

4.2. Patterns in the value-added of EU pharmaceutical exports and imports

Aggregate trade data for the value-added of EU exports and imports of pharmaceuticals confirms the EU's current competitive position. However, the average value-added of medicines exported from the EU to the USA is significantly lower than the average value-added of medicines imported to the EU from the USA, while innovators and producers of higher value medicines from China and India are catching up. As outlined in Figure 8 below, the average export price for 100 kg of pharmaceuticals exported outside the EU27 amounted to approx. EUR 13,700 over the period 2016-2020, while the average import price amounted to EUR 16,800. On average, the price per kg (quantity) of EU imports of pharmaceuticals from the USA is almost twice as high as the price of EU pharmaceutical exports to the USA. In other words, the value added of US pharmaceutical exports to the EU is roughly twice as high as the value added of EU pharmaceutical exports to the USA. For EU-China trade, the price of EU pharmaceutical exports to China is, on average, nine times higher than the price of EU pharmaceutical imports from China. By contrast, the average price of EU pharmaceutical exports to India is about the same as the average price of pharmaceutical imports from India.

[28] See WIPO (2015). WIPO Guide to Using Patent Information, World Intellectual Property Rights Organisation.

FIGURE 8: AVERAGE VALUE-ADDED OF EXTRA-EU PHARMACEUTICAL EXPORTS AND IMPORTS, PRICE/ QUANTITY RATIO, IN EUR PER 100 KG, AVERAGE OVER THE PERIOD 2016-2020

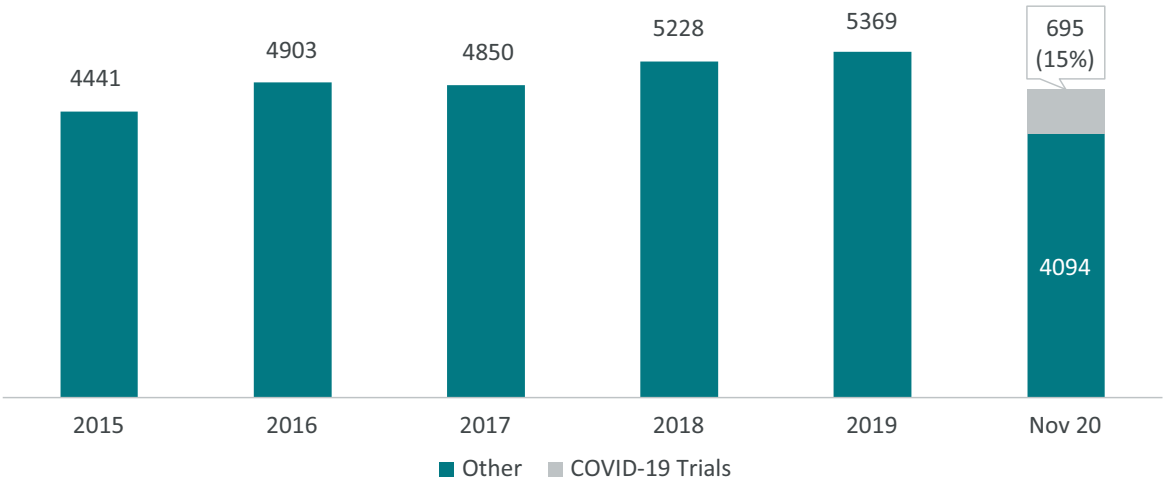


Source: Own calculations based on the EU's Comext data. Data underlying the calculations: trade values expressed in EUR; quantity expressed in unit of 100 kg. Data gaps have been excluded from the calculations.

4.3. The EU's pharmaceutical innovation gap

The recently published pharmaceutical "Pipeline Review 2021" (IQVIA/EFPIA 2021) shows that EU innovators are substantially lagging behind the USA in the innovation of new medical treatments. The report finds that the volume of clinical trials for multiple treatments has increased since 2015 with oncology having the most extensive pipeline. At the same time, excluding trials related to COVID-19, which accounted for about 15% of the clinical pipeline in 2020, clinical activity in other areas has decreased when compared to 2019 (see Figure 9).

FIGURE 9: FULL PIPELINE, NUMBER OF TRIALS STARTED IN 2015 UNTIL NOVEMBER 2020



Source: IQVIA/EFPIA Pipeline Review 2021.

The IQVIA/EFPIA report provides detailed statistics for active studies broken down by the geographical location of the innovator and therapeutic areas. It is shown that innovators from Europe are significantly lagging in active studies in several areas of treatment when compared to the USA, and in some cases, Asia and Australia/Oceania. As outlined by Figure 10, EU innovators account for 20% of all active studies for Alzheimer's[29] (USA: 43%; Asia: 9%), 20% for haemophilia A&B and ophthalmological disorders (USA: 68%; Asia: 9%), 20% for cell therapies[30] (USA: 50%; Asia: 9%), 7% for non-alcoholic steatohepatitis[31] (NASH) (USA: 68%; Asia: 10%), 8% for the human immunodeficiency virus[32] (HIV) (USA: 63%; Asia: 8%, and 10% for Hepatitis B[33] (USA: 34%; Asia: 25%).

Overall, the data shows that, in the future, EU Member States will likely become increasingly dependent on innovative medicines that are temporarily protected by patents and market exclusivity rights held by non-EU rights holders in many therapeutic areas. It should be

[29] According to the report, Alzheimer's is one of Europe's largest public health crises and the most common cause of dementia (60-80% of all dementia patients); today approx. 8.3 million patients suffer from Alzheimer's disease across Europe. Due to the anticipated rapid growth of the over-65 segment of the population, this number is expected to nearly double over the next 35 years, reaching 15.9 million in Europe by 2050.

[30] The EFPIA report reveals that the USA has over twice as many active studies in the area of Chimeric antigen receptor cell type (CAR-T) therapy than Europe. Cell therapy, in general, is the administration of viable, often purified cells into a patient's body for the treatment of a disease. Two common types include (1) stem cell transplants (SCT) and (2) CAR-T therapy. CAR T-cell is a form of cell therapy that involves modifying a patient's T-cells to recognize and attack cancer cells. CAR-Ts are a promising therapy for haematological cancers, modifying T-cells to target cancer antigens.

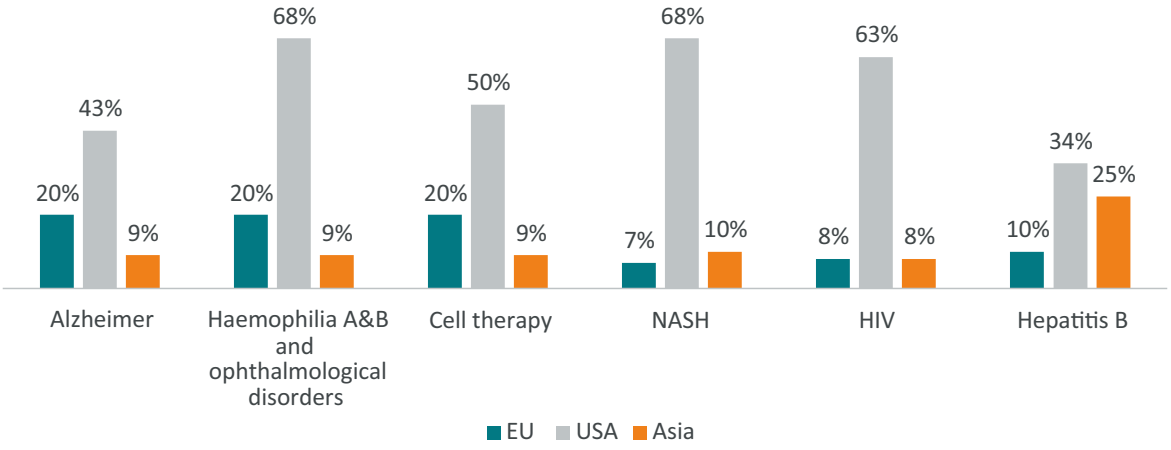
[31] In the case of active studies in this particular area, Europe is surpassed by both the USA and Asia. The prevalence rate of NASH in European countries is expected to increase by more than 40% by 2030. NASH is the unnatural build-up of fat in the liver as part of non-alcoholic fatty liver disease (NAFLD), causing inflammation and leading to fibrosis and cirrhosis of the liver. NASH is also becoming the leading cause for liver transplants.

[32] HIV remains one of the major public health issues globally, with more than 2 million people infected in Europe alone. The EFPIA report reveals that both the USA and Asia had a greater number of active studies in this area than Europe, as of November 2020. Curative therapies for HIV and chronic hepatitis B eradicate the virus from patients' organisms, saving them from life-long treatments. For HIV, two key approaches to curative therapy development are being investigated: eradication (or sterilisation) therapies are aimed at removing the viral reservoir from a patient's organism, whereas the goal of functional therapies is to maintain a sustainable infection level in the absence of medical intervention (ART).

[33] In this area of research, Europe is surpassed in terms of number of active studies by the USA, Asia, and the Australia/Oceania region (4.7 million patients diagnosed in the EU). Chronic hepatitis B infections pose a challenge to healthcare systems, being one of the leading causes of liver cancer. Current therapies effectively suppress hepatitis B virus, but need to be continued over the patient's lifetime. With 61 ongoing trials and the majority of pipeline activity still in the early stages, this area is likely to continue bringing innovation.

noted though that many of these rights holders produce and sell their products in the EU, based on patent and other market exclusivity rights that allow joint R&D and the licensing of production and distribution rights.

FIGURE 10: FULL PIPELINE, NUMBER OF TRIALS STARTED IN 2015 UNTIL NOVEMBER 2020



Source: IQVIA/EFPIA Pipeline Review 2021.

4.4. Trends in drug development costs

Incentives for investment in R&D and drug development have generally become more important over the past four decades as it became more expensive and more time consuming to develop a new drug and get approval for it. Everything else being equal, higher drug development costs reduce the commercial value of pharmaceutical IPRs. The effective commercial value of a pharmaceutical patent is driven by two factors: costs and revenues. Costs are composed of R&D costs, product development costs, international drug approval costs, the costs of manufacturing, and costs related to marketing and the distribution of the drug. These costs have to be adjusted for the risk of failure, which is considerable. Revenues, on the other hand, are primarily determined by product life cycles, time of marketing exclusivity, prices and, usually, national market size(s). In general, the profitability of a certain drug depends on the capability of patent owners to raise sufficient revenues over a given period of time, i.e. revenues that exceed the fixed drug development and variable production and marketing costs. In practice, the economic success of a new drug depends on a number of uncertainties that affect the cost structure of companies and their effective ability to collect sufficient revenues in fragmented national markets over a certain time period.

Even though there have been many advances in pharmaceutical research over the past 60 to 70 years, efficiencies in commercial drug development research noticeably declined. The rate of failure in drug development is exceptionally high as researchers have to study thousands of compounds before turning substances into a marketable product that generate value for patients. For clinical drug development success rates, for example, BIO Industry Analysis (2016) calculates that the overall likelihood of approval (LOA) from the first clinical trial phase (Phase I) was only 9.6% between 2006 and 2015, and 11.9% for all indications outside the field of oncology. The report also states that Phase II clinical programmes continue to suffer from the lowest success rate of the four development phases, with only 30.7% of developmental candidates advancing to Phase III.

Many studies demonstrate that the cost and time of drug development has increased tremendously since the 1960s. Scannell et al. (2012) report that the number of new drugs approved per USD billion spent on R&D has "halved about every 9 years" since the 1950s. This decline corresponds to a 80-fold productivity drop after adjustment for inflation. Investigating the underlying forces of the "loss of productivity" in drug research, Scannell et al. discuss four factors that they consider to be primary causes:

1) The "better than the Beatles" problem, according to which shifts in R&D for new therapeutic fields with lower approval probabilities cause higher attrition rates. This is, to a large extent, driven by incentives in reimbursement systems and health technology assessments (HTAs) that are intended to trigger developers to go for the "difficult" parts, especially oncology and orphan drugs, and to pay on the basis of outcomes (Adkins et al. 2017). These are exactly the therapeutic areas where it is difficult to pass the market approval tests, with incentives that leave policymakers not knowing whether they are going to contribute to the dual goals of improving outcomes and controlling costs.
2) The "cautious regulator" problem, which arises due to the regulators' increased risk awareness (lower risk tolerance) over time and, therefore, the higher trial and patient safety assurance costs (for additional regulatory provisions, see also EU 2012 and WHO 2012).
3) A "throw money at it" tendency, which means that companies assign many scientific resources to certain projects in order to be the first to launch a new drug.
4) The "basic research – brute force" bias, according to which there is a tendency in the industry to overestimate the ability of advances in basic research and brute force screening methods.

While these factors generally contributed to a relative decline in research productivity, there are also lower performance rates in general research that can be attributed to the industry's trend of seeking "precise effects" from molecules rather than broader therapeutic potential, whereby the targeting of certain therapeutic effects comes with longer and more complex trial and error activities. In this context, DiMasi et al. (2016) outlines that higher company

out-of-pocket costs for individual drugs and higher failure rates for drugs tested on human subjects were the major reasons behind rising drug development costs. Higher expenditures arose from higher clinical trial complexity, larger clinical trial sizes, a higher cost from the medical sector for inputs used for development, changes in protocol design to include efforts to gather Health Technology Assessment information, and testing on comparator drugs to accommodate payment demands for comparative effectiveness data. The authors calculate an increase in drug development costs of 145% from 2003 to 2013. Taken together, these developments significantly impacted on the drug development costs of those companies that intensely engage in research in innovative medicines.

The above-mentioned effects impact different stages of development and have considerably inflated the average cost of drug development over time. Several recent studies indicate that the costs of drug development often amount to up to several billions of USD (EUR) per drug (see Table 5 for an overview of various "average cost" estimates), demonstrating the need for internationally strong IPRs to ensure sustained private sector investment in the development of new medicines and therapies.

TABLE 5: ESTIMATES OF RESEARCH AND DEVELOPMENT COSTS OF INNOVATIVE NEW MEDICINES

Study	Period under investigation	Cost estimates
Morgan et al. (2011): The cost of drug development: A systematic review	Meta-analysis of studies published between 1980 and 2009	- Estimates of the cost of drug development ranged more than 9-fold, from USD 92 million cash (USD 161 million capitalised) to USD 883.6 million cash (USD 1.8 billion capitalised) - Authors argue that a lack of transparency limits many studies
Mestre-Ferrandiz et al. (2012): The R&D Cost of a New Medicine	pre-2002 data trial and R&D data	- Authors identified 11 studies published since 1979 that estimate mean R&D costs of a successful new drug - The most recent estimate is USD 1.9 billion - Authors report a tenfold increase from the 1979 estimate of USD 199 million (expressed in 2011 prices). - Authors own estimate: R&D costs per new drug of USD 1.5 billion (expressed in 2011 prices); out-of-pocket cost and ex capital cost: USD 1.01 billion
Herper, M. (2013): How Much Does Pharmaceutical Innovation Cost? A Look At 100 Companies	2003-2013	- For companies that have launched more than three drugs, the median cost per new drug is USD 4.2 billion - For companies that have launched more than four drugs, the median cost per new drug is USD 5.3 billion
DiMasi et al. (2016): Innovation in the pharmaceutical industry: New estimates of R&D costs	1995-2007	- Pre-tax out-of-pocket per approval is USD 1.4 billion (2013 dollars) - Pre-tax capitalised per approval is USD 2.6 billion (2013 dollars) - Total capitalised costs were found to have increased at a real annual rate of 8.5% - With post-approval R&D costs, the estimate increases to USD 2.9 billion (2013 dollars)

Source: ECIPE research.

4.5. Implications for the conception of strategic autonomy of Europe's innovative pharmaceutical industry

Trends in drug development costs, together with the EU's lack of innovation activity as well as global developments in pharmaceutical innovation, have shown that, overall, the EU's pharmaceutical sector can only maintain high value-added production and a high degree of international competitiveness if it remains attractive to research- and knowledge-intensive companies that have the financial resources and scientific capacities to innovate and manufacture in the EU.

Although pharmaceutical IPRs are not the only policy instrument to incentivise investments in innovation, the absence of them would significantly reduce private-sector innovation and pharmaceutical production, as patents and other market exclusivity rights are an integral part of pharmaceutical companies' long-term innovation and production strategies. At the same time, policies aiming at reducing the number of years of patent validity, with less protection granted by data exclusivity and supplementary protection rights, and prescriptive IPR polices aiming to steer investments (a deviation from universal and open outcome-oriented research incentives) would impact on pharmaceutical companies' choices regarding the geographical location of investments in research capacities and production facilities.

Looking at the EU, a decline of the strength of IPRs relative to other jurisdictions would likely cause divestment in the EU and the offshoring of research and production activities to countries that show similar institutional characteristics,[34] provide stronger IPR protection and have the gravity of large(r) markets. These countries include the USA, Japan and, increasingly, China, Brazil other large emerging market economies. In the EU, the negative impacts would likely be strongest in Member States that are still home to intensive R&D and a high share of high value-added production in total pharmaceutical production.

Maintaining an internationally strong IRP incentive regime in the EU is also key to moderating the economic impacts of industry trends. As reported by Akkari et al. (2016), technological and scientific knowledge in the pharmaceutical industry is increasingly spreading globally, implying that competition with big incumbent companies from the USA or the EU ("Big Pharma") is likely to increase in the future. Based on industry data, the authors project that large multinational pharmaceutical companies, of which many are headquartered in the EU and the USA, will have to "seek a greater penetration in pharmaceutical emerging markets".

[34] Such as economic freedoms, the quality of education, access to technology and skilled labour, the strength of the rule of law and the quality of governmental institutions.

Accordingly, an increase in the relative strength of IPRs in these markets as compared to the EU (or a relative decline in the EU) could cause investment-intensive European companies to relocate even more R&D and production capacity to "pharmerging" economies.

On aggregate, an internationally competitive IPR regime in the EU could moderate the relative decline in the attractiveness of EU Member States as a location for pharmaceutical investment, R&D and the production of high value-added medicines. By contrast, weaker IPRs would contradict the political objective for the EU to remain a global leader in pharmaceutical innovation and a production hub for innovative and high value-added medicines.

5. SCENARIO ANALYSIS OF THE ECONOMIC IMPACT OF A DECLINE IN THE VALUE-ADDED OF EU PHARMACEUTICAL PRODUCTION

Together with other determinants of private-sector investment, such as political stability, the availability of skilled labour, attractive corporate tax regimes, and an open international trade and investment regime, internationally competitive IPRs will remain key for pharmaceutical companies to keep operating and/or investing in the EU in the future. EU policy experiments that discount the impact of IPRs on pharmaceutical innovation and the longer-term effects on high value-added production could result in a relocation of R&D and manufacturing sites to jurisdictions outside the EU, and less investments in new research projects and production capacities in the EU. Such experiments include:

- reductions of effective patent terms, data exclusivity rights and patent term extensions (including supplementary protection certificates);
- political interference in companies' innovation and investment strategies, such as the abolition of universal IPR-based incentives; and
- various modes of compulsory licensing.

While it is difficult to estimate the precise economic impacts of such policies, a relative erosion of IPR incentives for investments in innovation in the EU as compared to other jurisdictions would in the medium to long term cause a decline of high value-added pharmaceutical production in the EU. Lower levels of production and value-added in the EU would result in less revenues, less profits and less funding available for investments and R&D spending, potentially creating a downward spiral for production and employment in the sector.

It is exemplarily demonstrated below how reduced investment in innovation in the EU could, in the medium to long term, impact on key industry indicators. The forward-looking analysis is based on hypothetical assumptions and accounts for the considerable importance of pharmaceutical IPRs in Western European countries, whose pharmaceutical industries are characterised by high investment activity, high R&D spending and high value-added production.

5.1. Methodological considerations

We employ EU Member State data, which is outlined in Section 3.2, to estimate the hypothetical value of production losses in EU pharmaceutical production, forgone investment and decreases in pharmaceutical employment in the EU. Based on the previous discussion, it is assumed that a relative decline of the strength of pharmaceutical IPRs in the EU would in the medium to long term result in less investments in innovation in the EU

and, over time, lower value-added production. We study three hypothetical scenarios that reflect different "generics to innovative medicines ratios" in the EU's overall pharmaceutical production mix, i.e. relatively low value-added production versus relatively high value-added production. It should be noted that IPR revisions of a different nature and extent would cause economic consequences of differing magnitudes. The scenarios analysed below do not reflect specific IPR policy changes or combinations thereof. Also, the impacts of an IPR reform in the EU will hinge on how IPRs and other determinants of investment in non-EU countries evolve over time.

As detailed industry data for the value of the EU's production of generics, on the one hand, and original (innovative) medicines, on the other, is unavailable, we use industry information about production characteristics in major generics-producing countries in the EU as a starting point. According to CA Market Monitor (2020), for example, pharmaceutical production in Central and Eastern European (CEE) countries, such as Bulgaria, Czechia, Hungary, Poland, Romania and Slovenia, is dominated by the production of generic medicines.[35] Assuming that, overall, the pharmaceutical value-added in (the above mentioned) CEE countries is driven by the production of off-patent (generics) drugs rather than innovative R&D and the production of high value-added medicines, key CEE production indicators are used to derive potential impacts on EU Member States and the EU as a whole from shifts in EU pharmaceutical production towards a generics-driven production mix. More specifically, empirical data for production, tangible investment and R&D spending are used to estimate the comparative-static impact from a shift in overall EU production away from R&D-based innovative medicines towards a more generics-driven production mix.

Country-specific data for the production value per employee are used for a comparative-static analysis.[36] Thereby, observed industry data are replaced by hypothetical though empirically observable data that reflect different ratios of innovative medicines relative to generic medicines in the EU27 production mix.[37] Replacing observed data by hypothetical but empirically derived data allows us to draw important lessons for policymakers about the potential medium- to long-term impacts on EU production, investments in innovation and production capacities, and employment that would result from a gradual shift towards less IP-intensive production in the EU27. It should be noted that this approach, like any economic impact assessment, general equilibrium or econometric analysis, has limitations. As the analysis is comparative-static, the estimates should be read as hypothetical

[35] It is reported that "generics manufacturing in particular relies on three factors: low costs, reliable supply chains, and a skilled workforce – including a regulatory team able to spot products coming off patent. CEE has all these factors, making it a prime manufacturing location for the rest of Europe and beyond." (CA Market Monitor 2020, p. 1)

[36] Comparative-static estimations compare two different economic outcomes, before and after a change in some underlying exogenous parameters. It allows the comparison of two different equilibrium states, after a process of adjustment.

[37] All relevant industry indicators are outlined in Table 1, Table 2 and Table 3 in Section 3.2.

comparable analysis that need to be put into perspective with the status quo, assuming "everything else being/remaining equal". The analysis does not account for future changes in global competition, R&D, and innovation and manufacturing capacities, nor does it explicitly account for increased competition in pharmaceutical manufacturing within the EU27, which is likely to be much more intense if overall EU production becomes more generics-driven.

It should also be noted that this analysis does not allow conclusions to be drawn about the length of the economic adjustment process that is triggered by an exogenous shock, which would cause an increase in the generics to innovative medicines ratio, such as a decline in the relative strength of IPR incentives for R&D and innovation in the EU. Accordingly, the estimates provided below should not be taken by their precise face value. The estimates should be considered as indicators for the overall direction and potential magnitude of impacts on the level of high value-added production, investments, R&D spending and employment in the EU, taking into consideration the nature and likelihood of future changes in the EU's IPR policy and IPR policymaking in other jurisdictions, as well as changes in industry behaviour and global trends in pharmaceutical R&D and manufacturing activities.

We analyse three hypothetical scenarios, which are described in Table 6 below. To calculate the potential changes in pharmaceutical production, investment, R&D spending and employment, the EU countries' observed economic indicators for annual production, investment and R&D spending are replaced by the 1st-, 2nd- and 3rd-quartile values of the overall EU27 sample.

TABLE 6: DESCRIPTION OF SCENARIOS

Scenario	Description of scenario
Scenario 1: Severe degeneration towards generics-driven pharmaceutical industry across the EU27	EU27 sample 1st-quartile estimates are applied for production value per employee, investments in intangibles per employee and R&D spending per employee. Estimated changes in direct employment in the pharmaceutical industry are derived from changes to the value of overall production, which is derived from the production value per employee estimate.
Scenario 2: Significant deterioration of the innovative medicines to generic medicines ratio in the EU27 production mix, particularly for countries characterised by value-added production	EU27 sample 2nd-quartile (sample median) estimates are applied for production value per employee, investments in intangibles per employee and R&D spending per employee. Estimated changes in direct employment in the pharmaceutical industry are derived from changes to the value of overall production, which is derived from the production value per employee estimate.
Scenario 3: Less significant deterioration of the innovative medicines to generic medicines ratio in the EU27 production mix, deteriorating only in countries characterised by value-added production (mainly Western European EU Member States)	EU27 sample 3rd-quartile estimates are applied for production value per employee, investments in intangibles per employee and R&D spending per employee. Estimated changes in direct employment in the pharmaceutical industry are derived from changes to the value of overall production, which is derived from the production value per employee estimate. It should be noted that in this scenario industry indicators would improve in some EU Member States, mainly CEE countries. Increases in production, employment, investment and R&D spending can be attributed to the applied 3rd-quartile estimates, which are generally higher than observed indicators in CEE countries, but at the same time lower than those observed in countries with high value-added production. Assuming lower IPR incentives for investments in pharmaceutical research in the EU, Scenario 3 can be interpreted as a situation in which a large number of research-intensive pharmaceutical companies relocate both R&D and production capacities from Western European Member States to lower-cost CEE countries to compensate for the commercial losses that would accrue from lower IPR incentives in the EU (relocation to low-cost countries outside the EU is excluded from the analysis). Contrary to the estimates in Scenario 1 and Scenario 2, the impacts on annual investment and R&D spending should therefore not be interpreted as consecutive annual changes, but rather understood as temporary catching-up spending in pharmaceutical capacities in the EU. By contrast, in Scenario 3, the overall value of pharmaceutical production reflects a persistent loss in the value of pharmaceutical production due to an overall increase in the "generics to innovative medicines ratio" in the EU.

Source: Own compilation.

For the overall EU sample, the 1st-quartile estimate is used to estimate potential impacts from a "worst-case scenario" in which pharmaceutical production in the EU would severely "degenerate" towards generics-driven research and manufacturing activities. Such low value-added activities reflect currently observed production and investment characteristics in the pharmaceutical industry in most CEE countries.

Applying the 2nd-quartile estimate (sample median) in the second scenario reflects a significant deterioration in the innovative medicines to generic medicines ratio in the EU's overall research and production mix. Applying the 2nd-quartile estimate reflects a situation

in which research and production activities in EU Member States with high value-added production would become much more generics driven in the future compared to the status quo, while production and investment characteristics would largely remain unchanged in Member States where pharmaceutical manufacturing is already dominated by the production of low value-added generic medicines, mostly in CEE countries.

Using the 3rd-quartile estimate in the third scenario reflects a situation in which the innovative medicines to generic medicines ratio would be somewhat higher compared to the status quo in countries with low value-added production and a low investment-intensity of pharmaceutical production, mainly in CEE countries. At the same time, the innovative medicines to generic medicines ratio would still be significantly lower in countries that are currently leading in terms of high investment intensities and a high level of high value-added production, mainly Belgium, Denmark, Germany, Finland and Sweden. Similar considerations apply for tangible investments and R&D spending.

As outlined above, IPR revisions of a different nature and extent will cause economic consequences of differing magnitudes. The scenarios analysed here do not reflect specific IPR policy options or combinations thereof, and the impacts of an IPR reform in the EU would also hinge on how IPRs in other countries evolve over time. However, a few configurations are conceivable for Scenarios 1 and 2. For example, a significant reduction in the effective number of years of market exclusivity, e.g. reduced patent terms and shorter patent-term extensions, would likely cause innovators in the EU to relocate to jurisdictions outside the EU and have a deterring effect on non-EU investors, triggering divestment, offshoring of production, reduced licensing and delays in the launch of innovative medicines on EU markets. Similarly, the abolition of universal IP incentives for pharmaceutical research, as currently discussed at the EU level, could cause innovative companies to leave the EU, with negative medium- to long-term impacts on future innovation and associated losses in high value-added production in the EU. By contrast, limited compulsory licensing obligations would likely have a smaller negative effect on the longer-term development of overall EU investment in pharmaceutical R&D and the associated level of high value-added production in the EU.

The calculation procedure for estimates of changes in production (value), investment (value) and employment (number of employees) is described in more detail below:

(1) As concerns the estimated value of pharmaceutical production, we use the country-specific production value per employee indicator[38] as a starting point to estimate the potential impact on pharmaceutical production in individual EU Member States and the EU27 that

[38] Based on Eurostat's SBS database.

would result from shifts in overall EU research and manufacturing towards less IP-intensive research and production activities.

(2) For estimates of the impacts on investment and R&D, we use investment in intangibles[39] and R&D spending per employee[40] indicators as a starting point to estimate the potential impact on investments in intangibles and overall R&D spending in individual EU Member States and the EU27 that would result from a shift of EU R&D and manufacturing towards less IP-intensive production activities.

(3) For estimates of the impacts on employment, we apply the estimates from (1), i.e. the estimated changes in the production value, to estimate potential changes in the level of pharmaceutical employment. We distinguish between two methodologies: one estimation is based on constant average costs of personnel (CACP) in the pharmaceutical industry, and one estimation based on constant labour costs in the overall EU27 industry (CLCI), i.e. labour costs across manufacturing sectors in the EU27.[41] The calculation of the CACP estimates is based on country-specific shares of total personnel costs in the pharmaceutical sector for the total production value of pharmaceuticals in the respective country. Assuming constant shares, estimated production values from (1) are taken to derive estimates for the total costs of personnel in the three scenarios. Assuming constant average costs of personnel, the total estimated costs of personnel in a given country are then divided by the observed average costs of personnel in this country in 2018, which results in the estimated number of employees for each scenario.

The calculation of the CLCI estimates is based on country-specific labour costs in industry across the manufacturing sectors in the EU. This approach allows us to account for relatively large differences in the levels of wages and salaries paid across manufacturing sectors in the EU Member States. Eurostat's industry data indicate that the average wages and salaries across the industry are generally similar or even higher than the average wages and salaries paid in the pharmaceutical sector in countries with low value-added production (e.g. CEE countries). By contrast, Eurostat data indicate that average wages and salaries across the industry are generally lower than average wages and salaries paid in the pharmaceutical sector in countries with high value-added production (e.g. Western European countries). As the production of generic medicines is, overall, less skill- and knowledge-intensive than the development and production of innovative medicines, the labour employed in generics production is generally more substitutable. As a result, a shift from a high value-added production to a low value-added production of pharmaceuticals would likely result in a

[39] Based on Eurostat's SBS database.

[40] Base on EFPIA (2019) data surveyed for the year 2017.

[41] Industry, except construction (compensation of employees plus taxes minus subsidies). See the description provided by Eurostat. Available at https://ec.europa.eu/eurostat/cache/metadata/en/lc_lci_lev_esms.htm

downward pressure on future wages and salaries paid in the pharmaceutical sector in EU Member States in which more innovative pharmaceutical companies are currently located, mainly Western European countries.

5.2. Estimated changes in production, investment, R&D spending and employment

For pharmaceutical production, investment in intangibles, R&D spending and employment in the pharmaceutical industry, EU27 estimates are reported in Figure 11, Figure 12, Figure 13, and Figure 14 below. Estimates for individual countries are provided in Table 7 below as well as in Table 16 to Table 20 in Appendix I.

As regards Scenario 1 (severe degeneration towards a generics-driven pharmaceutical industry across the EU27), the estimates indicate that the value of pharmaceutical production in the EU27 would decrease substantially if overall production in the EU would shift towards generic medicines. Similarly, associated annual investments in intangibles as well as overall R&D spending in the EU would decrease substantially if EU production would become less IP-intensive. The decrease in the production value would result in a significant decline in employment in the EU's pharmaceutical sector. While investment-driven employment is not included in the estimates, additional employment losses can be expected from lower investment levels, which would affect suppliers and other contracting firms. The largest losses in pharmaceutical production would be experienced in those EU Member States in which production is currently characterised by a relatively high share of knowledge- and IP-intensive pharmaceutical production activities, high levels of investment in intangibles, high levels of R&D spending, and a high number skilled and well-paid employees.

For Scenario 1, overall pharmaceutical production is estimated to decline by EUR 218 billion (-73%), overall investment in intangibles in the pharmaceutical sector is estimated to decline by EUR 4.4 billion (-41%), overall R&D spending in the pharmaceutical sector is estimated to decline by EUR 17 billion (-46%), and the total number of employees in the pharmaceutical industry is estimated to decline by approx. 388,000 employees (CLCI estimate; -64%) to 440,000 employees (CACP estimate; -73%).

As regards Scenario 2 (significant deterioration in the innovative medicines to generic medicines ratio in the EU27 production mix), the estimates are generally lower compared to Scenario 2. The estimates indicate that the value of pharmaceutical production in the EU27 would decrease considerably if overall pharmaceutical production would become less IP-intensive. Annual investments in intangibles as well as overall R&D spending in the EU would also decline, as would EU employment in the pharmaceutical industry. Additional employment losses can be expected from lower investment levels, affecting suppliers and contracting firms. The largest losses in pharmaceutical production would be registered in EU Member States

in which production is currently characterised by a relatively high share of knowledge and IP-intensive pharmaceutical production activities, high levels of investment in intangibles, high levels of R&D spending, and a high number of skilled and well-paid employees.

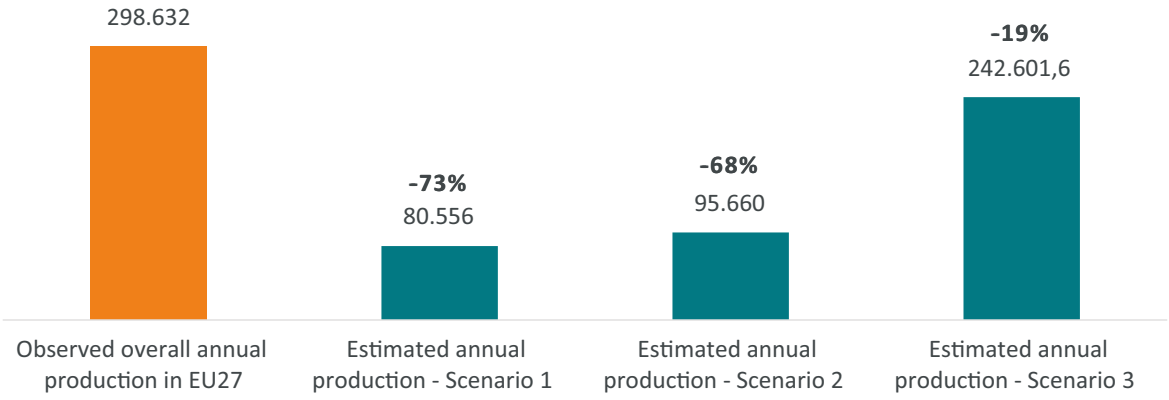
For Scenario 2, overall pharmaceutical production is estimated to decline by EUR 202 billion (-68%), overall investment in intangibles in the pharmaceutical sector is estimated to decline by EUR 2.2 billion (-20%), overall R&D spending in the pharmaceutical sector is estimated to decline by EUR 14 billion (-31%), and the total number of employees in the pharmaceutical industry is estimated to decline by approx. 348,000 employees (CLCI estimate; -58%) to 409,000 employees (CACP estimate; -68%).

For Scenario 3 (a less significant deterioration in innovative medicines to generic medicines ratio in the EU27 production mix), the estimated changes (losses) are generally lower compared to Scenarios 1 and 2. In Scenario 3, industry indicators would improve in some EU Member States, mainly CEE countries. Increases in production, employment, investment and R&D spending can be attributed to the application of 3rd-quartile estimates, which are generally higher than observed indicators in CEE countries, but at the same time lower than those observed in countries with high-value added production. Assuming lower IPR incentives for investments in pharmaceutical research in the EU, Scenario 3 can be interpreted as a situation in which a large number of research-intensive pharmaceutical companies relocate both R&D and production capacities from Western European Member States to less expensive CEE countries to compensate for the commercial losses that would accrue from lower IPR incentives in the EU; relocation to low-cost countries outside the EU is excluded from the analysis. Contrary to the estimates in Scenario 1 and Scenario 2, the impacts on annual investment and R&D spending should therefore not be interpreted as consecutive annual changes, but rather understood as temporary catch-up spending in pharmaceutical capacities in the EU. By contrast, in Scenario 3, the overall value of pharmaceutical production reflects a persistent loss in the value of pharmaceutical production due to an overall increase in the "generics to innovative medicines ratio" in the EU.

The estimates for Scenario 3 indicate that the value of pharmaceutical production would increase in countries currently characterised by a relatively high share of less knowledge and less IP-intensive pharmaceutical production activities, relatively low levels of investment in intangibles and relatively low levels of R&D spending. By contrast, compared to the status quo, the estimated value of pharmaceutical production would be lower in countries currently characterised by a relatively high share of knowledge and IP-intensive pharmaceutical production activities, relatively high levels of investment in intangibles and relatively high levels of R&D spending.

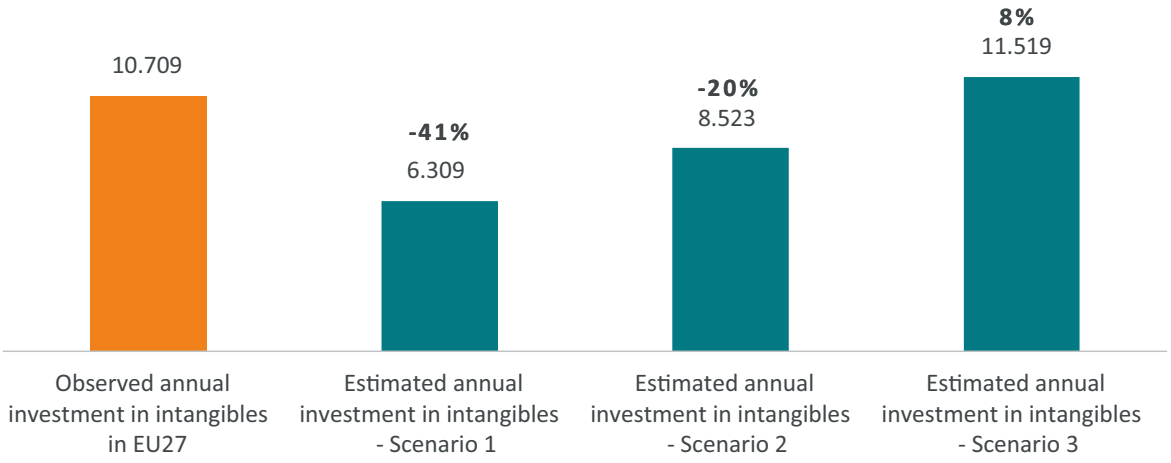
For Scenario 3, overall pharmaceutical production in the EU is estimated to decline by EUR 56 billion (-19%), overall investment in intangibles in the EU's pharmaceutical sector is estimated to increase by EUR 810 million (+8%; driven by the hypothetical amount of temporary catch-up investment created in CEE countries), overall R&D spending in the pharmaceutical sector is estimated to increase by EUR 6.3 billion (+28%; driven by the hypothetical increase in R&D spending in CEE countries), and the total number of employees in the pharmaceutical industry is estimated to increase by approx. 42,000 employees (CLCI estimate; +7%) or decline by 113,000 employees (CACP estimate; -19%, reflecting the overall reduction of the value of EU pharmaceutical production). According to the CLCI estimate, a less significant deterioration of the innovative medicines to generic medicines ratio across the EU27 could result in more employment, but substantially lower wages and salaries per average employee in the pharmaceutical industry in Western European countries due to a significant reduction in the value-added per employees.

FIGURE 11: ESTIMATED CHANGES IN THE OVERALL VALUE OF ANNUAL PRODUCTION OF PHARMACEUTICALS, EU27, BY SCENARIO



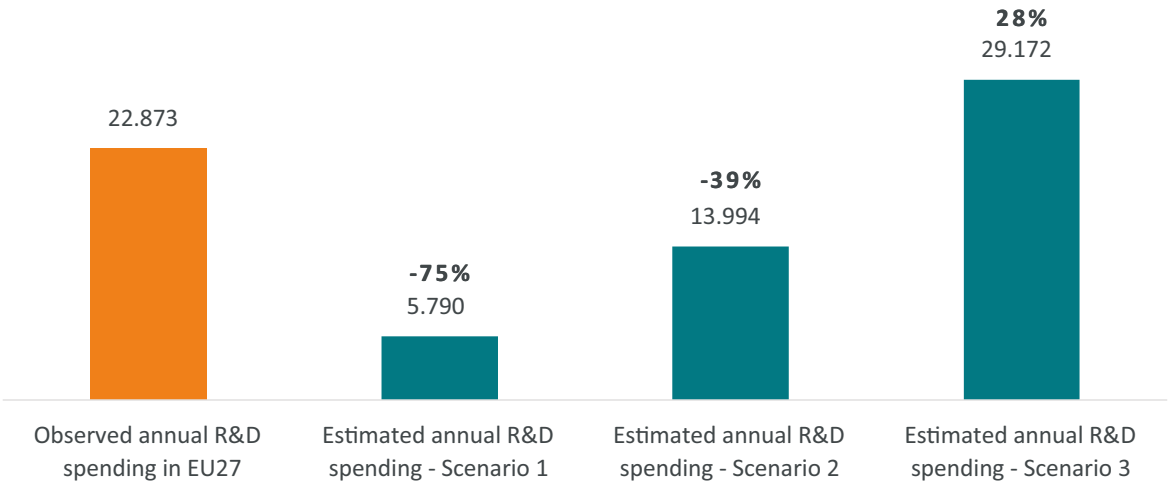
Source: Own estimation. Note: Numbers represent percentage changes compared to observed data in 2018 (production value).

FIGURE 12: ESTIMATED CHANGES IN ANNUAL INVESTMENT IN INTANGIBLES, EU27, BY SCENARIO



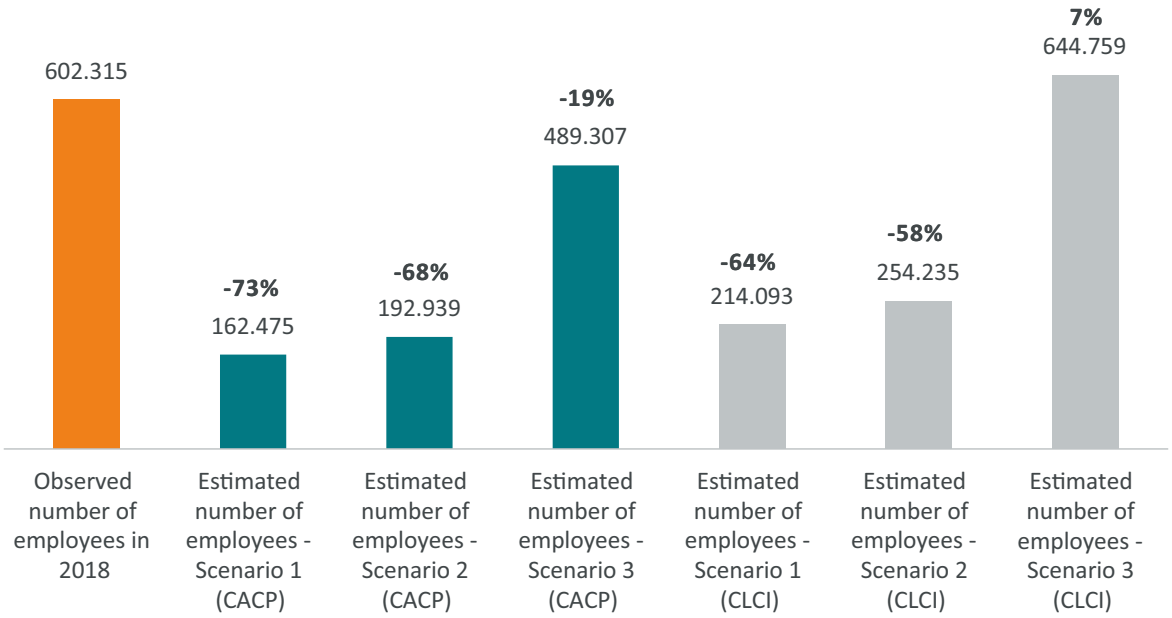
Source: Own estimation. Note: Numbers represent percentage changes compared to observed data in 2018 (investment in intangibles).

FIGURE 13: ESTIMATED CHANGES IN ANNUAL R&D SPENDING, EU-27, BY SCENARIO



Source: own estimation. Note: Numbers represent percentage changes compared to observed data in 2017 (R&D spending).

FIGURE 14: ESTIMATED CHANGES IN THE NUMBER OF EMPLOYEES IN THE EU27 PHARMACEUTICAL INDUSTRY, BY SCENARIO



Source: Own estimation. Note: Numbers represent percentage changes compared to observed data in 2018 (production value, number of employees).

TABLE 7: HEAT MAP OF ESTIMATED PERCENTAGE CHANGES IN PRODUCTION, INVESTMENT, R&D SPENDING AND EMPLOYMENT, BY EU MEMBER STATE

	Changes in the overall value of pharmaceutical production			Changes in investment in intangibles			Changes in R&D spending			Changes in employment (CAPC)		
	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3
Belgium	-88%	-85%	-63%	-62%	-49%	-30%	-92%	-81%	-61%	-88%	-85%	-63%
Czechia	-6%	12%	184%	-11%	21%	63%	31%	217%	560%	-6%	12%	184%
Denmark	-78%	-74%	-34%	-54%	-38%	-17%	-85%	-64%	-25%	-78%	-74%	-34%
Germany	-65%	-58%	6%	-37%	-15%	15%	-78%	-47%	10%	-65%	-58%	6%
Estonia	26%	49%	279%	-21%	6%	44%	n/a	n/a	n/a	26%	49%	279%
Greece	-27%	-13%	120%	12%	52%	105%	131%	458%	1064%	-27%	-13%	120%
Spain	-56%	-47%	34%	-36%	-14%	16%	-60%	-4%	100%	-56%	-47%	34%
Croatia	-11%	5%	167%	8%	45%	96%	17%	182%	488%	-11%	5%	167%
Italy	-67%	-61%	0%	-36%	-13%	17%	-59%	0%	108%	-67%	-61%	0%
Cyprus	-7%	10%	180%	-43%	-23%	4%	-80%	-52%	0%	-7%	10%	180%
Latvia	51%	79%	355%	177%	275%	407%	n/a	n/a	n/a	51%	79%	355%
Hungary	0%	19%	201%	-22%	5%	42%	6%	157%	436%	0%	19%	201%
Malta	-13%	3%	161%	-29%	-4%	29%	n/a	n/a	n/a	-13%	3%	161%
Netherlands	-68%	-62%	-4%	n/a	n/a	n/a	-80%	-53%	-1%	-68%	-62%	-4%
Austria	-51%	-41%	49%	-50%	-33%	-9%	-46%	31%	173%	-51%	-41%	49%
Poland	14%	36%	244%	25%	69%	128%	-29%	71%	257%	14%	36%	244%
Portugal	-16%	0%	154%	-55%	-40%	-18%	-24%	83%	280%	-16%	0%	154%
Romania	58%	87%	374%	-4%	30%	76%	0%	142%	404%	58%	87%	374%
Slovakia	67%	99%	404%	97%	167%	260%	n/a	n/a	n/a	67%	99%	404%
Finland	-70%	-65%	-10%	-19%	9%	47%	-78%	-46%	13%	-70%	-65%	-10%
Sweden	-82%	-78%	-45%	-60%	-46%	-28%	-89%	-73%	-44%	-82%	-78%	-45%
EU27	-73%	-68%	-19%	-41%	-20%	8%	-75%	-39%	28%	-73%	-68%	-19%

Source: Own estimation. Note: Numbers represent percentage changes compared to observed data in 2018 (production value, investment in intangibles, number of employees) and 2017 (R&D spending). Due to missing data, no estimates are reported for Bulgaria, Ireland, France, Lithuania, Luxembourg and Slovenia.

To sum up, the numbers suggest that a degeneration of Europe's current investment- and innovation-driven pharmaceutical sector towards a more generics-driven (off-patent) industry would in the medium to long term result in substantial decreases in overall pharmaceutical production in the EU, the number of persons employed in pharmaceutical companies, and wages and salaries in the EU – which appears to be at odds with the objectives of increasing production and innovation in Europe. This is true whether the changes to IPRs are radical or more moderate. Given the wealth of literature on the positive impacts of IPRs on innovation, it appears questionable whether such a policy shift would lead to sustained high levels of R&D, as indicated by the analysis of economic impacts from a deterioration of the innovative medicines to generics ratio in the EU. From a point of view of strategic autonomy, looking at ensuring resilience to vulnerabilities and the capacity to attract investment in R&D, the overall outcome of such an approach would be negative.

The largest losses in investment, R&D spending, pharmaceutical production and employment would be experienced in those EU Member States where production is currently characterised by high levels of investment in intangibles, high levels of R&D spending, high shares of high value-added production, and a high number skilled and relatively well-paid employees, i.e. mainly Western European countries. Some CEE countries may be able to offset the effects from divestment in Western Europe. However, due to increasing competition from (large) emerging market economies outside the EU, the magnitude of the offsetting effect is highly uncertain.

6. CONCLUSIONS

The previous analysis has shown that EU pharmaceutical innovators are still strong and internationally competitive in developing, producing and exporting innovative and high value-added medicines. On aggregate, the EU's pharmaceutical industry is only surpassed by US innovators, whose research and production activities tend to generate a significantly higher value-added for a broad spectrum of pharmaceutical products.

EU policymakers are generally right to focus on safeguarding the strategic – or long-term – autonomy of the pharmaceutical industry, if this implies ensuring global innovation leadership. Accordingly, any concept of strategic autonomy or sovereignty for the pharmaceutical industry needs to factor in the needs of Europe's research-intensive pharmaceutical companies, which are exposed to rising drug development costs and increasing international competition.

EU policymakers need to take a medium- to long-term perspective by accounting for the long-term link between IPRs and investments in innovation and associated high value-added production in the EU. EU ambitions to reduce supply chain dependencies and improve affordable access to medicines are generally merited. However, none of the currently proposed measures would in any way improve the innovation capacity and future competitiveness of Europe's pharmaceutical industry. The current proposals are unfit for facilitating global innovation leadership and sustaining a high level of high value-added production (of innovative medicines) and skilled employment in the EU's pharmaceutical sector.

Short-sighted policy experiments, such as localisation requirements or an erosion of universal IPRs for investments in drug development projects miss the fact that the EU as a whole needs regulation in place to increase pharmaceutical companies' incentives to invest in R&D and modern production capacities in the EU in the future. Focusing on the offshoring and affordability concerns while ignoring the need for reliable and internationally competitive IPR incentives for innovation risks reducing the sustainability of Europe's historically strong pharmaceutical innovation clusters.

An erosion of IPR incentives in the EU as compared to other jurisdictions could accelerate the relative decline in European companies' international competitiveness vis-à-vis businesses from the USA and large emerging market economies, such as China and India. In the medium to long term, weaker IPR incentives for investments in pharmaceutical research in the EU would likely cause a gradual transition of high value-added production to Central and Eastern European countries and non-EU jurisdictions that offer a more attractive mix of IPR protection on the one hand, and lower R&D and production costs on the other.

REFERENCES

Akkari, A., Munhoz, I., Tomikoa, J. dos Santos, N. and dos Santos, R. (2016). Pharmaceutical innovation: differences between Europe, USA and 'pharmerging' countries, *Gest. Prod.,* São Carlos, v. 23, no. 2

Barnett, J.M. (2017). Why is Everyone Afraid of IP Licensing?, Center for Law and Social Science Research Papers Series No. CLASS17-16, Legal Studies Research Papers Series No. 17-14. *Harvard Journal of Law & Technology,* Special Symposium: Private Law and Intellectual Property 123 (2016-2017)

Bilir, L. (2014). Patent Laws, Product Life-Cycle Lengths, and Multinational Activity. *American Economic Review.* Available at https://pubs.aeaweb.org/doi/pdfplus/10.1257/aer.104.7.1979

Bio Industry Analysis (2016), Clinical Development Success Rates 2006-2015, available at https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

Bochenek, T. and co-authors (2018). Systematic measures and legislative and organizational frameworks aimed at preventing or mitigating drug shortages in 28 European and Western Asian countries. Front. Pharmacol., 8 (2018), p. 942. Available at https://www.sciencedirect.com/science/article/pii/S0378517320301551#b0030

CA Market Monitor (2020). What the doctor ordered: Pharma drives economic growth in Central Europe. Available at https://castlereagh.net/what-the-doctor-ordered-pharma-drives-economic-growth-in-central-europe/

de Beer, J. (2016). Evidence-Based Intellectual Property Policymaking: An Integrated Review of Methods and Conclusions. The Journal of World Intellectual Property, 19, Issue 5-6, November 2016

de Weerdt, E., Simoens, S. Casteels, M. and Huys, I. (2015). Toward a European definition for a drug shortage: a qualitative study. Front. Pharmacol., 6 (2015), p. 253. Available at https://www.sciencedirect.com/science/article/pii/S0378517320301551#b0055

DiMasi, J.A., Grabowski, H.G and Hansen, R.W. (2016), Innovation in the pharmaceutical industry: New estimates of R&D costs, *Journal of Health Economics* (47), May 2016, p. 20-33

Dolon (2020). Estimated impact of EU Orphan Regulation on incentives for innovation. Available at https://dolon.com/dolon/wp-content/uploads/2020/10/Estimated-impact-of-EU-Orphan-Regulation-on-incentives-for-innovation.pdf

EFPIA (2021). EFPIA response to Inception Impact Assessment on Orphan and Paediatric Regulations. 14 January 2021. Available at https://efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-response-to-inception-impact-assessment-on-orphan-and-paediatric-regulations/

EFPIA (2020), Resilience and recovery: EFPIA response to the publication of the EU recovery plan, May 2020. Available at https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/resilience-and-recovery-efpia-response-to-the-publication-of-the-eu-recovery-plan/

EUIPO (2019). IPR-intensive industries and economic performance in the European Union. Industry-Level Analysis Report, September 2019 Third edition. A joint project between the European Patent Office and the European Union Intellectual Property Office. September 2019. Available at https://euipo.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/documents/IPContributionStudy/IPR-intensive_industries_and_economicin_EU/WEB_IPR_intensive_Report_2019.pdf

European Commission (2021a). Updating the 2020 New Industrial Strategy: Building a stronger Single Market for Europe's recovery. Available at https://ec.europa.eu/info/sites/default/files/communication-industrial-strategy-update-2020_en.pdf

European Commission (2021b). Trade Policy Review – An Open, Sustainable and Assertive Trade Policy. Available at https://eur-lex.europa.eu/resource.html?uri=cellar:5bf4e9d0-71d2-11eb-9ac9-01aa75ed71a1.0001.02/DOC_1&format=PDF

European Commission (2021c). Strategic dependencies and capacities. Accompanying the Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Updating the 2020 New Industrial Strategy: Building a stronger Single Market for Europe's recovery. May 2021. Available at https://ec.europa.eu/info/sites/default/files/swd-strategic-dependencies-capacities_en.pdf

European Commission (2020a). Press release. Pharmaceutical Strategy – Timely patient access to affordable medicines. 2 June 2020. Available at https://ec.europa.eu/commission/presscorner/detail/en/ip_20_2173

European Commission (2020b). Pharmaceutical Strategy – Timely patient access to affordable medicines. 2 June 2020. Available at https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines

European Commission (2020c). A New Industrial Strategy for Europe. 10 March 2020. Available at https://ec.europa.eu/info/research-and-innovation/research-area/industrial-research-and-innovation/industrial-policy_en

European Commission (2020d). Inception impact assessment for the Revision of the EU legislation on medicines for children and rare diseases. DG SANTE. 25 November 2020. Available at https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12767-Revision-of-the-EU-legislation-on-medicines-for-children-and-rare-diseases

European Commission (2020e). Joint evaluation of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products

European Commission (2020f). Synopsis Report, Pharmaceutical Strategy for Europe. 25 November 2020. Available at https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_swd2020-286_en.pdf

European Commission (2020g). Final Report Summary examining the replies to the public consultation on the Pharmaceutical Strategy for Europe – Timely Patient Access to Affordable Medicines. Available at https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_consultationreport_en.pdf

European Commission (2018). Impact Assessment accompanying the document Proposal for a Regulation of the European Parliament and of the Council amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products. Available at https://ec.europa.eu/docsroom/documents/29463

Eurostat (2021). International trade in medicinal and pharmaceutical products. Available at https://ec.europa.eu/eurostat/statistics-explained/index.php?title=International_trade_in_medicinal_and_pharmaceutical_products

Eurostat (2015). Patent Statistics: Concordance IPC V8 – NACE REV.2 (version 2.0)

EvaluatePharma (2020). World Preview 2020. Available at https://fondazionecerm.it/wp-content/uploads/2020/07/EvaluatePharma-World-Preview-2020_0.pdf

FDZ (2017). A Novel Technology-Industry Concordance Table Based on Linked Inventor-Establishment Data. 07/2017. Available at http://doku.iab.de/fdz/reporte/2017/MR_07-17_EN.pdf

Gaessler, F. and Wagner, S. (2018). Patents, Data Exclusivity, and the Development of New Drugs. Max Planck Institute for Innovation and Competition and ESMT European School of Management and Technology, June 2019. Available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3401226

Guinea, O. and Espés, A. (2021). International EU27 pharmaceutical production, trade, dependencies and vulnerabilities: a factual analysis. ECIPE 2021

Guinea, O. (2020). Key Trade Data Points on the EU27 Pharmaceutical Supply Chain. ECIPE Publication, July 2020. Available at https://ecipe.org/wp-content/uploads/2020/07/Pharmaceutical-data_July-2020.pdf

Health Strategy (2020). Press release. A French-German Initiative for the European Recovery from the Coronavirus Crisis. 18 May 2020. Available at https://www.bundesregierung.de/resource/blob/997532/1753772/414a4b5a1ca91d4f7146eeb2b39ee72b/2020-05-18-deutsch-franzoesischer-erklaerung-eng-data.pdf?download=1

Herper, M. (2013), How Much Does Pharmaceutical Innovation Cost? A Look At 100 Companies, Forbes – *Pharma and Healthcare,* 11 August 2013. Available at: https://www.forbes.com/sites/matthewherper/2013/08/11/the-cost-of-inventing-a-new-drug-98-companies-ranked/#52dfb4aa2f08

HMA-EMA (2019). Good practice guidance for communication to the public on medicines' availability issues, Recommendations for EU national competent authorities and EMA to ensure adequate public information, July 2019. Available at https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/good-practice-guidance-communication-public-medicines-availability-issues_en.pdf

IQVIA/EFPIA (2021). Pipeline Review 2021. Available at https://www.efpia.eu/publications/downloads/efpia/iqviaefpia-pipeline-review-2021/

LABIOTECH (2020). EU Launches Pharma Strategy, Raising Both Hopes and Questions. Article from 4 December 2020. Available at: https://www.labiotech.eu/trends-news/eu-pharma-biotech-ip/

Lee, I. and Kim, E. (2019). Factors Affecting the Outbound Open Innovation Strategies in Pharmaceutical Industry: Focus on Out-Licensing Deal. *Journal of Open Innovation: Technology, Market, and Complexity,* MDPI, Open Access Journal, 5(4), September 2019.

Malva, A.D. and Santarelli, E. (2016). Intellectual Property Rights, Distance to the Frontier, and R&D: Evidence from Microdata. *Eurasian Business Review* 6, no. 1. Available at https://link.springer.com/article/10.1007/s40821-015-0022-4

Medicines for Europe (2021). About the generics medicines group. Available at https://www.medicinesforeurope.com/generic-medicines/who-we-are/

Medicines for Europe (2016). Market overview – European generic medicines market, policy overview. Available at https://www.medicinesforeurope.com/wp-content/uploads/2016/11/Market-Review-2016-Generic-medicines-policies.pdf

Mestre-Ferrandiz, J., Sussex, J. and Towse, A. (2012). The R&D Cost of a New Medicine, Office of Health Economics, December 2012

Morgan, S., Grootendorst, P, Lexchin, J., Cunningham, C. and Greyson, D. (2011). The cost of drug development: a systematic review. *Health Policy,* April 2011

Musazzi, U., di Giorgio, D. and Minghetti, P. (2020). New regulatory strategies to manage medicines shortages in Europe. *International Journal of Pharmaceutics,* Volume 579, 15 April 2020. Available at https://www.sciencedirect.com/science/article/pii/S0378517320301551#b0055

Neves, P.C., Afonso, O., Silva, D. and Sochira, E. (2021). The link between intellectual property rights, innovation, and growth: A meta-analysis. *Economic Modelling,* 97, April 2021, pp. 196-209

Pugatch, M. and Chu, R. (2011). The strength of pharmaceutical IPRs vis-à-vis foreign direct investment in clinical research: Preliminary findings. *Journal of Commercial Biotechnology,* 17, 4.

Results Healthcare (2020). Outsourced Pharmaceutical Manufacturing 2020. Current trends and future prospect

RND (2020). Arzneimittelproduktion: Altmaier will gemeinsames EU-Projekt. Article from 25 March 2020. Available at https://www.rnd.de/politik/arzneimittel-peter-altmaier-will-gemeinsame-eu-produktion-von-medikamenten-PN24LLQJOPHFA537XVNSETWQY4.html

Thomas, B. and Chugan, P.K. (2019). Determinants of Licensing Decisions: A Study of Pharmaceutical Industry. Business, Economy and Environment: The New Normal. Eds. Shamik Shome, Parag Rijwani and Deepak Danak, Himalaya Publishing House Pvt. Ltd., Mumbai for Institute of Management, Nirma University, Ahmedabad, January 2019

Scanell, J.W., Blanckley, A., Boldon, H. and Warrington, B. (2012), Diagnosing the Decline in Pharmaceutical R&D Efficiency, *Nature Reviews, Drug Discovery,* Volume 11, March 2012

UNCTAD-ICTSD (2003). Indicators of the Relative Importance of IPRs in Developing Countries. Issue Paper No. 3, published by the International Centre for Trade and Sustainable Development (ICTSD) and the United Nations Conference on Trade and Development (UNCTAD)

Vision Research Reports (2020). Active Pharmaceutical Ingredients (API) Market 2020 Size, Global Trends, Comprehensive Research Study, Development Status, Opportunities, Future Plans, Competitive Landscape and Growth by Forecast 2027. September 2020. Available at https://bit.ly/36b8Vb3

Wakap, S. et al. (2019). Estimating point prevalence of rare diseases: analysis of the Orphanet database. *European Journal of Human Genetics,* Volume 28, pp. 165-173

WIPO (2009). Intellectual Property Rights and Pharmaceuticals: Challenges and Opportunities for Economic Research. The Economics of Intellectual Property. Published be the World Intellectual Property Organisation

Vicente, V. and Simoes, S. (2014). Manufacturing and export provisions: Impact on the competitiveness of European pharmaceutical manufacturers and on the creation of jobs in Europe. *Journal of Generic Medicines,* Vol. 11(1-2) 35-47

ANNEX

I. Pharmaceutical products list by category and combined nomenclature

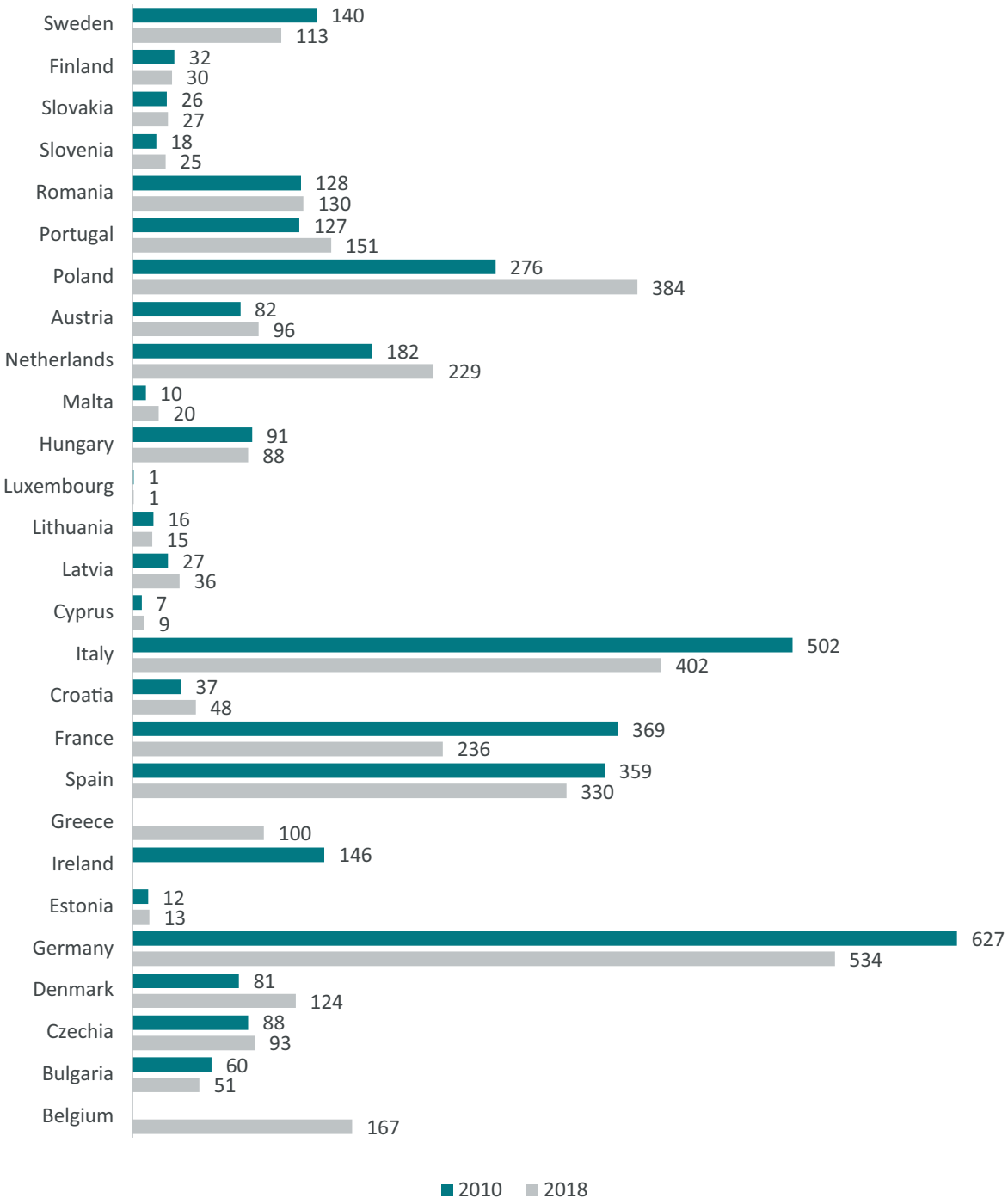
TABLE 8: PHARMACEUTICAL PRODUCTS LIST BY CATEGORY AND COMBINED NOMENCLATURE

Category	Name	CN (8 digits)
1	Finished pharmaceutical products (FPPs)	30021500; 30043100; 30043200; 30043900; 30044100; 30044200; 30044300; 30044900; 30045000; 30046000; 30049000
2	Antibiotic FPPs	30041000; 30042000
3	Vaccines for human medicine	30022000
4	Active pharmaceutical ingredients (APIs)	29146200; 29146980; 29163910; 29182100; 29182200; 29182300; 29189940; 29214600; 29214900; 29221400; 29221900; 29222900; 29223100; 29224100; 29224400; 29224920; 29225000; 29232000; 29241100; 29242400; 29242910; 29251200; 29252900; 29263000; 29319000; 29322020; 29331190; 29331990; 29332100; 29332910; 29333100; 29333200; 29333300; 29333935; 29334100; 29334910; 29335200; 29335390; 29335400; 29335500; 29335995; 29336940; 29337100; 29337200; 29337900; 29339190; 29339950; 29341000; 29342020; 29343090; 29349100; 29349990; 29359090; 29362100; 29362200; 29362300; 29362400; 29362500; 29362600; 29362700; 29362800; 29362900; 29369000; 29371100; 29371200; 29371900; 29372100; 29372200; 29372300; 29372900; 29375000; 29379000; 29381000; 29389030; 29391100; 29391900; 29392000; 29393000; 29394100; 29394200; 29394300; 29394400; 29394900; 29395100; 29395900; 29396100; 29396200; 29396300; 29396900; 29397100; 29397990; 29398000; 29420000; 30019098; 30021300
5	Antibiotic APIs	29411000; 29412080; 29413000; 29414000; 29415000; 29419000
6	Semi-finished products (SFPs)	30021400; 30031000; 30032000; 30033100; 30033900; 30034100; 30034200; 30034300; 30034900; 30036000; 30039000

Source: Guinea (2021).

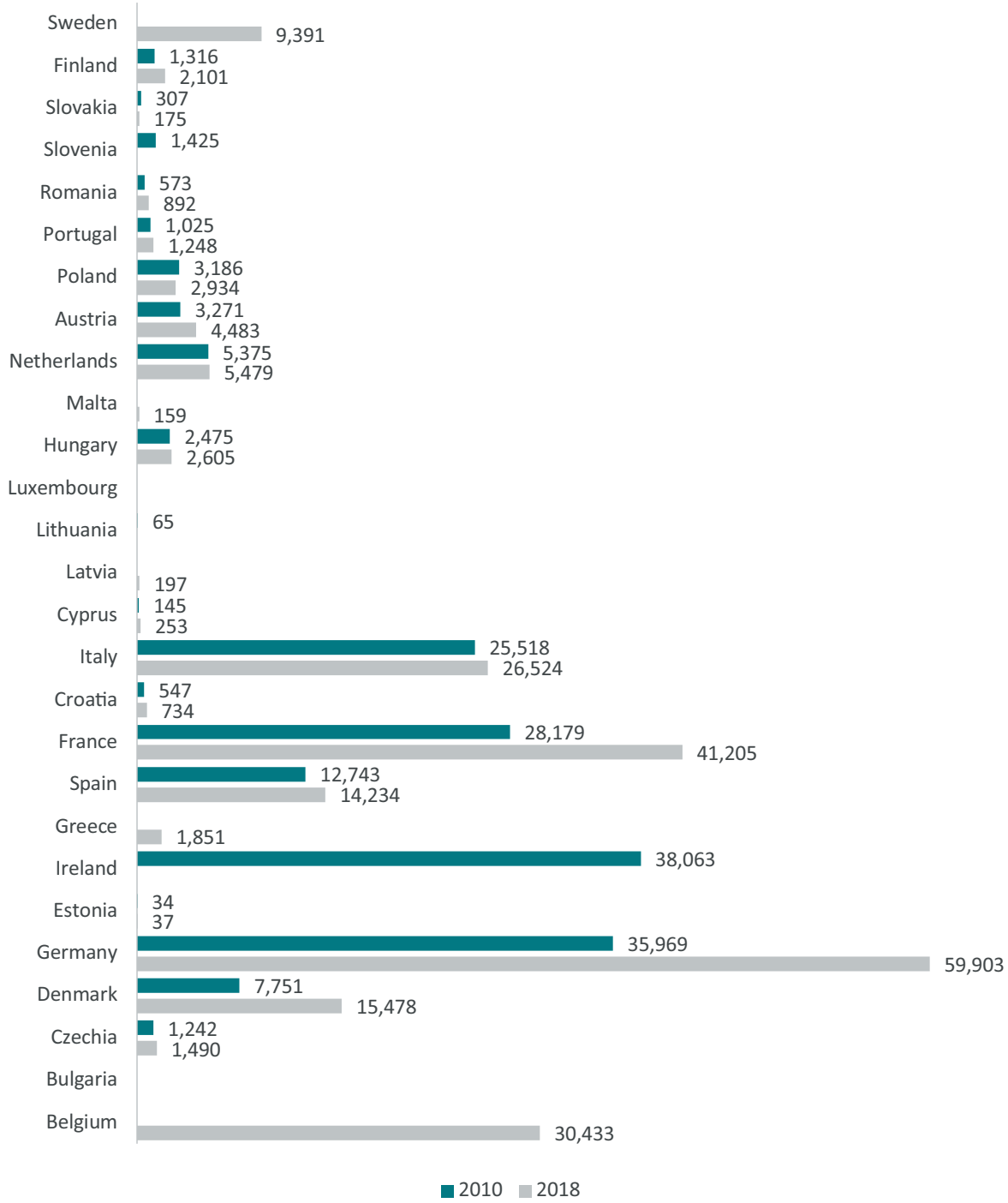
II. Production, employment and investment in the EU's pharmaceutical industry

FIGURE 15: NUMBER OF ENTERPRISES, MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS, EU27



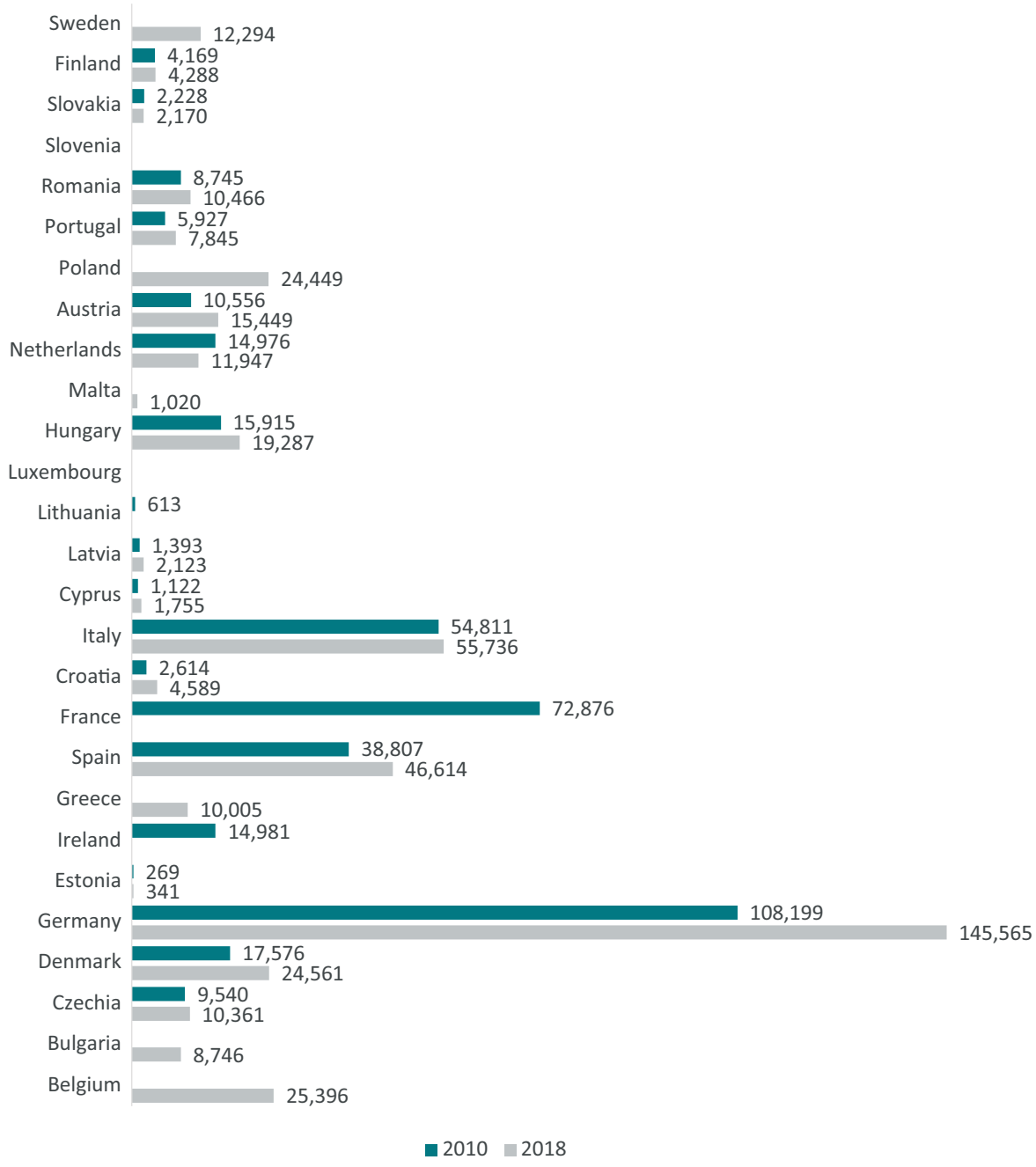
Source: Eurostat, Annual enterprise statistics for special aggregates of activities (NACE Rev. 2).

FIGURE 16: VALUE OF ANNUAL PRODUCTION, IN MILLION EUR, MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS, EU27



Source: Eurostat, Annual enterprise statistics for special aggregates of activities (NACE Rev. 2).

FIGURE 17: NUMBER OF EMPLOYEES, IN FULL-TIME EQUIVALENTS, MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS, EU27

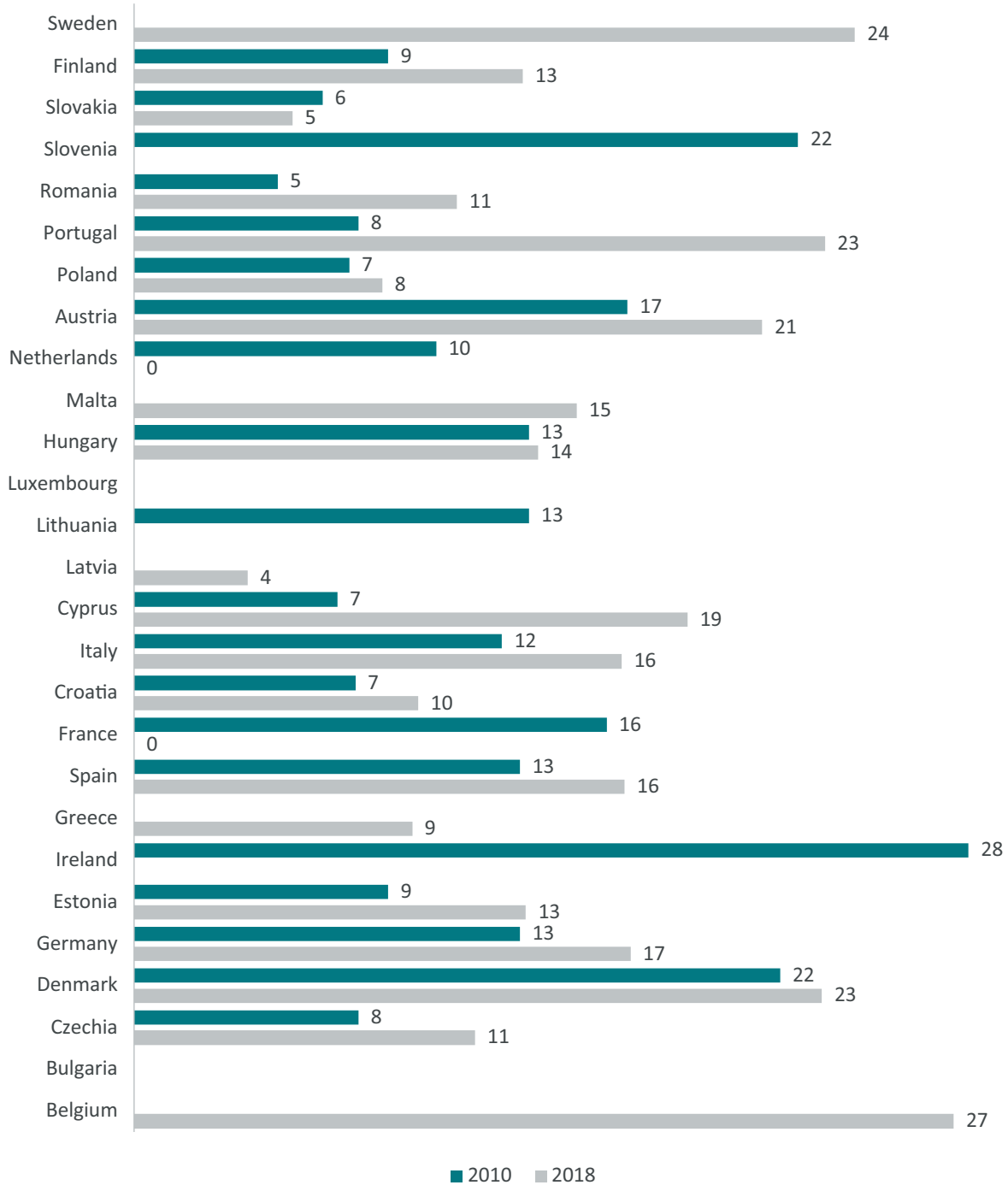


Source: Eurostat, Annual enterprise statistics for special aggregates of activities (NACE Rev. 2).

FIGURE 18: WAGES OF FULL-TIME EQUIVALENT, MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS, EU27

Source: Own calculations based on Eurostat, Annual enterprise statistics for special aggregates of activities (NACE Rev. 2).

FIGURE 19: INVESTMENT PER PERSON EMPLOYED, IN 1,000 EUR, MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS, EU27



Source: Own calculations based on Eurostat, Annual enterprise statistics for special aggregates of activities (NACE Rev. 2).

III. Value-added of EU27 pharmaceutical exports and imports, top-10 by average trade value for the period 2016 to 2020

TABLE 9: VALUE-ADDED OF EXTRA-EU PHARMACEUTICAL EXPORTS AND IMPORTS, TOP-10 BY AVERAGE TRADE VALUE FOR THE PERIOD 2016 TO 2020

EXPORTS	PRICE / QUANTITY [EUR/100kg]				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	9,895	11,133	13,746	100%	100%
300490	8,299	8,523	8,888	45%	72%
300215	n/a	n/a	222,898	18%	1%
300210	59,898	78,974	76,982	n/a	n/a
300220	48,648	71,917	105,072	7%	1%
300212	n/a	n/a	40,084	4%	2%
300439	29,526	35,048	40,569	4%	2%
3004S5	32,270	39,897	54,120	4%	1%
300420	9,522	9,198	9,188	2%	3%
300432	14,879	17,028	16,091	2%	2%
300390	5,798	7,825	21,390	2%	1%
IMPORTS	**PRICE / QUANTITY [EUR/100kg]**				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	12,323	11,615	16,756	100%	100%
300490	13,387	13,344	14,169	42%	49%
300210	53,749	70,154	83,666	n/a	n/a
300215	n/a	n/a	280,717	20%	2%
300212	n/a	n/a	21,585	6%	6%
300214	n/a	n/a	969,136	5%	0%
300390	7,112	13,384	42,035	5%	2%
300220	68,737	75,622	128,325	4%	0%
300439	47,508	37,590	42,304	3%	2%
300420	14,811	9,264	15,209	1%	2%
300290	5,510	5,895	12,638	2%	2%

Source: Own calculations based on EU Comext data. Data underlying the calculations: trade values expressed in EUR; quantity expressed in unit of 100 kg.

TABLE 10: VALUE-ADDED OF EU27-US PHARMACEUTICAL EXPORTS AND IMPORTS, TOP-10 BY AVERAGE TRADE VALUE FOR THE PERIOD 2016 TO 2020

EXPORTS	PRICE / QUANTITY [EUR/100kg]				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	36,543	36,499	38,844	100%	100%
300490	41,624	29,628	23,126	38%	71%
300215	n/a	n/a	417,911	29%	2%
300210	135,613	145,077	184,428	n/a	n/a
300220	158,163	280,728	273,818	9%	1%
300212	n/a	n/a	97,159	3%	1%
300214	n/a	n/a	2,422,938	2%	0%
300431	127,819	302,176	188,311	2%	1%
300290	45,304	44,460	85,784	3%	1%
300439	41,569	55,805	87,118	3%	1%
300440	5,219	96,273	110,946	n/a	n/a
IMPORTS	**PRICE / QUANTITY [EUR/100kg]**				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	328	52,127	70,026	100%	100%
300490	593	83,897	81,259	31%	18%
300210	440	91,714	157,983	n/a	n/a
300215	n/a	n/a	n/a	20%	5%
300212	n/a	n/a	n/a	14%	33%
300220	840	329,688	666,073	6%	2%
300214	n/a	n/a	n/a	7%	1%
300390	156	35,068	91,153	4%	6%
300290	83	18,342	35,951	5%	9%
300213	n/a	n/a	n/a	3%	0%
300420	361	72,943	59,168	1%	1%

Source: Own calculations based on EU Comext data. Data underlying the calculations: trade values expressed in EUR; quantity expressed in unit of 100 kg.

TABLE 11: VALUE-ADDED OF EU27-CHINA PHARMACEUTICAL EXPORTS AND IMPORTS, TOP-10 BY AVERAGE TRADE VALUE FOR THE PERIOD 2016 TO 2020

EXPORTS	PRICE / QUANTITY [EUR/100kg]				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	9,883	13,435	15,836	100%	100%
300490	8,993	11,837	13,790	52%	65%
300210	19,722	34,761	40,383	n/a	n/a
300215	n/a	n/a	62,232	6%	2%
300220	26,054	36,393	124,200	13%	1%
300212	n/a	n/a	21,464	5%	4%
300439	13,985	26,277	52,855	5%	2%
300432	7,296	11,355	15,668	5%	6%
300420	9,558	8,119	17,489	3%	3%
300290	8,556	22,594	31,773	2%	2%
300431	41,693	45,833	35,365	2%	1%
IMPORTS	**PRICE / QUANTITY [EUR/100kg]**				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	1,130	1,515	1,742	100%	100%
300490	4,264	7,172	12,555	29%	4%
300590	487	617	601	21%	62%
300190	307,739	448,575	530,522	25%	0%
300215	n/a	n/a	29,364	3%	1%
300510	648	829	795	7%	17%
300650	478	532	594	4%	11%
300420	1,601	2,368	2,046	2%	2%
300120	5,612	96,587	187,928	2%	0%
300210	3,733	4,511	4,284	n/a	n/a
300310	28,337	16,633	18,712	1%	0%

Source: Own calculations based on EU Comext data. Data underlying the calculations: trade values expressed in EUR; quantity expressed in unit of 100 kg.

TABLE 12: VALUE-ADDED OF EU27-INDIA PHARMACEUTICAL EXPORTS AND IMPORTS, TOP-10 BY AVERAGE TRADE VALUE FOR THE PERIOD 2016 TO 2020

EXPORTS	PRICE / QUANTITY [EUR/100kg]				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	8,022	5,106	8,880	100%	100%
300490	5,801	3,027	4,867	36%	61%
300220	38,514	33,615	74,962	24%	4%
300210	21,746	22,153	16,272	n/a	n/a
300215	n/a	n/a	24,220	8%	4%
300212	n/a	n/a	19,345	7%	4%
300431	33,442	53,176	26,288	7%	2%
300420	8,469	5,985	3,354	3%	7%
300290	31,294	4,385	6,973	3%	5%
300439	20,658	22,134	18,450	3%	2%
3004S5	27,245	17,678	19,060	n/a	n/a
IMPORTS	**PRICE / QUANTITY [EUR/100kg]**				
HS Code	2006-2010	2011-2015	2016-2020	2016-2020 share weighted by 2020 trade value	2016-2020 share weighted by 2020 traded quantity
30	3,516	3,635	3,871	100%	100%
300490	4,626	4,221	4,069	85%	79%
300420	4,857	4,611	5,577	3%	2%
300339	11,999	8,620	7,347	3%	2%
300390	1,335	966	1,120	2%	7%
300215	n/a	n/a	155,987	0%	0%
300410	3,711	4,315	3,889	3%	3%
300590	686	826	840	1%	4%
300660	908	5,633	5,612	0%	0%
300210	43,919	43,609	74,674	n/a	n/a
300440	3,863	3,196	3,668	n/a	n/a

Source: Own calculations based on EU Comext data. Data underlying the calculations: trade values expressed in EUR; quantity expressed in unit of 100 kg.

IV. EU pharmaceutical manufacturing

TABLE 13: EU SOLD PRODUCTION, EXPORT, IMPORTS AND TRADE BALANCE OF PHARMACEUTICAL PRODUCTS IN 2019, BY PRODUCT CATEGORY, VALUE IN BILLION EUR

Product code and description	Sold production 2019	Exports 2019	Imports 2019	Trade balance
21103110 - Lactones (excluding coumarin, methylcoumarins and ethylcoumarins)	n/a	n/a	n/a	n/a
21106050 - Human blood; animal blood prepared for therapeutic, prophylactic or diagnostic uses; cultures of micro-organisms; toxins (excluding yeasts)	n/a	n/a	n/a	n/a
21202120 - Antisera and other blood fractions	n/a	n/a	n/a	n/a
21202140 - Vaccines for human medicine	n/a	n/a	n/a	n/a
21201380 - Other medicaments of mixed or unmixed products, p.r.s., n.e.c.	64.4	86.5	37.0	49.6
21202125 - Antisera, other immunological products which are directly involved in the regulation of immunological processes and other blood fractions	27.6	47.2	27.3	19.9
21202145 - Vaccines for human medicine	17.7	12.5	2.4	10.1
21201270 - Medicaments containing corticosteroid hormones, their derivatives and structural analogues, put up in measured doses or for retail sale	11.0	12.4	2.7	9.7
21201260 - Medicaments containing insulin but not antibiotics, for therapeutic or prophylactic uses, put up in measured doses or for retail sale	7.8	3.3	0.0	3.3
21103159 - Compounds containing a pyrimidine ring (whether or not hydrogenated) or piperazine ring in the structure (excluding malonylurea (barbituric acid) and its derivatives)	6.0	6.3	3.9	2.3
21201360 - Medicaments containing vitamins, provitamins, derivatives and intermixtures thereof, for therapeutic or prophylactic uses, put up in measured doses or for retail sale	5.1	0.8	0.2	0.6
21201180 - Medicaments of other antibiotics, p.r.s.	4.9	4.4	1.5	3.0
21201320 - Other medicaments for therapeutic or prophylactic uses, of HS 3003, n.p.r.s.	3.9	4.5	4.7	- 0.2
21202340 - Opacifying preparations for X-ray examinations; diagnostic reagents designed to be administered to the patient	3.1	1.4	0.1	1.3
21105200 - Hormones, prostaglandins, thromboxanes and leukotrienes, natural or reproduced by synthesis; derivatives and structural analogues thereof, including chain modified polypeptides, used primarily as hormones	3.1	4.0	6.3	- 2.3
21105400 - Antibiotics	2.9	1.2	2.9	- 1.7
21201340 - Medicaments of alkaloids or derivatives thereof, p.r.s.	2.8	2.5	0.4	2.1

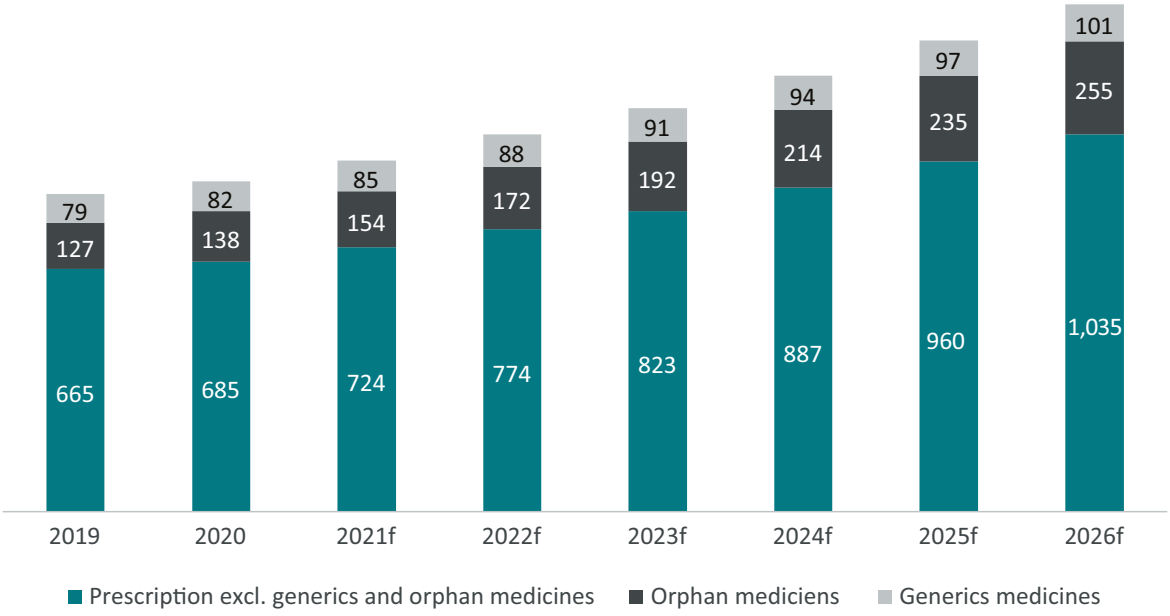
Product code and description	Sold pro-duction 2019	Exports 2019	Imports 2019	Trade balance
21106040 - Glands and other organs or substances for therapeutic or prophylactic use, n.e.c. (excluding blood and extracts of glands or other organs)	2.2	0.7	1.2	- 0.6
21105100 - Provitamins and vitamins, natural or reproduced by synthesis (including natural concentrates), derivatives thereof used primarily as vitamins, and intermixtures of the foregoing, whether or not in any solvent	2.0	1.1	1.3	- 0.2
21202200 – Chemical contraceptive preparations based on hormones or spermicides	1.9	2.5	0.0	2.4
21201250 – Medicaments containing hormones but not antibiotics, for therapeutic or prophylactic uses, not put up in measured doses or for retail sale (excluding insulin)	1.9	0.1	0.2	- 0.1
21202160 – Vaccines for veterinary medicine	1.8	1.1	0.2	0.9
21201310 – Medicaments of alkaloids or derivatives thereof, n.p.r.s.	1.4	0.0	0.0	0.0
21106055 – Human blood; animal blood prepared for therapeutic, prophylactic or diagnostic uses; cultures of micro-organisms; toxins (excluding yeasts)	1.2	3.5	1.2	2.3
21201150 – Medicaments of other antibiotics, n.p.r.s.	1.2	0.1	0.0	0.1
21202420 – Adhesive dressings or similar articles; impregnated or coated with pharmaceutical substances; or put up in forms for retail sale	1.0	0.6	0.4	0.1
21102060 – Acyclic amides and their derivatives, and salts thereof (including acyclic carbamates)	0.9	0.2	0.3	- 0.0
21105300 – Glycosides and vegetable alkaloids, natural or reproduced by synthesis, and their salts, ethers, esters and other derivatives	0.9	0.6	0.4	0.1
21202440 – Wadding, gauze, etc., with pharmaceutical substances, p.r.s., n.e.c.	0.8	0.6	0.7	- 0.1
21202320 – Blood-grouping reagents	0.7	0.1	0.1	0.0
21201160 – Medicaments of penicillins, streptomycins or derivatives thereof, in doses or p.r.s.	0.6	0.9	0.1	0.8
21102040 – Quaternary ammonium salts and hydroxides; lecithins and other phosphoaminolipids, whether or not chemically defined	0.6	0.3	0.3	0.0
21103130 – Compounds containing an unfused pyrazole ring (whether or not hydrogenated) in the structure	0.6	0.7	0.7	- 0.0
21102070 – Cyclic amides and their derivatives, and salts thereof (including cyclic carbamates) (excluding ureines and their derivatives, and salts thereof)	0.5	0.5	1.6	- 1.1
21103200 – Sulphonamides	0.5	3.7	1.9	1.8
21104000 – Sugars, pure (excluding glucose, etc.); sugar ethers and salts, etc.	0.4	0.2	0.1	0.1

Product code and description	Sold production 2019	Exports 2019	Imports 2019	Trade balance
21201130 – Medicaments containing penicillins or derivatives thereof, with a penicillanic acid structure, or streptomycins or their derivatives, for therapeutic or prophylactic uses, n.p.r.s.	0.4	0.0	0.0	- 0.0
21103119 – Lactones (excluding phenolphthalein; 1-Hydroxy-4-[1-(4-hydroxy-3-methoxycarbonyl-1-naphthyl)-3-oxo-1H,3H-benzo[de]isochromen-1-yl]-6-octadecyloxy-2-naphthoic acid; 3¿-Chloro-6¿-cyclohexylaminospiro[isobenzofuran-1(3H),9¿-xanthen]-3-one; 6¿-(N-Ethyl-p-toluidino)-2¿-methylspiro[isobenzofuran-1(3H),9¿-	0.4	n/a	n/a	n/a
21103170 – Compounds containing an unfused triazine ring (whether or not hydrogenated) in the structure (excluding melamine)	0.2	0.2	0.3	- 0.2
21106020 – Extracts of glands or other organs or of their secretions (for organo-therapeutic uses)	0.2	0.1	0.1	0.0
21102020 – Glutamic acid and its salts	0.1	0.0	0.0	- 0.0
21102010 – Lysine and its esters, and salts thereof	0.1	0.0	0.3	- 0.3
21103180 – Compounds containing a phenothiazine ring-system (whether or not hydrogenated); not further fused	0.1	0.0	0.0	0.0
21202460 - First-aid boxes and kits	0.1	0.0	0.1	- 0.0
21101070 – Esters of salicylic acid and their salts (excluding of O-acetylsalicylic acid)	0.0	0.0	0.0	- 0.0
21101050 – O-acetylsalicylic acid; its salts and esters	0.0	0.0	0.0	0.0
21202430 – Sterile surgical catgut	0.0	0.1	0.2	- 0.1
21101030 – Salicylic acid and its salts	0.0	0.0	0.0	0.0
21103117 – Phenolphthalein; 1-Hydroxy-4-[1-(4-hydroxy-3-methoxycarbonyl-1-naphthyl)-3-oxo-1H,3H-benzo[de] isochromen-1-yl]-6-octadecyloxy-2-naphthoic acid; 3'-Chloro-6'-cyclohexylaminospiro[isobenzofuran-1(3H),9'-xanthen]-3-one; 6'-(N-Ethyl-p-toluidino)-2'-methylspiro[isobenzofuran-1(3H),9'-xanthen]-3-one; Meth	0.0	n/a	n/a	n/a
21103140 – Hydantoin and its derivatives	0.0	0.0	0.0	- 0.0
21103155 – Malonylurea (barbituric acid) and its derivatives, and salts thereof	0.0	0.0	0.0	- 0.0
21201230 – Medicaments containing insulin but not antibiotics, for therapeutic or prophylactic uses, not put up in measured doses or for retail sale	0.0	0.0	0.0	- 0.0
Total	**183.4**	**205.1**	**101.4**	**103.7**

Source: EU's Prodcom database.

V. Market size of pharmaceutical products

FIGURE 20: WORLDWIDE TOTAL PRESCRIPTION DRUG SALES, 2019 TO 2026, IN BILLION USD



Source: EvaluatePharma (2020). World Preview 2020. Forecasted numbers are provided for the period 2021 to 2026.

TABLE 14: TOTAL PHARMACEUTICAL SALES AND SALES OF GENERICS IN THE EU27, IN MILLION EUR, EX-FACTORY PRICES

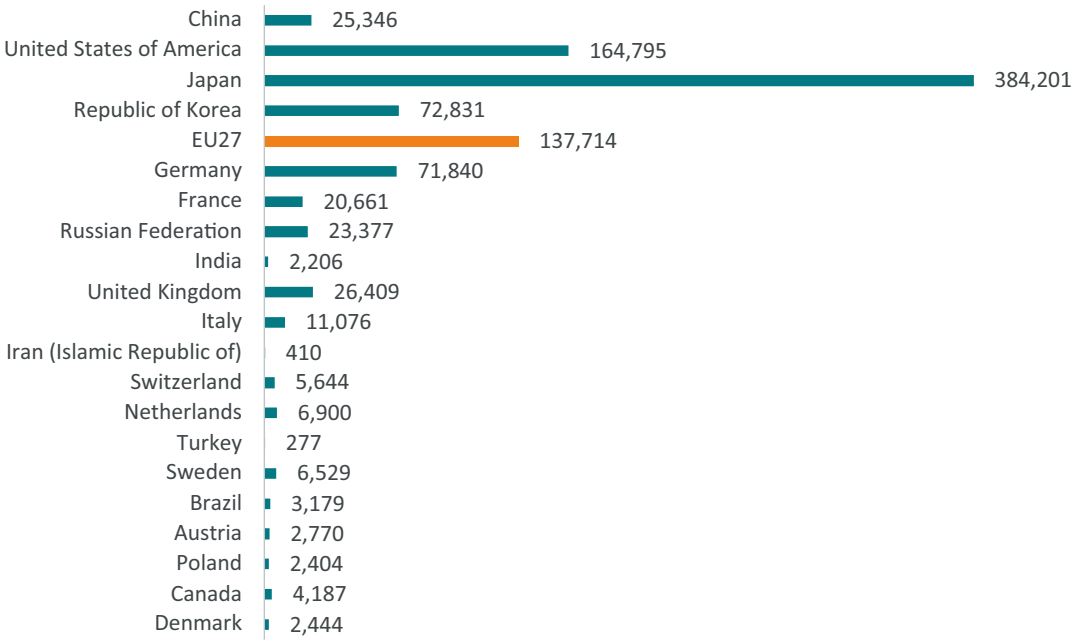
	Total pharmaceutical sales at ex-factory prices in 2018	Total pharmaceutical sales at ex-factory prices in 2017	Generics sales in percentage of total pharmaceutical sales in 2017	2018 generics sales estimate on basis of 2017 generics shares on total sales (value at ex-factory prices)
Austria	4,213	3,657	40%	1,698
Belgium	5,067	4,771	17%	841
Bulgaria	1,089	1,026	48%	523
Croatia	764	710	43%	329
Cyprus*	189	180	26%	48
Czech Republic*	2,578	1,639	26%	670
Denmark	2,584	2,445	31%	804
Estonia	301	290	19%	58
Finland	2,373	2,333	26%	617
France	28,419	28,362	19%	5,456
Germany	32,525	30,815	31%	10,148
Greece	5,141	4,890	23%	1,157
Hungary	2,242	2,225	38%	843
Ireland	2,013	1,977	16%	318
Italy	26,945	25,959	59%	15,898
Latvia*	277	225	26%	72
Lithuania	602	538	26%	157
Luxembourg	n/a	n/a	n/a	n/a
Malta*	77	77	26%	20
Netherlands	5,086	5,052	18%	936
Poland	6,352	5,744	53%	3,360
Portugal	3,056	2,983	23%	691
Romania	2,522	2,547	28%	706
Slovakia	1,287	1,216	20%	254
Slovenia	613	587	25%	154
Spain	16,028	15,595	22%	3,510
Sweden	3,990	3,917	20%	806
Total EU27 ex Luxembourg	**156,333**	**149,760**	**32%**	**50,072**

Source: Sales data for 2018 were taken from EFPIA (2019). Sales data for 2017 were taken from EFPIA (2018). Estimates for the market shares of generics sales in total sales were taken from EFPIA (2018). * indicates that the market share estimates for generics were not available for these countries and were replaced by the median estimate calculated for countries with available data (26%).

VI. Patents as technology innovation indicators

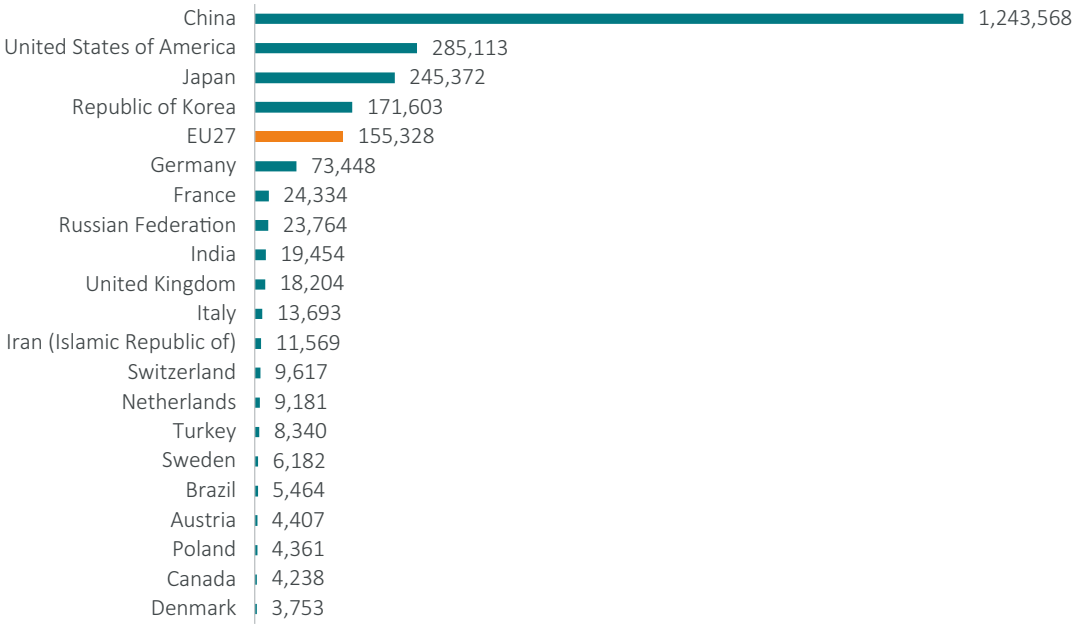
a. Overall patenting activity across industries

FIGURE 21: 2000 – FILINGS MADE BY APPLICANTS AT THEIR HOME OFFICE



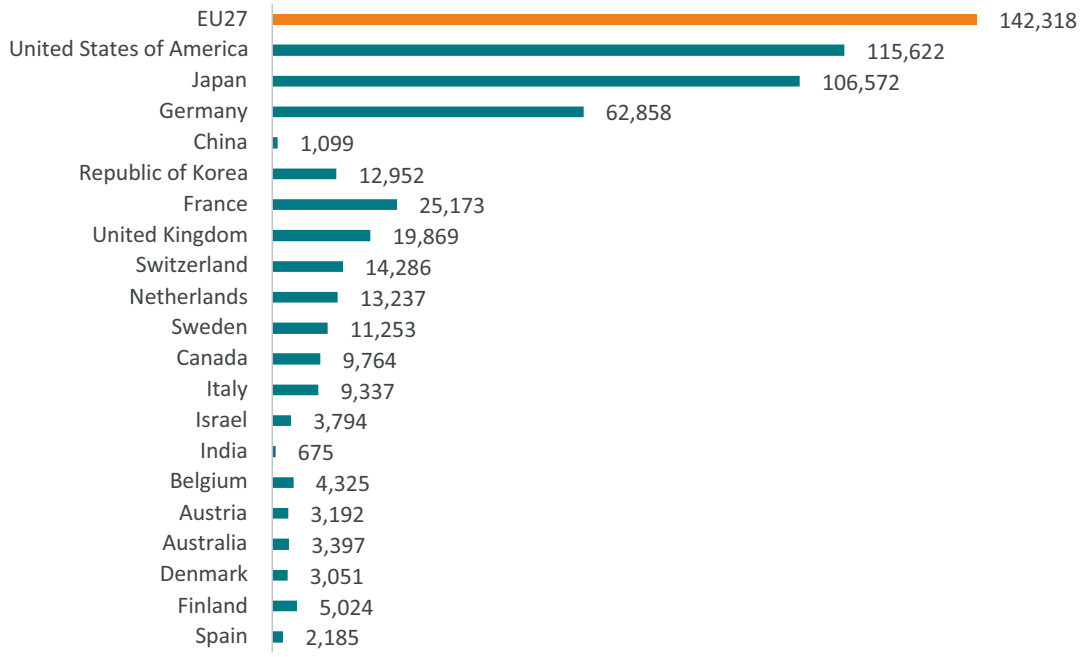
Source: WIPO.

FIGURE 22: 2019 – FILINGS MADE BY APPLICANTS AT THEIR HOME OFFICE



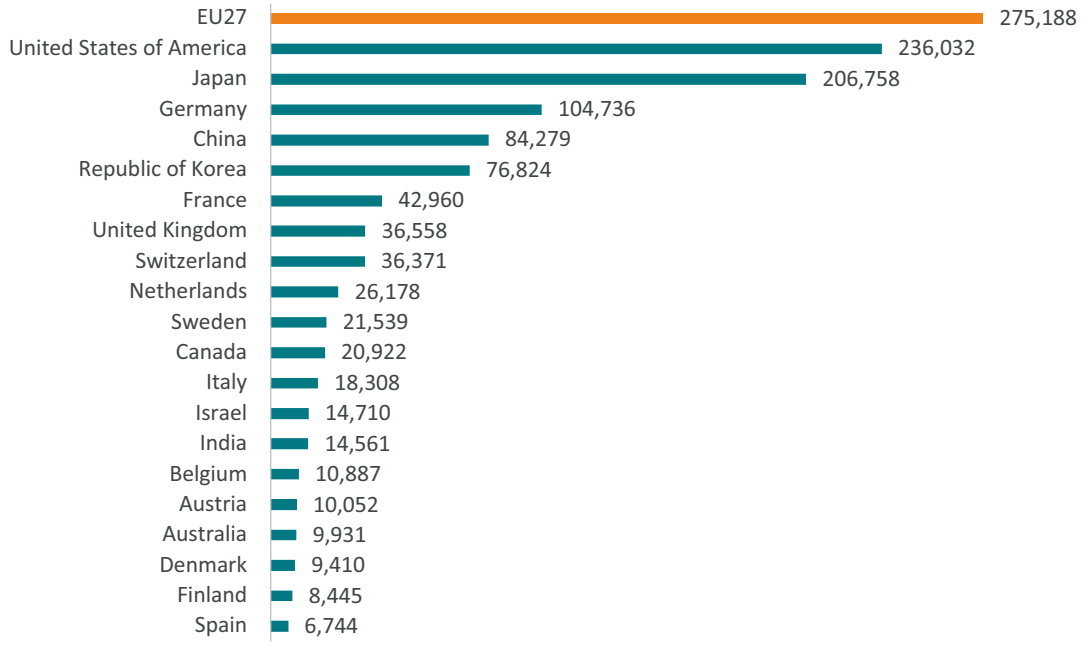
Source: WIPO.

FIGURE 23: 2000 – FILINGS ABROAD FROM THE APPLICANT'S ORIGIN



Source: WIPO.

FIGURE 24: 2019 – FILINGS ABROAD FROM THE APPLICANT'S ORIGIN



Source: WIPO.

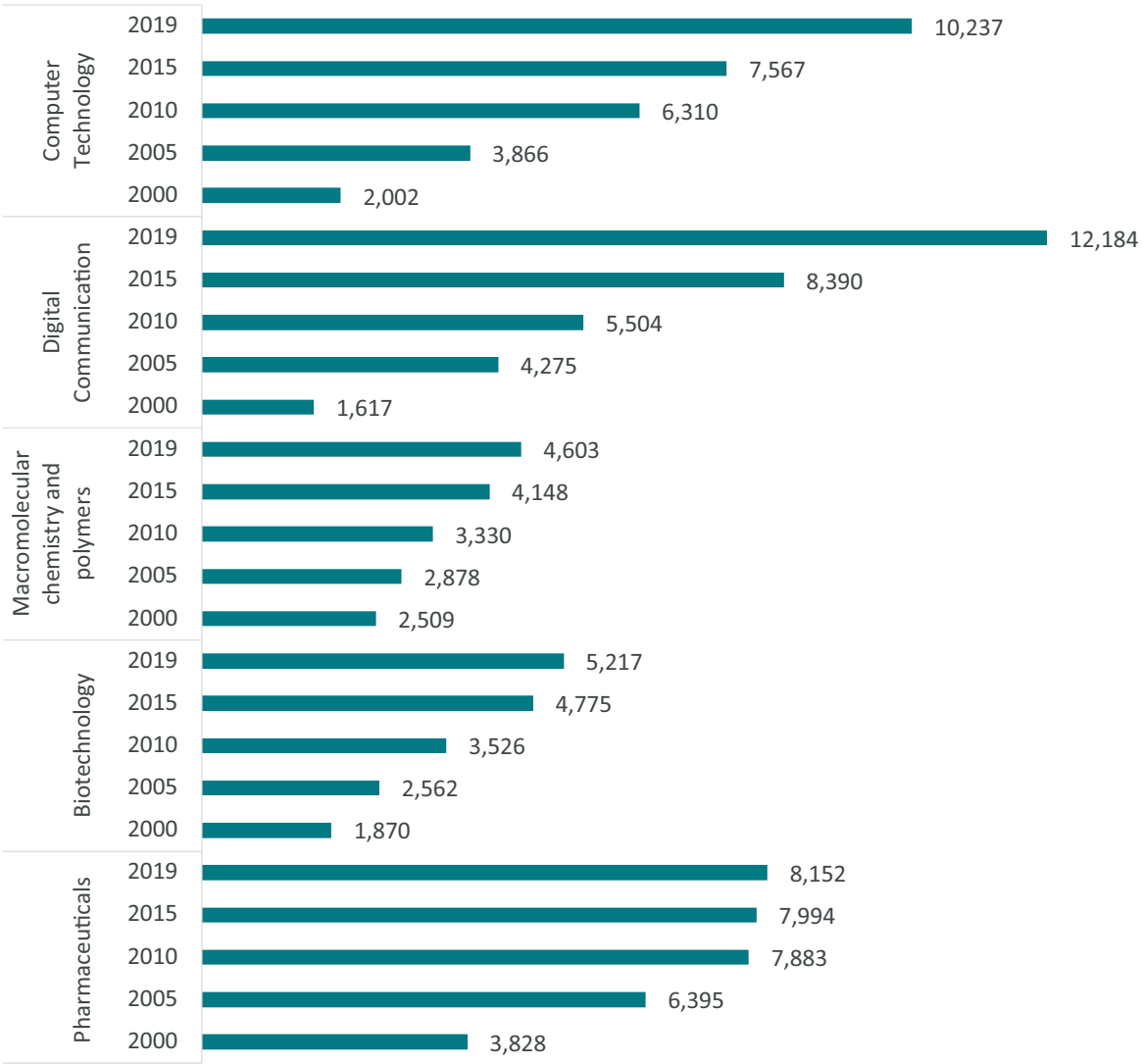
b. Patent grants and publications by technology

TABLE 15: PATENT GRANTS IN BIOTECHNOLOGY SECTORS, ABSOLUTES AND ANNUAL GROWTH RATES, 2000-2019

		2000	2005	2010	2015	2019	CAGR 2000-2005	CAGR 2005-2010	CAGR 2005-2010	CAGR 2010-2015	CAGR 2015-2019
1	China	122	659	1,870	5,076	8,618	40.1%	40.1%	23.2%	22.1%	14.1%
2	United States of America	4,212	3,682	4,887	7,079	8,301	-2.7%	-2.7%	5.8%	7.7%	4.1%
3	Republic of Korea	307	966	848	1,700	2,244	25.8%	25.8%	-2.6%	14.9%	7.2%
4	Japan	1,551	1,403	2,219	2,597	2,184	-2.0%	-2.0%	9.6%	3.2%	-4.2%
5	Germany	585	901	1,230	1,468	1,501	9.0%	9.0%	6.4%	3.6%	0.6%
6	Switzerland	210	327	450	778	1,024	9.3%	9.3%	6.6%	11.6%	7.1%
7	France	375	513	565	908	949	6.5%	6.5%	1.9%	10.0%	1.1%
8	United Kingdom	385	418	593	649	786	1.7%	1.7%	7.2%	1.8%	4.9%
9	Netherlands	225	247	340	572	604	1.9%	1.9%	6.6%	11.0%	1.4%
10	Denmark	135	198	303	413	493	8.0%	8.0%	8.9%	6.4%	4.5%
11	Russian Federation	230	920	390	420	487	32.0%	32.0%	-15.8%	1.5%	3.8%
12	Belgium	70	125	208	297	410	12.3%	12.3%	10.7%	7.4%	8.4%
13	Canada	212	222	280	267	290	0.9%	0.9%	4.8%	-0.9%	2.1%
14	Sweden	92	146	145	174	224	9.7%	9.7%	-0.1%	3.7%	6.5%
15	Italy	132	111	191	208	211	-3.4%	-3.4%	11.5%	1.7%	0.4%
16	Australia	80	111	173	220	206	6.8%	6.8%	9.3%	4.9%	-1.6%
17	Spain	77	110	193	221	200	7.4%	7.4%	11.9%	2.7%	-2.5%
18	Israel	49	75	116	182	190	8.9%	8.9%	9.1%	9.4%	1.1%
19	Poland	8	15	22	97	129	13.4%	13.4%	8.0%	34.5%	7.4%
20	Austria	48	59	103	97	126	4.2%	4.2%	11.8%	-1.2%	6.8%
21	EU27	1,870	2,562	3,526	4,775	5,217	6.5%	6.5%	6.6%	6.3%	2.2%
22	Top 20	9,105	11,208	15,126	23,423	29,177	4.2%	4.2%	6.2%	9.1%	5.6%
23	Total	9,331	11,609	15,784	24,360	30,257	4.5%	4.5%	6.3%	9.1%	5.6%

Source: WIPO.

FIGURE 25: TOTAL NUMBER OF PATENTS GRANTS BY TECHNOLOGY, EU27 APPLICANT ORIGIN, 2000-2019



Source: WIPO. Indicators: total count by applicant's origin (equivalent count). WIPO statistics database. Last updated: January 2021.

VII. Scenario analysis

TABLE 16: ESTIMATED CHANGES IN THE OVERALL ANNUAL PRODUCTION OF PHARMACEUTICALS, EU MEMBER STATES AND EU27, BY SCENARIO

Country	Observed number of employees (2018)	Observed production value per employee in million EUR (2018)	Observed overall production in million EUR (2018)	Observed production value per employee, 1st quartile	Estimated annual production – Scenario 1	Percentage change	Observed production value per employee, 2nd quartile (median)	Estimated annual production – Scenario 1	Percentage change	Observed production value per employee, 3rd quartile	Estimated annual production – Scenario 1	Percentage change
Belgium	28,278	1.1	30,433	0.1	3,782	-88%	0.2	4,491	-85%	0.4	11,389.9	-63%
Bulgaria	8,814			0.1	1,179		0.2	1,400		0.4	3,550.1	
Czechia	10,494	0.1	1,490	0.1	1,404	-6%	0.2	1,667	12%	0.4	4,226.8	184%
Denmark	25,306	0.6	15,478	0.1	3,385	-78%	0.2	4,019	-74%	0.4	10,192.8	-34%
Germany	157,424	0.4	59,903	0.1	21,055	-65%	0.2	25,002	-58%	0.4	63,407.6	6%
Estonia	346	0.1	37	0.1	46	26%	0.2	55	49%	0.4	139.4	279%
Ireland				0.1			0.2			0.4		
Greece	10,095	0.2	1,851	0.1	1,350	-27%	0.2	1,603	-13%	0.4	4,066.1	120%
Spain	47,341	0.3	14,234	0.1	6,332	-56%	0.2	7,519	-47%	0.4	19,068.1	34%
France			41,205	0.1			0.2		-100%	0.4		-100%
Croatia	4,859	0.2	734	0.1	650	-11%	0.2	772	5%	0.4	1,957.1	167%
Italy	65,852	0.4	26,524	0.1	8,807	-67%	0.2	10,459	-61%	0.4	26,524.0	0%
Cyprus	1,755	0.1	253	0.1	235	-7%	0.2	279	10%	0.4	706.9	180%
Latvia	2,225	0.1	197	0.1	298	51%	0.2	353	79%	0.4	896.2	355%
Lithuania				0.1			0.2			0.4		
Luxembourg				0.1			0.2			0.4		
Hungary	19,479	0.1	2,605	0.1	2,605	0%	0.2	3,094	19%	0.4	7,845.8	201%
Malta	1,033	0.2	159	0.1	138	-13%	0.2	164	3%	0.4	416.1	161%
Netherlands	13,124	0.4	5,479	0.1	1,755	-68%	0.2	2,084	-62%	0.4	5,286.1	-4%
Austria	16,550	0.3	4,483	0.1	2,213	-51%	0.2	2,628	-41%	0.4	6,666.0	49%
Poland	25,090	0.1	2,934	0.1	3,356	14%	0.2	3,985	36%	0.4	10,105.8	244%
Portugal	7,856	0.2	1,248	0.1	1,051	-16%	0.2	1,248	0%	0.4	3,164.3	154%
Romania	10,507	0.1	892	0.1	1,405	58%	0.2	1,669	87%	0.4	4,232.0	374%
Slovenia			:	0.1			0.2			0.4		
Slovakia	2,185	0.1	175	0.1	292	67%	0.2	347	99%	0.4	880.1	404%
Finland	4,684	0.4	2,101	0.1	626	-70%	0.2	744	-65%	0.4	1,886.6	-10%
Sweden	12,799	0.7	9,391	0.1	1,712	-82%	0.2	2,033	-78%	0.4	5,155.2	-45%
EU27	**602,315**	**0.5**	**298,632**	**0.1**	**80,556**	**-73%**	**0.2**	**95,660**	**-68%**	**0.4**	**242,601.6**	**-19%**

Source: Own estimations.

TABLE 17: ESTIMATED CHANGES IN INVESTMENT IN INTANGIBLES IN THE PHARMACEUTICAL INDUSTRY, EU MEMBER STATES AND EU27, BY SCENARIO

Country	Observed number of employees (2018)	Observed investment in intangibles per person employed in 1,000 EUR (2018)	Observed investment in intangibles in million EUR (2018)	Observed investment in intangibles per employee, 1st quartile	Estimated annual investment in intangibles – Scenario 1	Percentage change	Observed investment in intangibles per employee, 2nd quartile (median)	Estimated annual investment in intangibles – Scenario 2	Percentage change	Observed investment in intangibles per employee, 3rd quartile	Estimated annual investment in intangibles – Scenario 3	Percentage change
Belgium	28,278	27.4	777	10.5	296	-62%	14.2	400	-49%	19.1	541	-30%
Bulgaria	8,814			10.5	92		14.2	125		19.1	169	
Czechia	10,494	11.4	123	10.5	110	-11%	14.2	148	21%	19.1	201	63%
Denmark	25,306	23.0	582	10.5	265	-54%	14.2	358	-38%	19.1	484	-17%
Germany	157,424	16.6	2,615	10.5	1,649	-37%	14.2	2,228	-15%	19.1	3,011	15%
Estonia	346	13.1	5	10.5	4	-21%	14.2	5	6%	19.1	7	44%
Ireland				10.5			14.2			19.1		
Greece	10,095	9.3	94	10.5	106	12%	14.2	143	52%	19.1	193	105%
Spain	47,341	16.4	777	10.5	496	-36%	14.2	670	-14%	19.1	905	16%
France			1,645	10.5		-100%	14.2		-100%	19.1		-100%
Croatia	4,859	9.5	47	10.5	51	8%	14.2	69	45%	19.1	93	96%
Italy	65,852	16.3	1,075	10.5	690	-36%	14.2	932	-13%	19.1	1,259	17%
Cyprus	1,755	18.5	32	10.5	18	-43%	14.2	25	-23%	19.1	34	4%
Latvia	2,225	3.8	8	10.5	23	177%	14.2	31	275%	19.1	43	407%
Lithuania				10.5			14.2			19.1		
Luxembourg				10.5			14.2			19.1		
Hungary	19,479	13.5	263	10.5	204	-22%	14.2	276	5%	19.1	373	42%
Malta	1,033	14.8	15	10.5	11	-29%	14.2	15	-4%	19.1	20	29%
Netherlands	13,124			10.5	137		14.2	186		19.1	251	
Austria	16,550	21.0	350	10.5	173	-50%	14.2	234	-33%	19.1	317	-9%
Poland	25,090	8.3	210	10.5	263	25%	14.2	355	69%	19.1	480	128%
Portugal	7,856	23.1	184	10.5	82	-55%	14.2	111	-40%	19.1	150	-18%
Romania	10,507	10.8	114	10.5	110	-4%	14.2	149	30%	19.1	201	76%
Slovenia				10.5			14.2			19.1		
Slovakia	2,185	5.3	12	10.5	23	97%	14.2	31	167%	19.1	42	260%
Finland	4,684	13.0	61	10.5	49	-19%	14.2	66	9%	19.1	90	47%
Sweden	12,799	24.1	338	10.5	134	-60%	14.2	181	-46%	19.1	245	-28%
EU27	**602,315**	**17.7**	**10,709**	**10.5**	**6,309**	**-41%**	**14.2**	**8,523**	**-20%**	**19.1**	**11,519**	**8%**

Source: Own estimations.

TABLE 18: ESTIMATED CHANGES IN R&D SPENDING IN THE PHARMACEUTICAL INDUSTRY, EU MEMBER STATES AND EU27, BY SCENARIO

Country	Observed number of employees (2018)	Observed R&D spending per person employed in 1,000 EUR (2017/2018)	Observed R&D spending in million EUR (2017)	Observed investment per employee, 1st quartile	Estimated annual R&D spending – Scenario 1	Percentage change	Observed R&D spending per employee, 2nd quartile (median)	Estimated annual R&D spending – Scenario 2	Percentage change	Observed R&D spending per employee, 3rd quartile	Estimated annual R&D spending – Scenario 3	Percentage change
Belgium	28,278	124.1	3,508	9.6	272	-92%	23.2	657	-81%	48.4	1,370	-61%
Bulgaria	8,814			9.6	85		23.2	205		48.4	427	
Czechia	10,494	7.3	77	9.6	101	31%	23.2	244	217%	48.4	508	560%
Denmark	25,306	64.5	1,632	9.6	243	-85%	23.2	588	-64%	48.4	1,226	-25%
Germany	157,424	43.9	6,918	9.6	1,513	-78%	23.2	3,658	-47%	48.4	7,625	10%
Estonia	346			9.6	3		23.2	8		48.4	17	
Ireland			305	9.6		-100%	23.2		-100%	48.4		-100%
Greece	10,095	4.2	42	9.6	97	131%	23.2	235	458%	48.4	489	1064%
Spain	47,341	24.2	1,147	9.6	455	-60%	23.2	1,100	-4%	48.4	2,293	100%
France			4,451	9.6		-100%	23.2		-100%	48.4		-100%
Croatia	4,859	8.2	40	9.6	47	17%	23.2	113	182%	48.4	235	488%
Italy	65,852	23.2	1,530	9.6	633	-59%	23.2	1,530	0%	48.4	3,189	108%
Cyprus	1,755	48.4	85	9.6	17	-80%	23.2	41	-52%	48.4	85	0%
Latvia	2,225			9.6	21		23.2	52		48.4	108	
Lithuania				9.6			23.2			48.4		
Luxembourg				9.6			23.2			48.4		
Hungary	19,479	9.0	176	9.6	187	6%	23.2	453	157%	48.4	943	436%
Malta	1,033			9.6	10		23.2	24		48.4	50	
Netherlands	13,124	48.9	642	9.6	126	-80%	23.2	305	-53%	48.4	636	-1%
Austria	16,550	17.8	294	9.6	159	-46%	23.2	385	31%	48.4	802	173%
Poland	25,090	13.6	340	9.6	241	-29%	23.2	583	71%	48.4	1,215	257%
Portugal	7,856	12.7	100	9.6	76	-24%	23.2	183	83%	48.4	380	280%
Romania	10,507	9.6	101	9.6	101	0%	23.2	244	142%	48.4	509	404%
Slovenia			180	9.6		-100%	23.2		-100%	48.4		-100%
Slovakia	2,185			9.6	21		23.2	51		48.4	106	
Finland	4,684	42.9	201	9.6	45	-26%	23.2	109	79%	48.4	227	13%
Sweden	12,799	86.3	1,104	9.6	123	-64%	23.2	297	-12%	48.4	620	-44%
EU27	**602,315**	**38.0**	**22,873**	**9.6**	**5,790**	**-46%**	**23.2**	**13,994**	**31%**	**48.4**	**29,172**	**28%**

Source: Own estimations.

TABLE 19: ESTIMATED CHANGES IN EMPLOYMENT IN PHARMACEUTICAL PRODUCTION, EU MEMBER STATES AND EU27, BY SCENARIO, CACP-BASED ESTIMATES

						Scenario 1			Scenario 2			Scenario 3		
Country	Observed number of employees (2018)	Observed total personnel costs in million EUR (2018)	Observed average costs of personnel in EUR (2018)	Observed overall production in million EUR (2018)	Observed share of total personnel costs in total production value	Estimated total costs of personnel in million EUR, based on estimated overall production, 1st quartile	Percentage change	Estimated number of employees – Scenario 1 (CACP)	Estimated total costs of personnel in million EUR, based on estimated overall production, 2nd quartile	Percentage change	Estimated number of employees – Scenario 2 (CACP)	Estimated total costs of personnel in million EUR, based on estimated overall production, 3rd quartile	Percentage change	Estimated number of employees – Scenario 3 (CACP)
Belgium	28,278	3,087.7	109,191	30,433	10%	383.7	-88%	3,514.2	455.67	-85%	4,173.1	1,155.6	-63%	10,583.3
Bulgaria	8,814	87.8	9,961					-			-	-	-100%	-
Czechia	10,494	254.5	24,252	1,490	17%	239.8	-6%	9,887.5	284.75	12%	11,741.4	722.2	184%	29,777.1
Denmark	25,306	2,680.9	105,939	15,478	17%	586.2	-78%	5,533.7	696.16	-74%	6,571.3	1,765.5	-34%	16,665.3
Germany	157,424	14,025.9	89,096	59,903	23%	4,929.8	-65%	55,330.9	5,854.12	-58%	65,705.5	14,846.5	6%	166,633.9
Estonia	346	9.1	26,301	37	25%	11.4	26%	435.1	13.59	49%	516.7	34.5	279%	1,310.3
Ireland														
Greece	10,095	383.2	37,959	1,851	21%	279.5	-27%	7,363.4	331.92	-13%	8,744.1	841.8	120%	22,175.6
Spain	47,341	2,701.0	57,054	14,234	19%	1,201.5	-56%	21,058.7	1,426.77	-47%	25,007.2	3,618.4	34%	63,420.1
France		8,282.9		41,205	20%									
Croatia	4,859	134.9	27,763	734	18%	119.5	-11%	4,303.8	141.89	5%	5,110.7	359.8	167%	12,961.2
Italy	65,852	4,781.0	72,602	26,524	18%	1,587.5	-67%	21,866.2	1,885.20	-61%	25,966.2	4,781.0	0%	65,852.0
Cyprus	1,755	52.9	30,142	253	21%	49.1	-7%	1,629.5	58.33	10%	1,935.0	147.9	180%	4,907.4
Latvia	2,225	49.2	22,112	197	25%	74.3	51%	3,359.3	88.21	79%	3,989.2	223.7	355%	10,116.8
Lithuania														
Luxembourg														
Hungary	19,479	586.3	30,099	2,605	23%	586.3	0%	19,479.0	696.23	19%	23,131.3	1,765.7	201%	58,662.7
Malta	1,033	34.9	33,785	159	22%	30.3	-13%	895.9	35.94	3%	1,063.9	91.2	161%	2,698.1
Netherlands	13,124	960.2	73,164	5,479	18%	307.6	-68%	4,204.2	365.27	-62%	4,992.5	926.3	-4%	12,661.3
Austria	16,550	1,320.3	79,776	4,483	29%	651.9	-51%	8,172.0	774.18	-41%	9,704.3	1,963.4	49%	24,610.8
Poland	25,090	572.0	22,798	2,934	19%	654.3	14%	28,699.5	776.97	36%	34,080.7	1,970.5	244%	86,431.2
Portugal	7,856	256.6	32,663	1,248	21%	216.1	-16%	6,615.6	256.60	0%	7,856.0	650.8	154%	19,923.4
Romania	10,507	168.3	16,018	892	19%	265.2	58%	16,554.5	314.89	87%	19,658.5	798.6	374%	49,855.3
Slovenia														
Slovakia	2,185	45.9	21,007	175	26%	76.8	67%	3,655.0	91.18	99%	4,340.3	231.2	404%	11,007.3
Finland	4,684	284.8	60,803	2,101	14%	84.9	-70%	1,396.8	100.86	-65%	1,658.7	255.8	-10%	4,206.7
Sweden	12,799	1,069.5	83,561	9,391	11%	195.0	-82%	2,333.1	231.51	-78%	2,770.6	587.1	-45%	7,026.4
EU27	**602,315**	**43,978.2**	**73,015**	**298,632**	**15%**	**11,863.1**	**-73%**	**162,474.6**	**14,087.49**	**-68%**	**192,938.9**	**35,726.9**	**-19%**	**489,306.6**

Source: Own estimations.

TABLE 20: ESTIMATED CHANGES IN EMPLOYMENT IN PHARMACEUTICAL PRODUCTION, EU MEMBER STATES AND EU27, BY SCENARIO, CLCI-BASED ESTIMATES

Country	Labour cost per hour in industry (except construction, compensation of employees plus taxes minus subsidies) in EUR	Average number of usual weekly hours	Estimated annual labour cost in industry (except construction) in EUR	Estimated number of employees – Scenario 1 (CLCI)	Estimated number of employees – Scenario 2 (CLCI)	Estimated number of employees – Scenario 3 (CLCI)
Belgium	44.7	37.2	86,468	4,438	5,270	13,365
Bulgaria	6	40.4	12,605	-	-	-
Czechia	14.1	39.9	29,255	8,197	9,734	24,685
Denmark	48.5	33.4	84,235	6,960	8,265	20,959
Germany	41.8	34.7	75,424	65,361	77,616	196,840
Estonia	13.3	37.9	26,212	437	518	1,315
Ireland	33.4	36.5	63,393	-	-	-
Greece	17.2	41.8	37,386	7,476	8,878	22,516
Spain	24.9	37.5	48,555	24,745	29,385	74,521
France	40.2	37.4	78,181	-	-	-
Croatia	10.3	39.6	21,210	5,634	6,690	16,966
Italy	29.7	36.9	56,988	27,857	33,080	83,894
Cyprus	13.6	39	27,581	1,781	2,115	5,363
Latvia	10.4	38.6	20,875	3,558	4,226	10,717
Lithuania	9.9	38.8	19,974	-	-	-
Luxembourg	35.9	37.4	69,818	-	-	-
Hungary	10.6	39.3	21,662	27,066	32,140	81,511
Malta	13.2	39.6	27,181	1,114	1,322	3,354
Netherlands	39.9	30.3	62,866	4,893	5,810	14,735
Austria	39.8	36.4	75,333	8,654	10,277	26,062
Poland	10.7	40.1	22,312	29,325	34,824	88,315
Portugal	12.8	39.2	26,092	8,282	9,835	24,941
Romania	7.3	39.8	15,108	17,551	20,842	52,858
Slovenia	19.5	39.5	40,053	-	-	-
Slovakia	13.7	39.9	28,425	2,701	3,208	8,135
Finland	37	36.5	70,226	1,209	1,436	3,642
Sweden	41.4	36.3	78,147	2,495	2,963	7,513
EU27	**28.8**	**37**	**55,411**	**214,093**	**254,235**	**644,759**

Source: Own estimations.