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CHARACTERISTICS OF INNOVATION IN THE PHARMACEUTICAL INDUSTRY

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LIST OF ABBREVIATIONS

angl. – angleško

AI – (sl. umetna inteligenca); artificial intelligence

BRICS – (sl. Brazilija, Rusija, Indija, Kitajska in Južna Afrika); Brazil, Russia, India, China and South Africa

CEEDD – (sl. Center odličnosti za eksterno odkrivanje zdravil); Centre of Excellence for External Drug Discovery

CIS – (sl. raziskava o inovacijah v Skupnosti); Community Innovation Survey

COVID-19 – (sl. koronavirusna bolezen 2019); Coronavirus Disease 2019

CTI – (sl. Center za terapevtske inovacije); Center for Therapeutic Innovation

C21 – (sl. NACE koda za proizvodnjo farmacevtskih surovin in preparatov); NACE code for Manufacture of basic pharmaceutical products and pharmaceutical preparations

DMAIC – (sl. definicija-mera-analiza-izboljšava-kontrola); Define-Measure-Analyse-Improve-Control

EC – (sl. Evropska komisija); European Commission

EFTA – (sl. Evropsko združenje za prosto trgovino); European Free Trade Association

EFPIA – (sl. Evropska federacija farmacevtske industrije in združenj); European Federation of Pharmaceutical Industries and Associations

EU – (sl. Evropska unija); European Union

EU-15 – (sl. Avstrija, Belgija, Danska, Finska, Francija, Nemčija, Grčija, Irska, Italija, Luksemburg, Nizozemska, Portugalska, Španija, Švedska, Združeno kraljestvo); Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and United Kingdom

EU-27 – (sl. Avstrija, Belgija, Bolgarija, Ciper, Češka republika, Danska, Estonija, Finska, Francija, Nemčija, Grčija, Irska, Italija, Latvija, Litva, Luksemburg, Madžarska, Malta, Nizozemska, Poljska, Portugalska, Romunija, Slovaška, Slovenija, Španija, Švedska, Združeno kraljestvo); Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom

EU-28 – (sl. Avstrija, Belgija, Bolgarija, Ciper, Češka republika, Danska, Estonija, Finska, Francija, Nemčija, Grčija, Hrvaška, Irska, Italija, Latvija, Litva, Luksemburg, Madžarska, Malta, Nizozemska, Poljska, Portugalska, Romunija, Slovaška, Slovenija, Španija, Švedska, Združeno kraljestvo); Austria, Belgium, Bulgaria, Croatia Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and United Kingdom

EU-5 – (sl. Nemčija, Francija, Italija, Združeno kraljestvo in Španija); Germany, France, Italy, Great Britain and Spain

FDA – (sl. Uprava za živila in zdravila); Food and Drug Administration

FR – (sl. Francija); France

FTE – (sl. ekvivalent polne zaposlitve); full-time equivalent

GE – (sl. Nemčija); Germany

GDP – (sl. bruto domači proizvod); gross domestic product

GMP – (sl. dobra proizvodna praksa); good manufacturing practices

GSK – (sl. GlaxoSmithKline); GlaxoSmithKline

HIV – (sl. virus človeške imunske pomanjkljivosti); Human Immunodeficiency Virus

ICH – (sl. Mednarodna konferenca o usklajevanju tehničnih zahtev za registracijo zdravil za uporabo v humani medicini); International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

I – (sl. glavne inovacijske dejavnosti); innovation core activities

IMS – (sl. IMS Health (družba), pri čemer je IMS kratica za Mednarodno zdravstvno statistiko); IMS Health Incorporated, where IMS stands for Intercontinental Medical Statistics

IPR – (sl. pravice intelektualne lastnine); intellectual property rights

ISO – (sl. Mednarodna organizacija za standardizacijo); International Organization for Standardization

IT – (sl. informacijska tehnologija); information technology

ITA – (sl. Italija); Italy

KLEMS – (sl. kapital, delo, energija, materiali in storitve); capital (K), labour (L), energy (E), materials (M) and service (S)

M – (sl. proizvodnja farmacevtskih surovin in preparatov); manufacture of basic pharmaceutical products and preparations

MIST – (sl. Mehika, Indonezija, Južna Koreja in Turčija); Mexico, Indonesia, South Korea and Turkey

MIT – (sl. Inštitut za tehnologijo v Massachusettsu); Massachusetts Institute of Technology

M&A – (sl. združenja in prevzemi); mergers and acquisitions

NACE – (sl. nomenklatura gospodarskih dejavnosti); Nomenclature of Economic Activities

NASA – (sl. Nacionalna zrakoplovna in vesoljska uprava); National Aeronautics and Space Administration

NDF – (sl. nova oblika odmerka); new dosage form

NI – (sl. nova indikacija); new indication

NME – (sl. nova molekulska struktura); new molecular entities

NPV – (sl. neto sedanja vrednost); net present value

NSI – (sl. državni institut za statistiko); National Statistical Institute

NTD – (sl. zapostavljene tropske bolezni); neglected tropical diseases

OECD – (sl. Organizacija za gospodarsko sodelovanje in razvoj); Organisation for Economic Co-operation and Development

OTC – (sl. trgovanje na prostem trgu); over-the-counter

PIC/S – (sl. Shema sodelovanja farmacevtskih inšpekcij); Pharmaceutical Inspection Co-operation Scheme

P-O (drugs) – (sl. (zdravila) na recept); prescription-only (drugs)

ROI – (sl. donosnost naložb); return on investment

ROW – (sl. preostali svet); rest of the world

R&D – (sl. raziskave in razvoj); research and development

SARS – (sl. sindrom akutnega oteženega dihanja); Severe Acute Respiratory Syndrome

SI – (sl. Slovenija); Slovenia

SL – (sl. slovensko); Slovenian

TQM – (sl. celostno obvladovanje kakovosti); total quality management

US – (sl. Združene države Amerike); United States

VAT – (sl. davek na dodano vrednost); value-added tax

WIIW – (sl. Dunajski insitut za mednarodne ekonomske študije); Vienna Institute for International Economic Studies

4P – (sl. štiri temeljne kategorije inovativnosti); four core categories of innovations

INTRODUCTION

The pharmaceutical industry or pharma involves the discovery, development, manufacturing and sale of drugs by public and private companies (Kitsis, 2011). Driven by an ageing population and novelty drugs that treat rare medical conditions, pharma is growing globally. Nevertheless, it has gone through several transitions in recent decades forcing, it to reshape its operating model and footprint (Pan & Gautam, 2016). As a result, two distinguishing segments were formed, i.e. innovation (originators) and generic.

Compared to other industries, pharma approaches research and development (hereinafter: R&D) uniquely and is driven by it. In addition, the pharmaceutical industry is characterised by the following: high regulation, product complexity quality requirements, a protracted drug-development process, intensive investment and patents that facilitate market exclusivity (Grabowski, 2004). As patent expirations could result in lost revenue, pharma companies seek to engage in partnerships, traditional collaborations, virtual R&D, crowdsourcing, innovation centres or open-source innovations (Schuhmacher, Gassmann & Hinder, 2016). Besides product and process innovation, companies are forced to focus on other types of innovation if they want to remain competitive (e.g. management innovation, business-model innovation and product-protection innovation) (Song & Han, 2016).

Due to the above, the pharmaceutical industry is seen as more successful than other industries. A structured representation of data regarding the pharmaceutical industry could thus provide prospects for other industries, as well as a better understanding for pharma itself of how pharmaceutical companies are changing and adapting their business models in order to maximise their innovative output, what strategies and future trends are important today, and how these activities are reflected in the amounts of funds companies invest in their R&D activities and human resources. With this in mind, this thesis aims to apply a top-down research approach that includes an analysis at the global level, the level of the European Union (hereinafter: the EU) and at the national level, i.e. Slovenia. The research questions to be answered are as follows:

Q1: What are the main characteristics of the pharmaceutical industry and its innovation?

Q2: What trends have shaped the industry in recent decades, what trends are expected to emerge in the future and how will they shape the business models of pharmaceutical companies and the industry as a whole?

Q3: How is the Slovenian pharmaceutical industry comparable to leading European countries in terms of innovation investments and the strategies it pursues?

Q4: How is value-added per employee related to investments in R&D?

Accordingly, the first section introduces a theoretical overview of the pharmaceutical industry at various levels, from the global level to Slovenia. The second section presents development of trends in different time periods, as well as future prospects. In addition, innovation is defined and innovation specifics in the pharmaceutical industry are outlined in the third section. The fourth section describes R&D and innovation in the pharmaceutical industry, while the fifth section shifts the analysis to an empirical perspective. Based on CIS data, R&D and innovation are analysed for Germany, France, Italy and Slovenia, and compared with EU data. Based on the EU KLEMS database, the comparative performance of the pharmaceutical industry with value-added and innovation at the aggregate level is examined.

1 CHARACTERISTICS OF THE PHARMACEUTICAL INDUSTRY

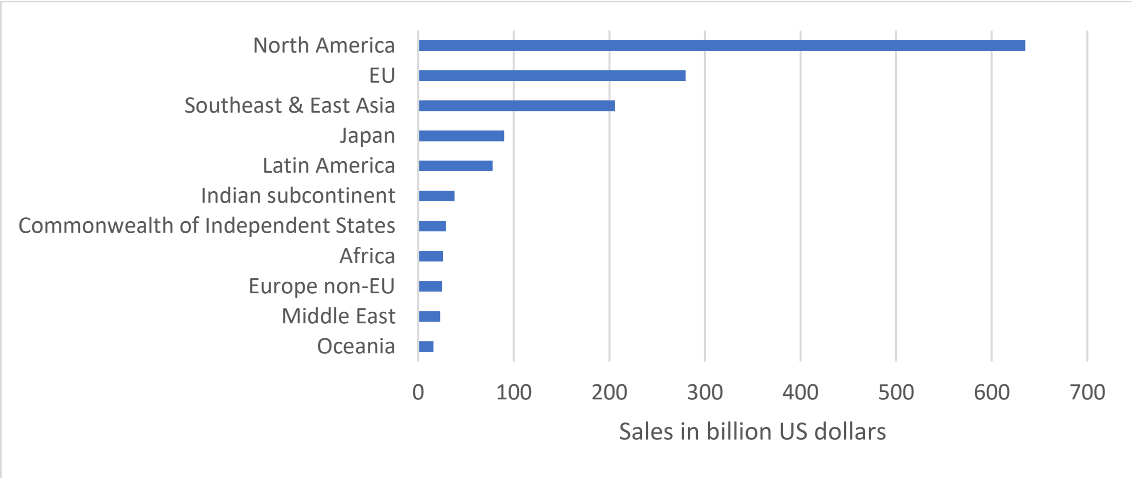
The pharmaceutical industry is defined as an industry that involves the discovery, development, manufacture and sale of drugs by both public and private companies. The pharmaceutical industry is widely known as pharma, a synonym used herein that the reader should bear in mind throughout the thesis (Kitsis, 2011). Globally, the pharmaceutical translation of science into successful products has improved life expectancy by two months, on average, each year (Munos, 2009). Its beginnings date back to the 19th century when health concerns about different diseases stimulated an interest in the healing powers and properties of minerals, plants and animals (Ascher, Bogdan, Dreszer & Zhou, 2015). Today, pharma is a globally growing industry, driven by an ageing population and novelty drugs used to treat rare medical conditions.

1.1 Global pharmaceutical industry

The last two decades have brought rapid growth to the global pharmaceutical market. In 2001, it was valued at around $290 billion in terms of global revenue, with this value tripling and settling at around $1.2 trillion in 2018 (IQVIA, 2019d). Throughout this period, the list of the largest pharmaceutical markets has remained unchanged, with the United States (hereinafter: the US) generating more than $460 billion in sales and thus earning its place at the top of the list in 2018. The US was followed by emerging markets (AstraZeneca, 2019b), which are defined as prosperous, developing countries in which investment opportunities come with high risk, but are expected to result in high income (Tannoury & Attieh, 2017). They comprised countries such as Russia, China, India and Brazil, which have experienced the fastest increase in sales and generated $211 billion in 2018 alone. Europe generated approximately $196 billion, while the remaining $110 billion in sales was recorded in the rest of the world (hereinafter: ROW) (AstraZeneca, 2019a).

Pharmaceutical sales in Brazil, Russia, India, China, and South Africa (hereinafter: BRICS), and Mexico, Indonesia, South Korea and Turkey (hereinafter: MIST) have doubled over the last five years (Tannoury & Attieh, 2017), while revenue is projected to grow further in the coming years. Figure 1 presents projected global sales for 2022 by region.

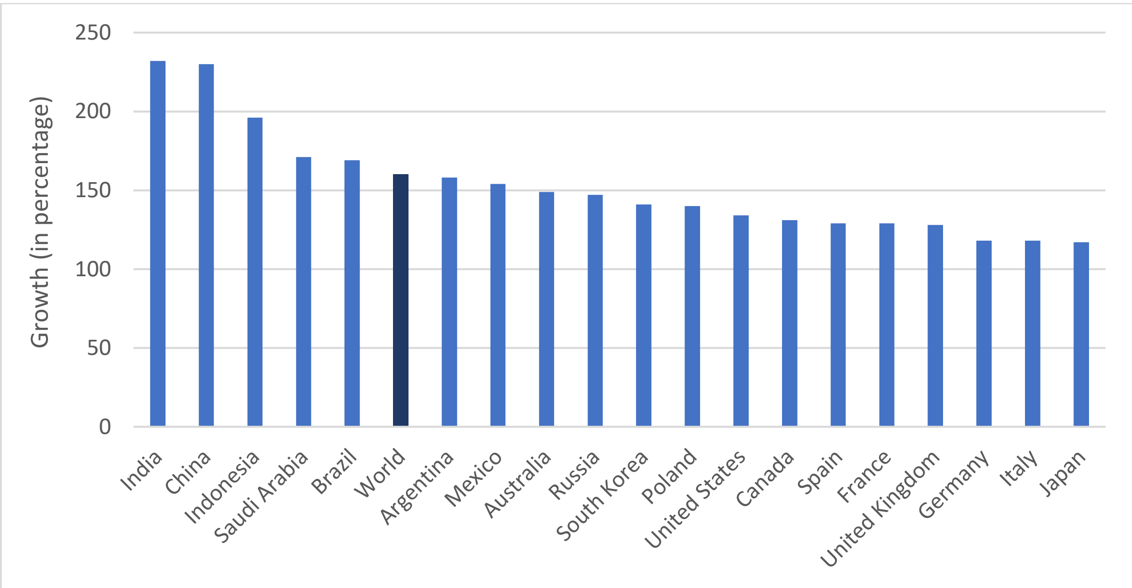
Figure 1: Projected global pharmaceutical sales for 2022 by region (in billion US dollars)



Source: AstraZeneca (2019b).

Although the US is expected to maintain its position as the largest market, its growth is projected to settle below the global average by 2030, most likely due to new generic products, the migration to over-the-counter medication, increased costs for customers and safety concerns. The three countries that are expected to thrive the most are India, China and Indonesia (Figure 2).

Figure 2: Global forecast of pharmaceutical sector growth from 2017 to 2030 by country (in %)



Source: Torreya Partners & OECD (2017).

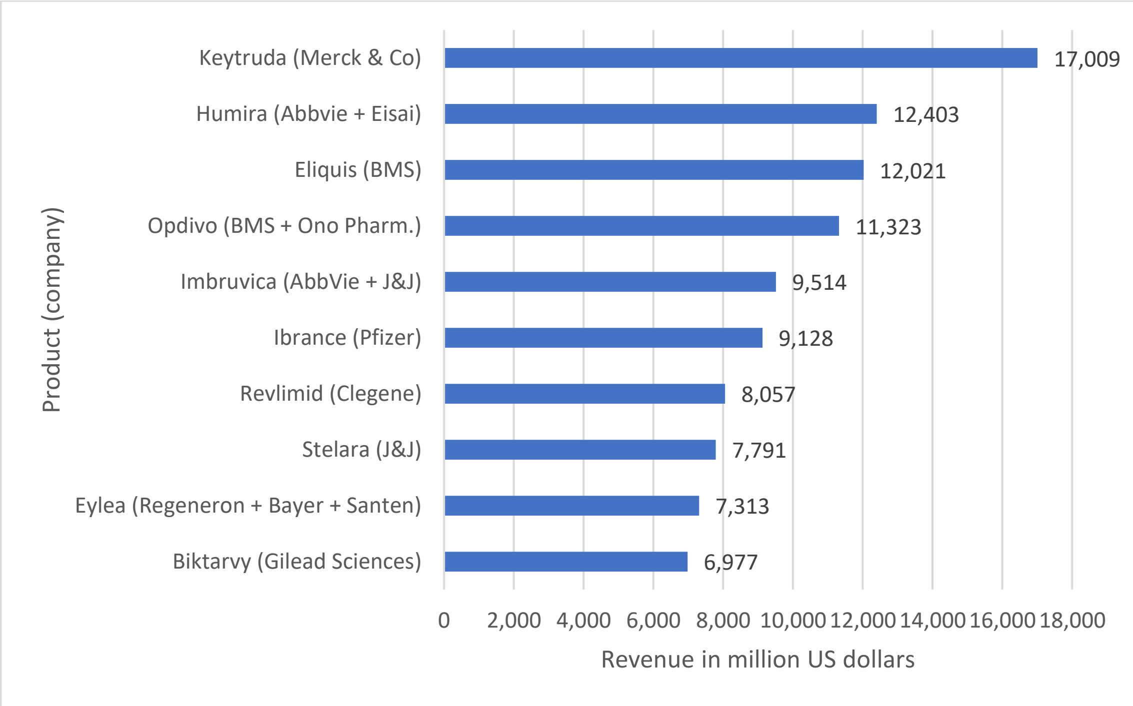
The top global pharmaceutical companies in 2018 were Pfizer, Merck and Johnson & Johnson from the US, and Novartis, Roche and Sanofi from Europe (AstraZeneca, 2019a). According to sales, oncology drugs, antidiabetics and respiratory drugs were the top three global therapeutic drug categories, generating $99.3 billion, $78.7 billion and $60.5 billion, respectively. In oncologic therapeutic drug development, drugs for non-small cell lung cancer and breast cancer were among the leaders (IQVIA, 2019e). In the period from 2014 to 2018, the highest compound annual growth in spending in the main therapeutic categories was recorded in autoimmune drugs (15.4%), followed by drugs for diabetes (15.2%), oncology (13.1%) and blood coagulation (13.1%), immunology (11.7%) and respiratory diseases (5.7%), antibiotics and vaccines (2.3%), and pain medicines (0.9%). In the same observed period, mental health and hypertension drug categories recorded negative compound annual growth rates of -2.6% for mental health drugs and -3.6% for hypertension drugs (IQVIA, 2019c).

Pharmaceutical products can be divided into two major groups, i.e. prescription and over-the-counter (hereinafter: OTC) or prescription-free medicines. OTC drugs represent a steadily growing market that generated $110 billion in global revenue in 2018, with Switzerland being the largest consumer of OTC remedies in that year, while the biggest players were Johnson & Johnson, GlaxoSmithKline (hereinafter: GSK) and Bayer AG. These medicines include digestives and intestinal remedies (15%), analgesic (21%), cold and cough remedies (30%), skin treatments (16%) and vitamins and minerals (18%). These products are accompanied by very low research and development costs, and have significantly lower margins than prescription drugs. There is, however, a high degree of consumer loyalty (e.g. to aspirin, paracetamol, ibuprofen and others), which makes them an attractive category. Sales and development in this segment are highly influenced by the overall global improvement in access to healthcare and pharmaceuticals, consumer behaviour and attitudes, and the increasing use of the internet and smartphones (e.g. online sales accounted for 43% of total sales in South Korea). Trends tend to drive their development towards products with higher proportions of natural ingredients, connected devices and eHealth (Brinckmann, 2019).

Globally, the top three drugs in terms of revenue generated in 2018 were as follows: Humira, which is produced by the US company AbbVie and generated almost $20 billion in revenue, a significant increase from the $18.4 billion generated the year before; Eliquis produced by Bristol-Myers Squibb and Pfizer, which generated slightly less than half of the sales of Humira; and Revlimid produced by Clegene. The reason behind the heavy use of Humira lies in the range of medical conditions it can treat, from rheumatoid and psoriatic arthritis to a number of autoimmune diseases. As a blockbuster drug (with annual global revenue in excess of $1 billion), Humira has a very significant effect on its producer AbbVie. Because Humira alone generates over 60% of the company's revenue and almost 80% of its revenue is generated by its top three products, the company could be exposed to the risk of heavy revenue losses from the expiration of patents. Biosimilars of Humira are already available on the market and will slowly increase their market shares. The aforementioned drug is thus expected to suffer from a sharp decrease in revenue until 2024 (Genetic Engineering and Biotechnology News, 2020). Potential losses from the expiration of patents are discussed further in section 4.2.

Figure 3 presents projections of the top 10 pharmaceutical products by revenue for 2024. It is interesting to observe how Humira is projected to occupy second place. The amount of revenue it generates, however, is expected to be a combination of revenue generated by its original producer AbbVie and the revenue projected to be generated by a generic equivalent made by the Japanese company Eisai.

Figure 3: Projected top 10 global pharmaceutical products by revenue in 2024 (in million US dollars)

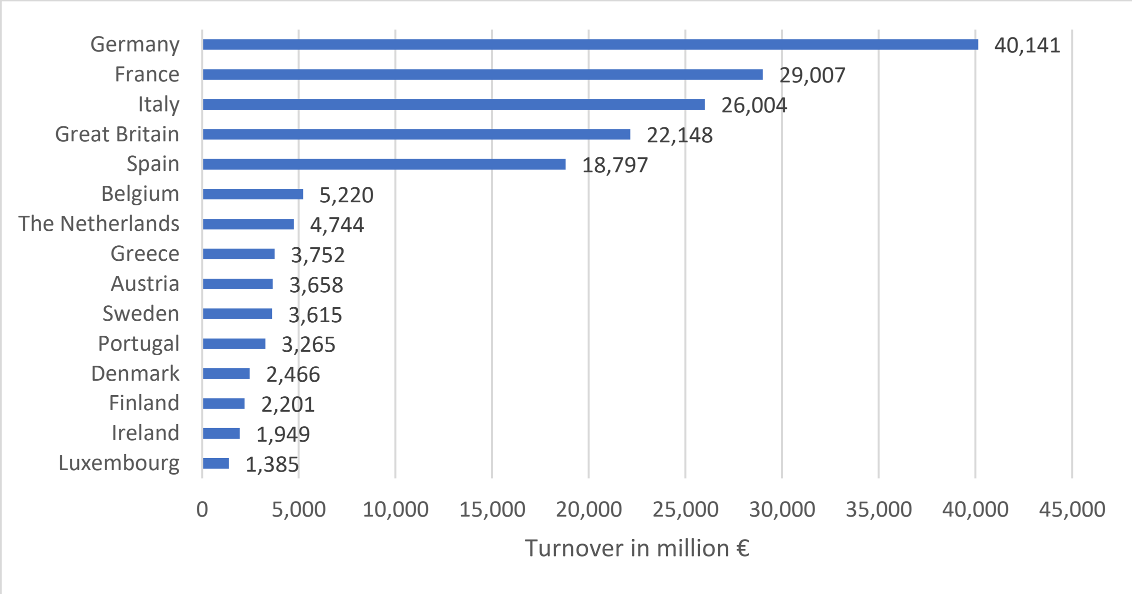


Source: Evaluate (2019f).

1.2 Pharmaceutical industry in Europe

The top five leading European pharmaceutical markets in 2017 were Germany, France, Italy, Great Britain and Spain (see Figure 4), which are also the five largest European countries and referred to as the EU-5 (IMS Health, 2018b). As seen in Figure 4, other EU countries lag far behind the EU-5. Poland was the biggest pharmaceutical market in Central and Eastern Europe in 2017, with more than €6 billion in turnover, and was followed by Romania (€2,700 million) and the Czech Republic (€2,300 million). Slovenia ranked 8th in the region with more than half a billion euros (€587 million) in revenue (IMS Health, 2018c).

Figure 4: Turnover of leading pharmaceutical markets in Europe in 2017 by country (in million €)



Source: IMS Health (2018b).

Although the average price structure of pharmaceutical products in Europe included tax of around 10% in 2016 (IMS Health, 2018a), the value-added tax (hereinafter: VAT) rate varies from country to country and is, according to data from 2018, also different for OTC drugs and prescription-only (hereinafter: P-O) drugs within specific countries (comparison presented in Figure 5) (European Commission, 2018a, 2018b). Germany is also the country that generates by far the highest sales on the OTC self-medication market (e.g. analgesics, cough and cold products, digestive remedies and skin treatment products). It generated more than €5.6 billion in sales in 2017, which is more than two times more than Poland, which ranked second with more than €2.5 billion in sales (AESGP, 2018).

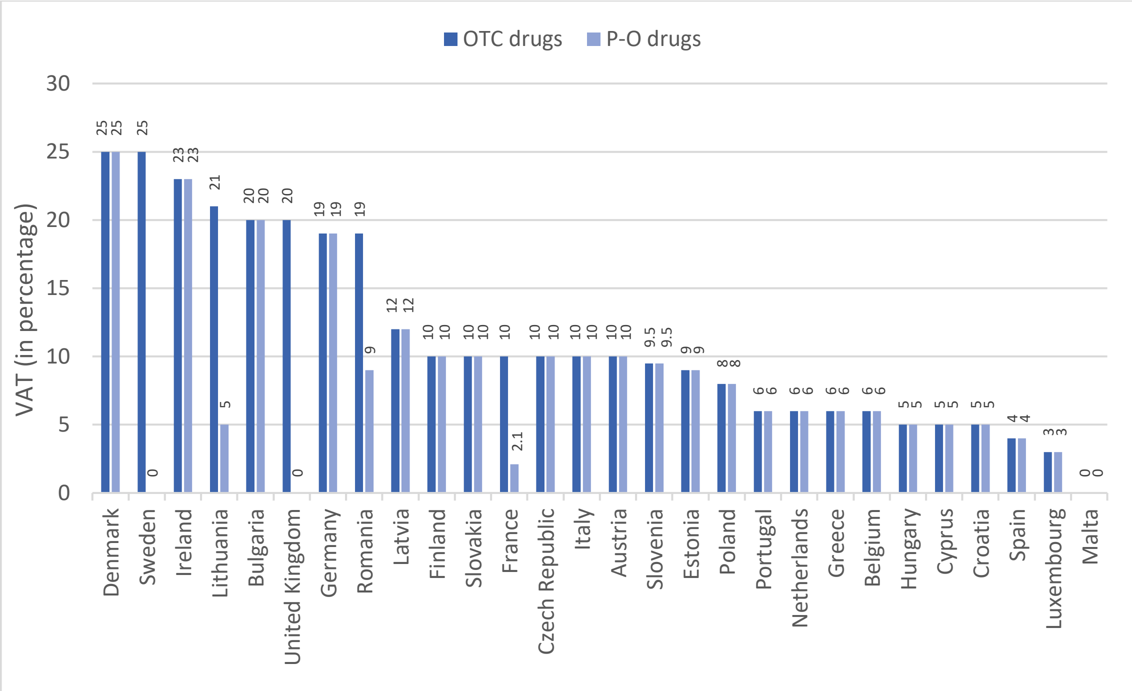
It is interesting to note that Switzerland, which invests the most in its R&D, has about 60,000 fewer employees than Germany (data for 2017). The number of employees in the pharmaceutical sector in different European countries is shown in Figure 6.

1.3 Analysis of the pharmaceutical industry in Slovenia

Germany, Switzerland and the UK are the top three countries in terms of pharmaceutical R&D investments. Table 1 shows investments by country, where our studied countries of Germany, France and Italy have the highest R&D investments, although the amounts differ slightly. Slovenia's R&D investments amount to €180 million, which is comparable to Finland and Hungary (Table 1). Given its size, however, Slovenia is in a relatively more competitive position than larger countries. Countries included in the analysis earmarked half of their R&D

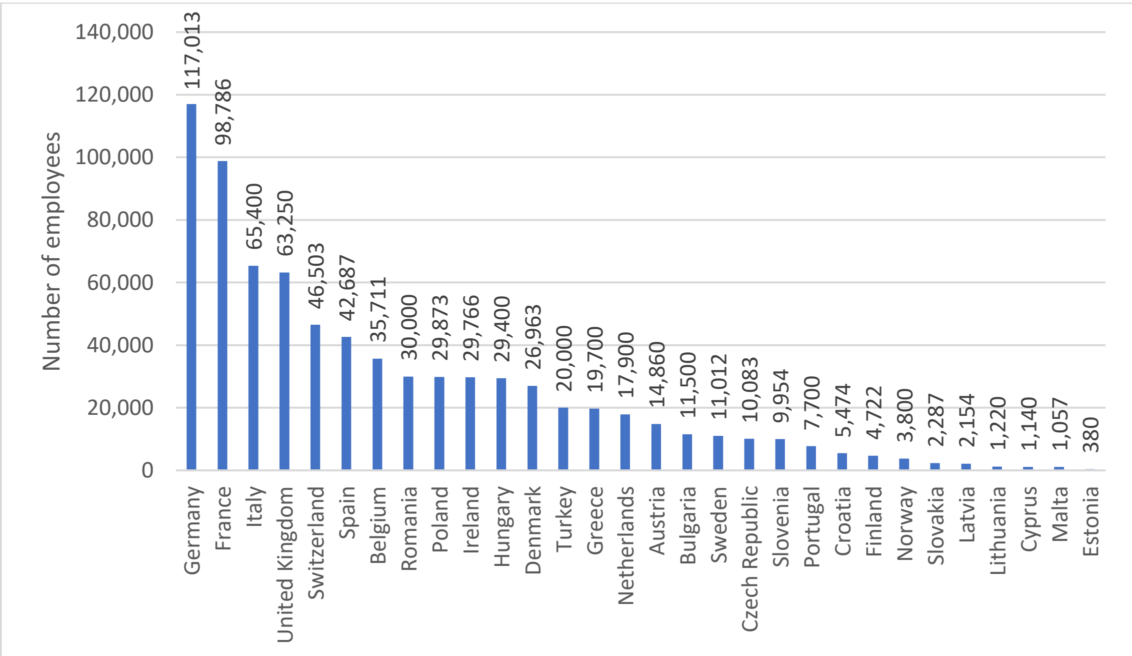
investments to clinical trials, followed by 19% for uncategorised and 16% for pre-human/pre-clinical trials (EFPIA, 2019e).

Figure 5: Comparison of the VAT rate on OTC and P-O drugs in Europe in 2018 by country (in %)



Source: European Commission (2018a, 2018b).

Figure 6: Total number of employees in pharmaceutical industry by country in 2017



Source: EFPIA (2019c).

Table 1: Pharmaceutical industry R&D investments (in million €) and number of employees (in total number) by country in 2019

	R&D investments (in million €)	**Number of employees**
Germany	6,918	117,013
Switzerland	6,105	56,503
United Kingdom	5,292	63,250
France	4,451	98,786
Belgium	3,508	35,711
Denmark	1,632	26,963
Italy	1,530	65,400
Spain	1,147	42,687
Sweden	1,104	11,012
Russia	856	n.a.
Netherlands	642	17,900
Poland	340	29,873
Ireland	305	29,766
Austria	294	14,860
Finland	201	4,722
Slovenia	180	9,954
Hungary	176	19,400
Norway	126	3,800
Romania	101	30,000
Portugal	100	7,700
Cyprus	85	1,140
Czech Republic	77	10,083
Turkey	66	20,000
Greece	42	19,700
Croatia	40	5,474
Bulgaria	n.a.	11,500
Estonia	n.a.	380
Iceland	n.a.	500
Latvia	n.a.	2,154
Lithuania	n.a.	1,220
Malta	n.a.	1,057
Slovakia	n.a.	2,287

Note: Due to incomplete data for some countries, the most recently available data was reported, as follows for R&D investments in million €: Slovenia and Turkey (2016), Sweden, Norway, Greece, France and Austria (2015), Cyprus and Ireland (2013), the Czech Republic (2012) and Croatia and the Netherlands (2011). Employment statistics was reported for Estonia, the Netherlands, Norway and Turkey from 2016, from 2014 for Sweden, from 2013 for Denmark and Lithuania, and from 2007 for Cyprus.

Source: EFPIA (2019e).

The pharmaceutical industry in Europe is considered an industry with a high number of employees and a high proportion of highly skilled workers, which is necessary for maintaining a high-level knowledge base. According to an analysis by the EFPIA (2019e), the number of employees in the countries included in the analysis amounted to 760,795. Of that total, 18% worked in Germany, 15% in France and 10% in Italy. These are the only three countries above the 10% threshold. The number of employees in Slovenia was 9,954 employees or 1.6% of the total. Detailed numbers are presented in Table 1. Slovenia ranked 16th in terms of R&D investments and 19th in terms of the number of employees (taking into account the same countries) (EFPIA, 2019e). In addition, Slovenia has a positive trade balance of approximately €1,469 million, meaning that its exports exceed its imports (€2,728 million and €1,259 million, respectively). Other major exporters are Switzerland, Germany, Ireland, Denmark, the Netherlands and Belgium, with a trade balance ranging from €39,694 million (Switzerland) to €7,631 million (Belgium). The data are summarised in Table 2 (EFPIA, 2019e).

Table 2: Imports, exports and balance of trade by country in 2017 (in million €)

Country	Imports	Exports	Balance of trade
Austria	8,976	9,942	966
Belgium	32,663	40,294	7,631
Bulgaria	1,294	893	-401
Croatia	1,048	1,144	96
Cyprus	245	278	33
Czech Republic	4,082	2,291	-1,791
Denmark	3,829	12,496	8,667
Estonia	359	82	-277
Finland	1,918	752	-1,166
France	24,694	28,653	3,959
Germany	47,672	75,118	27,446
Greece	3,092	1,190	-1,902
Hungary	3,971	5,015	1,044
Ireland	9,540	35,451	25,911
Italy	23,390	23,855	465
Latvia	598	438	-160
Lithuania	1,013	704	-309
Luxembourg	486	339	-147
Malta	183	265	82
Netherlands	23,520	31,729	8,209
Norway	2,061	669	-1,392
Poland	6,103	4,016	-2,087
Portugal	2,442	1,081	-1,361
Romania	2,962	749	-2,213
Russia	8,015	313	-7,702
Slovakia	1,709	330	-1,379
Slovenia	1,259	2,728	1,469
Spain	13,190	10,740	-2,450
Sweden	3,850	7,556	3,706
Switzerland	26,680	66,374	39,694
Turkey	3,938	775	-3,163
United Kingdom	29,850	29,776	-74

Source: EFPIA (2019e).

Taking into account public and private spending on healthcare, there was an increase in several countries and in Europe as a whole from 1980 to 2000 or 2010, followed by a decline from 2010 to 2017. Slovenia belongs to this group; it spent 8% of GDP on public and private healthcare in 2017. Spending by more developed countries and certain EU Member States (e.g. Germany, Switzerland, Sweden and the US) is higher than spending by Slovenia. These are primarily countries with steady growth in spending. Conversely, the proportion of GDP spent by countries that joined the EU with Slovenia or later (e.g. the Czech Republic, Hungary, Latvia and Estonia) is similar or lower. Total public and private spending on healthcare is presented in Table 3.

Table 3: Total public and private spending on healthcare by country for 1980, 1990, 2000, 2010, 2015 and 2017 (in % of GDP at market prices)

Country	1980	1990	2000	2010	2015	2017
Germany	8.1	8.0	9.8	11.0	11.1	11.3
Switzerland	6.6	7.9	9.8	10.7	11.9	12.3
United Kingdom	5.1	5.1	6.0	8.5	9.8	9.6
France	6.7	8.0	9.5	11.2	11.5	11.5
Belgium	6.1	7.1	9.2	10.2	10.3	10.3
Denmark	8.4	8.0	8.1	10.3	10.3	10.2
Italy	n.a.	7.0	7.6	9.0	9.0	8.9
Spain	5.0	6.1	6.8	9.0	9.1	8.8
Sweden	7.8	7.3	7.4	8.5	11.0	10.9
Netherlands	6.6	7.1	7.1	10.4	10.4	10.1
Poland	n.a.	4.3	5.3	6.4	6.3	6.7
Ireland	7.5	5.6	5.9	10.5	7.4	7.1
Austria	7.0	7.7	9.2	10.2	10.3	10.3
Finland	5.9	7.2	6.8	8.9	9.7	9.2
Slovenia	n.a.	n.a.	7.8	8.6	8.5	8.0
Hungary	n.a.	n.a.	6.8	7.5	7.1	7.2
Norway	5.4	7.1	7.7	8.9	10.1	10.4
Portugal	4.8	5.5	8.4	9.8	9.0	9.0
Czech Republic	n.a.	3.7	5.7	6.9	7.1	7.1
Turkey	2.4	2.5	4.6	5.1	4.1	4.2
Greece	n.a.	6.1	7.2	9.6	8.2	8.4
Estonia	n.a.	n.a.	5.2	6.3	6.5	6.7
Iceland	6.0	7.6	9.0	8.8	8.3	8.5
Latvia	n.a.	n.a.	5.4	6.1	5.7	6.3
Slovakia	n.a.	n.a.	5.3	7.8	6.9	7.1
Luxembourg	4.6	5.1	5.9	7.0	6.2	6.1
Europe	6.1	6.4	7.1	8.7	8.6	8.6
The US	8.2	11.3	12.5	16.4	16.8	17.2
Japan	6.2	5.8	7.2	9.2	10.9	10.7

Source: EFPIA (2019e).

2 KEY TRENDS IMPACTING THE PHARMACEUTICAL INDUSTRY

The pharmaceutical industry has gone through different periods, shaping it in the way that we know it today. These historical periods can be divided according to their characteristics, which are presented in section 2.1. Moreover, trends have led pharma to develop into two different camps, i.e. innovators and generics. The pharmaceutical industry is still growing steadily. For this reason, some future trends that will affect its innovation are reviewed, as well.

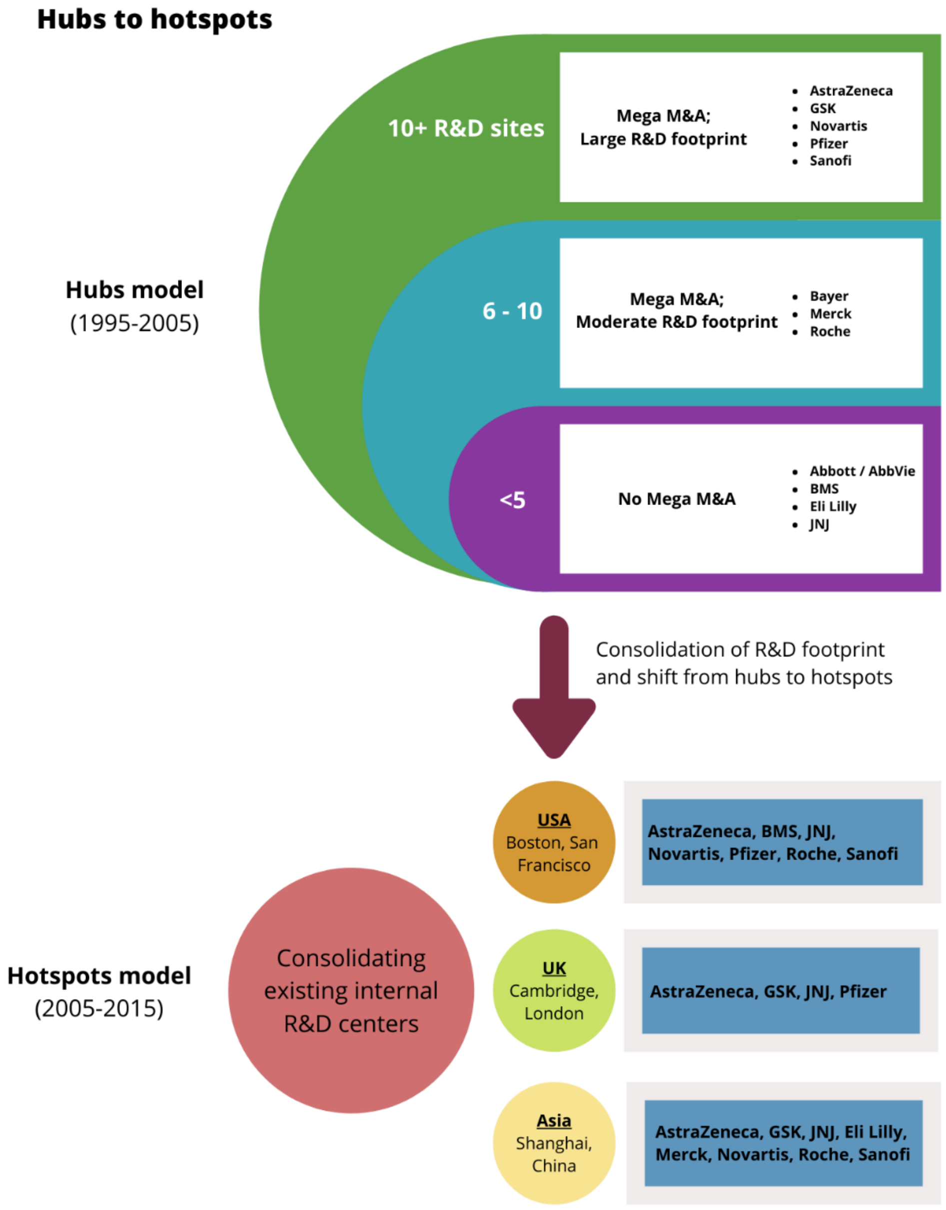
2.1 General trends

In recent decades, significant growth and exciting breakthroughs have characterised the industry. Big pharma has thus faced the need to redesign its business model and its footprint over time. Gautam and Pan (2016) conducted research on the key trends that have impacted major pharmaceutical companies over the past 20 years. In the 1990s and early 2000s, the most common model that pharma companies employed was that of a large-scale, well-diversified company present in several global hubs, drawing their revenue primarily from developed economies. Their analysis reviewed four trends that occurred between two concurrent time periods, from 1995 to 2005 and from 2005 to 2015, namely, massive to lean, hubs to hotspots, primary to specialty and West to East. Each of these are discussed below.

Massive to lean. First, massive to lean addressed the shift from intense “bigger is better” mergers and acquisitions (hereinafter: M&A) activity that strove for economies of scale and diversified portfolios, which resulted in bloated operations with large R&D hubs, enormous sales representative teams, large numbers of manufacturing facilities and matrixed governance layers with poor cultural integration of the resulting conglomerates. To contrast these results, big pharma began shifting towards a “leaner and focused” model in the second observed period, by pursuing the areas in which they were better than their competitors, and by divesting their non-core assets and focusing on fewer areas. Acquisitions in this period focused on the strategic rationale of building complementary capabilities rather than expanding portfolios, while some were driven by financial engineering, such as tax inversions. Only small players were in it to achieve economies of scale.

Hubs to hotspots. Second, the large number of acquisitions during the first period was triggered primarily by declining R&D productivity, which was also highlighted as a challenge of the global pharmaceutical industry by Paul et al. (2010) and Khanna (2012). However, Gautam and Pan (2016) reported that these acquisitions resulted in the formation of multiple independent research hubs in various locations owned by the same company with the aim of trying to solve the same scientific challenges, employing the so-called “more shots on goals” strategy. Hubs to hotspots explains the trend of big pharma companies to shrink their R&D footprint and establish fewer key centres, i.e. hotspots, for producing breakthrough science. This has enabled them to implement a much more open and collaborative model with better cooperation with external researchers, clinicians, academic institutions and biotech. Figure 7 graphically presents the transition from hubs to hotspots.

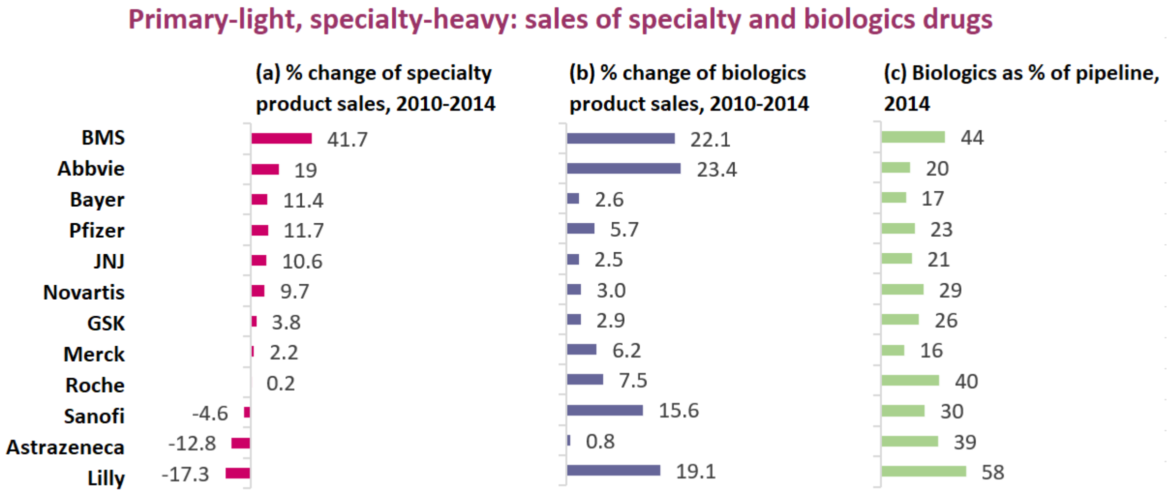
Figure 7: Graphical presentation of the transition from large hubs to innovation hotspots in the periods 1995-2005 and 2005-2015



Source: Gautam & Pan (2016).

Primary to specialty. The third trend Gautam and Pan (2016) discussed is primary to specialty, which addresses the fact that during the period from 1995 to 2005, the top-selling medicines were primary care, small-molecule therapies, which accounted for about 80% of revenue for most big pharma companies. Moreover, some of the biggest mergers were driven by blockbuster drugs. During the period from 2005 to 2015, however, major players shifted their focus from developing primary care and small-molecule medicines to better understanding diseases, and developing targeted and specialised medicines, to technology and science innovation for biologics, to personalised medicines and diagnostics to regulatory frameworks and development timelines, and to reimbursement and pricing. The same challenge was also discussed by other researchers, such as Kessel (2011) and IMS Health (2009). This shift was frequently initiated by targeted acquisitions. Today, most major players have an even distribution between primary care and specialty units. Specialty medicines and biologics also generated a growing stream of revenue in recent decades, with several major companies recording more than 10% absolute growth in the proportion of these products from 2010 to 2014 (Figure 8) (Gautam & Pan, 2016).

Figure 8: Percent change of specialty and biologics product sales from 2010 to 2014 and biologics as % of pipeline in 2014, by company



Source: IMS Health (2009).

West to East. The fourth trend, i.e. West to East focuses on major markets and has been seen before in literature, for example in research by Looney (2010) and Tannoury and Attieh (2017). Gautam and Pan (2016) reported that the leading global markets in the period from 1995 to 2005 were North America and Europe, with none of the leading companies deriving more than 20% of their revenue from emerging markets. In the period from 2005 to 2015, however, this proportion rose to at least 25% for most major companies. Euromonitor (2016) reported that as of 2016, the majority of the world's 30 megacities are situated in emerging economies. Tannoury and Attieh (2017) attributed this shift to increasing life expectancy, large populations and the growing prosperity of these countries, as well as flattened growth alongside the tight regulations of developed markets. They also pointed out that lifestyle changes in developing countries are accompanied by shifts in disease patterns (e.g. a rapid rise in diabetes, and oncologic and cardiovascular illnesses in emerging markets), mimicking their Western counterparts and thus making them solid markets for drug formulae that have been selling for decades, allowing major pharmaceutical players to market their global products on these new markets.

It should be pointed out that this trend mostly affects companies that had primary-care-focused portfolios and that have seen the expiration of patents in the US, Canada and Europe. The latter led to the up-selling of less expensive generic drugs that, on average, cost only about 20% of the price of their branded counterparts. Companies with a heavy biologics focus did not experience such a significant increase in revenue from emerging markets (Gautam & Pan, 2016). Furthermore, the increasing availability of biosimilar drugs is also an important factor in the paradigm shift (Tannoury & Attieh, 2017).

Emerging markets have also been increasing their innovation capabilities, especially China (Gautam & Pan, 2016). China is quickly emerging as a hotspot for global innovation due to investments of private and government capital, and a growing pool of home-grown and western-trained professionals (Gautam, 2015). Nevertheless, increasing revenue and the availability of workers at low-cost wages make emerging markets strong value sources for outsourcing activity, and can reduce drug development costs significantly due to the lower costs associated with performing clinical trials (ProText Knowledge Services, 2010).

Although emerging markets **are expanding the provision of healthcare, they are still searching for different ways to limit or lower their costs,** which can sometimes result in tight budget constraints that prevent patients from accessing innovative treatments. Another important factor here is political pressure through price controls and regulations. According to the European Commission (2009), there are policies in multiple countries that oblige pharmacists to dispense the cheapest product at all times and are therefore supporting sales of generic products. In China, for example, budget control policies have limited doctors' ability to prescribe a higher-priced international brand, although the quality of products from local generics has not yet reached a comparable level (Ascher, Bogdan, Dreszer & Zhou, 2015). Substandard generic and branded drugs spread due to corruption and may lead to a public health crisis (in terms of both a clinical and economic burden). It is surprising that only a small amount of poor quality drugs are falsified; the rest reach the market due to poor quality control, inappropriate packaging and storage, and due to poor manufacturing practices (Johnston & Holt, 2014). It is also concerning that, according to Cohen, Mrazek and Hawkins (2007), 25% of marketed drugs in third world countries (low- and middle-income countries) were of poor quality or substandard in 2007. In addition, Russian companies are granted price advantages and special access, while an effective price freeze is imposed on some imported medicines. The Brazilian government is trying to help its local producers by lowering long-term costs through a technology transfer agenda, which is supposed to guarantee volumes to market players (Ascher, Bogdan, Dreszer & Zhou, 2015).

Although emerging markets are promising for investors, there also bring many obstacles and challenges, such as the previously mentioned cost-containment policies, time constraints, underdeveloped health care infrastructures, corruption (bribery for certificates), economic crises and a shortage of expertise and training (Tannoury & Attieh, 2017).

As the outcome today, **big pharma companies are transforming into specialised companies** with a lean model, focusing on producing their research footprint in a few key innovation bio clusters and drawing their revenue from specialty products, biologics and emerging markets (Gautam & Pan, 2016).

Because the number of new discoveries is limited and the pipeline of research-driven pharmaceutical companies is shrinking, they cannot simply rely on new, patented products to replace their lost revenue from the expiration of patents. For this reason, they employ strategic behaviour and pursue **lifecycle extension strategies** (Song & Han, 2016). One of the strategic approaches companies tend to pursue is refilling their R&D pipelines by acquiring biotech companies (James, 2002). For example, when Lipitor's patent protection was close to its expiring, Pfizer acquired Wyeth Pharmaceuticals (Malik, 2009). Although the choice of which path to pursue when confronted with a patent cliff depends largely on a company's priorities, capabilities and opportunities, Song and Han (2016) developed a model of four generic strategic paths that may be pursued, i.e. prevention, innovation, extraction and adaptation. These strategies are furthermore discussed in section 3.2.

Additionally, Azad, Munisamy, Teng, Talib and Saona (2018) measured technical efficiency using the Malmquist total factor productivity index in Bangladesh, where the pharma industry met 97% of its local demand and was therefore self-sufficient in the period 2009 to 2013. Their results indicated that big pharma in the aforementioned country currently possesses expertise in **process patent activities** rather than in product patent, with both large and medium-sized companies introducing automation in their production plants. They found that the increase in productivity can be attributed entirely to technical advancement (adoption and development of new technological aspects) and not technical improvements. This is generating high profiles in production and sales. However, achieving long-term sustainability by purchasing patents and introducing automation may not be possible and will lead to future challenges. As they indicated in the study, product patent represents the basis for that, and establishing self-dependency in terms of innovation and the production of raw materials is crucial. We may conclude that this indicates a future trend in developing countries such as Bangladesh.

Industry 4.0 is also dictating trends in digitalisation (e.g. digitised manufacturing-internet of things, augmented and virtual reality, big data and analytics, artificial intelligence (hereinafter: AI), etc.). In the past, digitalisation was used by pharma companies primarily for manual tasks, with the main aim being the saving of time and effort. Today, however, computers are so advanced that they can spot patterns in images and digital data. Due to this ability, the process of diagnosing and treating diseases is becoming an increasingly data-driven practice. The time needed for analysis has been reduced to as little as one day, which is an enormous advancement. Companies are also combining and mixing different digital technologies, such as natural language processing and deep learning, with big data from sensors, consumer wearables and connected devices. This is extremely useful for identifying links in diseases and patterns for mutations, which are then used for manufacturing customised drugs at the individual level. Digitalisation has also brought machine learning and AI, which help scientists analyse previously generated mass data, and help them decide which experiments should be performed. Some algorithms can also predict the side effects of certain ingredients of a new drug, which speeds up the drug approval process (Statista, 2019).

2.2 Regulatory trends affecting the pharmaceutical industry

The manufacturing of pharmaceutical products has been one of the most regulated manufacturing environments for more than 50 years (Woodcock, 2004). Regulations that were imposed as good manufacturing practices (hereinafter: GMP) in the 1960s and the Pharmaceutical Inspection Co-operation Scheme (hereinafter: PIC/S GMP) guide in the 1970s have been the subject of constant review, adaptation and refinement ever since. One of the hottest topics in the pharmaceutical industry is the quality of medicinal products, which translates into patient protection. Awareness about its importance has been growing ever since the Food and Drug Administration (hereinafter: FDA) introduced the GMP, which aims to harmonise and guide the production of drugs worldwide. Since 2002, the FDA has been working on a new initiative for the 21st century, i.e. cGMP, which relate to both industrial and regulatory systems (Woodcock, 2004).

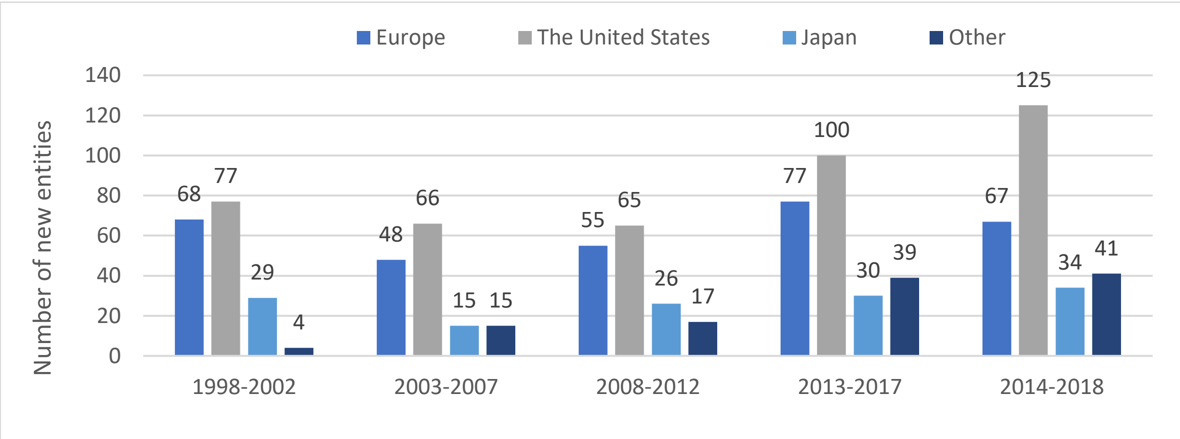
There are many guidelines from different organisations that are imposed and widely applied in the industry, such as the World Health Organization's guidelines on GMP, the FDA's guidelines on cGMP, EU guidelines, guidelines issued by the International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (hereinafter: ICH), the Define-Measure-Analyse-Improve-Control (hereinafter: DMAIC) model, which is a generic model of Six Sigma methodology, total quality management (hereinafter: TQM), the International Organization for Standardization (hereinafter: ISO) series and many more (Woodcock, 2004). Today, these regulations cover all aspects of pharmaceutical manufacturing, as well as complementary aspects, such as the packaging and distribution of products, documentation, outsourcing and data management. Recently, regulatory guidelines in pharma have been showing increased interest in the development of a trend in which they focus on areas such as data integrity (overall handling and data lifecycle process) (Tabersky, Woelfle, Ruess, Brem & Brombacher, 2018).

Although tough regulations can be perceived as a burden that restricts flexibility in innovation, these rules frequently stimulate the development of new innovative scientific approaches and technologies, and are increasing their level of complexity and quality requirements to that end (Tabersky, Woelfle, Ruess, Brem & Brombacher, 2018). For example, ICH Q3D is a new standard for measuring and controlling inorganic impurities in pharmaceuticals, which has been in effect since June 2016 (USP-NF, 2016). This standard replaced routine tests of concentrations in components with controls based on risk and permitted daily exposures (Li et al., 2015). By employing new state-of-the-art instruments, critical elemental impurities can be controlled to a significantly lower level, thus reducing the risk for patients (Tabersky, Woelfle, Ruess, Brem & Brombacher, 2018). This is just one example of how new regulations or amendments to existing regulations are improving quality and stimulating innovative solutions. They are encouraging companies to pursue innovation throughout their operations, not only in their core activities.

2.3 Differences between generics and innovators

Throughout the development of the pharmaceutical industry, companies have evolved into two distinguished segments, i.e. innovation (originators) and generic. Innovator companies focus on the discovery of novel treatments in the form of new indications (hereinafter: NIs), new molecular entities (hereinafter: NMEs), new drug delivery systems, or new dosage forms (hereinafter: NDFs) for existing and developing diseases (Aitken, Berndt & Cutler, 2009; Fischer, 1999). In the period 1998 to 2018, US pharmaceutical innovator companies created the largest number of new drugs, with Europe following directly behind the US (Pharmaceutical Executive, 2019). Figure 9 provides a closer look at the number of new chemical or biological entities developed in this period by region of origin.

Figure 9: Total number of new chemical or biological entities developed from 1992 to 2018 by region of origin



Source: EFPIA (2019b).

Because the process of developing a new drug is very protracted and requires intensive investments, innovator companies protect their investments with patents that grant them market exclusivity. However, after the patent protection expires, generic companies race to enter the market with generic equivalents. The generic business thus operates on revenue generated from the production of duplicates of innovator products (Grabowski, 2004). According to the FDA (2018): “A generic drug is identical—or bioequivalent—to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use”.

Generics do so by conducting limited R&D through which they prove the clinical equivalence of their generic product to the innovator’s product. It is also to their advantage that they do not have to perform any clinical trials. This is very cost beneficial for them and also makes it possible for their products to reach people who are unable to afford the costly innovator versions (Grabowski, 2004).

When the patent protection of drugs created by innovators expires, generic manufacturers enter the market by producing medications that are equivalent to the innovator's, but at a significantly lower price (between 50% and 80% lower), shifting the market competition structure from a monopoly to competition based on price due to the abbreviated and less-costly process they need to go through to get approval from the FDA, and thus dry up the innovator's profit streams (Pearce II, 2006). A global research paper published by Indxx (2016) revealed that governments dealing with ageing populations and increasing costs are actively encouraging and promoting the use of generic products because they lower costs, not only for patients but for the healthcare system as a whole. As a result, the volume of prescriptions of generic drugs accounted for 88% of the volume of all prescribed medications in 2016, with growing future prospects. This scenario was very much different in the past when generic drug makers were also obliged by law to go through the same process as branded drugs to receive approval. Because this entailed enormous financial investments, this scenario was changed with the Hatch-Waxman Act in 1984 (Trefis Team, 2015).

2.4 Future trends that will affect innovation in the pharmaceutical sector

Trends from 1995 to 2015 were presented in section 2.1. Building upon these, Gautam and Pan (2016) expect some trends to continue in the ten-year period from 2015 to 2025. The pharmaceutical industry will continue to face patent expirations, regulatory hurdles and R&D productivity, which is forcing pharmaceutical companies to revise business strategies with the aim of staying competitive on the market. Due to the diversity of strategies employed, companies might focus on:

- diversified business, ranging from diagnostics, generics, medical devices, innovative drugs, consumer health and animal health; or
- biopharma, solely through innovative drugs.

Major pharmaceutical companies will evolve further in the direction of the previously described four trends, i.e. massive to lean, hubs to hotspots, primary to specialty and West to East. Moreover, access to healthcare will have to become sustainable as well as affordable for all stakeholders, i.e. patients, governments and healthcare companies. This is one of the greatest challenges in the next decade and is especially relevant for emerging markets that represent from one third to one half of big pharma. New models will have to include, but not be limited to, the following: coverage assistance, tiered pricing and performance-based models (Gautam & Pan, 2016).

Healthcare and information technology (hereinafter: IT) are converging and will continue to converge over the coming decade. Healthcare and diagnostics are transforming due to big data and mobile health. Accordingly, the development of personalised and precise medicines might benefit from apps and wearable devices that measure the health parameters of patients, which will require the adaptation of pharmaceutical companies (Gautam & Pan, 2016).

From 1995 to 2005, the ten largest companies, notwithstanding the industry, were from the US and Europe. Today, at least half of these are from emerging markets. Because the pharmaceutical industry is highly limited by regulatory frameworks, emerging markets have not yet come in line with currently established companies from the developed world, i.e. Pfizer, Novartis, AstraZeneca and Merck. Nevertheless, developed markets are expected to further be challenged by companies from emerging economies (e.g. China, India, Korea and Brazil), striving to become global leaders. This, however, should be a more gradual rather than over-night process (Gautam & Pan, 2016).

Not only are emerging-market companies strengthening their position on domestic and global markets, there is also a growing interest in emerging markets by incumbent companies from the developed world as a place to outsource their operations. Because production and R&D costs are increasing, outsourcing is a way to keep prices low while benefiting from low-cost wages and human capital from emerging markets. Researchers mention the importance of shifting the production of patent-expired drugs to developing countries or, alternatively, investing in new patentable drugs. In addition, the population is ageing, purchasing power is increasing and diseases resulting from negative lifestyle habits are emerging in developing countries. These would be beneficial for pharmaceutical companies in the coming decade as an additional revenue stream. However, the characteristics that categorise them as “emerging” markets should not be forgotten, as they might be hindering successful establishment there and would require adapted strategies (Tannoury & Attieh, 2017).

Also, Barbieri, Huang, Pi and Tassinari (2017) report the ageing population as a recent trend that is having an influence on health-related goods and services. Changing the production strategies of pharmaceutical companies is affecting choices regarding what and where to produce medicines. Moreover, M&As are seen as a tool, especially by the Chinese government, to create bigger and more competitive players, and to take advantage of synergies. Vertical M&As were particularly efficient after the crisis in 2008. Therefore, a new wave of M&As might occur at pharmaceutical companies at a time when growth in the global economy is slowing down and leading to a new crisis triggered by limited economic activity during the coronavirus disease 2019 (COVID-19) epidemic.

With regard to COVID-19, the development of a vaccine against pandemic/epidemic diseases is another challenge. Not only COVID-19, but epidemics, in general, are problematic. Given the duration and high cost of developing a vaccine, as well as high attrition, developers usually engage in several successive steps with pauses to analyse data and verify manufacturing processes before the successful final outcome is confirmed. Severe Acute Respiratory Syndrome (hereinafter: SARS) and Zika cases demonstrated the need for faster vaccine development, as these two epidemics ended before the vaccines were developed, which had a huge financial impact on pharmaceutical manufacturers when funds provided by funding bodies were reallocated (Lurie, Saville, Hatchett & Halton, 2020). Also, Weiss (2020) emphasised that the development, approval and production processes normally take years, and presented the opposite case of preparedness for COVID-19. Because the new disease was expected in early 2018, teams across the globe were ready to start experimenting as soon as the first news regarding the outbreak in Wuhan emerged. There are six candidates for the COVID-19 vaccine. Human trials began within just three months, while manufacturing companies have already made preparations, meaning that readiness is at a higher level than in preceding pandemic situations, although there will be a need to choose between different vaccine candidates before actual manufacturing (Weiss, 2020). Taking into account all of these facts, the establishment of a global financial mechanism to support development and manufacturing in the event of pandemics/epidemics will be a key component in preparedness for future outbreaks (Lurie, Saville, Hatchett & Halton, 2020).

3 INNOVATION AND ITS IMPACT ON CORPORATE PERFORMANCE WITH A FOCUS ON THE PHARMACEUTICAL SECTOR

Today, innovation is an essential requirement that enables companies and countries to survive in and adapt to the turbulent environment of the competitive global economy (Fleury, Fleury & Borini, 2013), which has been characterised by the acceleration and global distribution of knowledge production, market expansion, fragmentation and virtualisation, the growing importance of sustainability, the rapid development of the technological and social infrastructure (Bessant & Venables, 2008), and growing consumer demand for versatile products and services (Schaarschmidt & Kilian, 2014). Sustainable innovation is driven by the constant development and implementation of new projects, which is not a simple task, but rather a complex non-linear process that takes place in clusters of innovation programmes (Xiang & Long, 2002, as cited in Chen, 2016).

3.1 Definition of innovation

The Organisation for Economic Co-operation and Development (hereinafter: OECD) and Eurostat (2018) define innovation as: “New or improved product or process (or a combination thereof) that differs significantly from the unit’s previous products or processes and that has been made available to potential users (product) or brought into use by the unit (process)”. Innovation, however, means more than inventions that are new to the world; it also means changes and ideas that are new to companies (adaptations and imitations) (Webster, 2004). Accordingly, two types of innovation can be distinguished, i.e. incremental innovations, meaning “doing what we already do but in a better way”, and radical innovations, meaning “new to the world” (Tidd & Bessant, 2018).

Four core categories of innovations exist and are referred to as the 4Ps. The framework also provides a map of four dimensions of innovation space that can be applied to any organisation. These 4Ps are as follows (Tidd & Bessant, 2018):

- product innovation (changes in an organisation's offer – products or services);
- process innovation (changes in the way an organisation creates or delivers its offer);
- position innovation (changes in the context in which an organisation introduces its offer – how it targets its offer and the story it tells about it); and
- paradigm innovation (changes an organisation imposes in the underlying mental models that frame what it does – business model innovation).

The 4Ps represent the core categories from which more specific categories can be derived. As pointed out by Chen (2016), for example, sustainable innovation is primarily influenced by three innovation capabilities: knowledge innovation (positively influenced by knowledge learning and knowledge creation ability), production innovation (driven by knowledge transferring ability and level of production equipment) and market innovation (as the result of good marketing and profit-making abilities). Older theories, based on technological and product innovation, are today accompanied by newly developed forms of innovation (which are much harder to duplicate), such as sustainable development and eco-innovation, institutional innovation (Wijen, Zoeteman, Pieters & van Seters, 2005), management innovation (Birkinshaw & Mol, 2006; Hamel, 2006), organisational innovation (Damanpour, Szabat & Evan, 1989), administrative innovation (Birkinshaw, Hamel & Mol, 2008) and business model innovation (Spieth, Schneckenberg & Matzler, 2016).

Companies can improve the efficiency of their static operational activities and their dynamic efficiency. Those who place greater emphasis on the latter tend to be more innovative. In deciding how much emphasis should be placed on each of the two, both systemic extra-companies and non-systematic individual factors must be considered (Arvanitis & Hollenstein, 2002; Crepon, Duguet & Kabala, 1996; Dosi, 1988; Geroski & Walters, 1995; Nelson, 1959; Schmookler, 1966).

Table 4 illustrates different aspects of innovation, which are further discussed in the remaining part of this section. In addition, reference to existing literature are made in the table.

The decision on how to actively innovate is supported by a number of stable and continuous practices and routines that nurture innovative activities (Hodgson, 1999). They include the level of encouragement of staff to constantly learn and work on developing their skills, methods of communication within a company (also organisational structure-decentralisation), managerial attitudes and management innovation (Birkinshaw, Hamel & Mol, 2008), and the use of effective ways to generate adequate profits that can come from innovative decisions. For example, highly innovative companies implement aggressive managerial approaches with a combination of more flexible management styles. They stimulate a creative climate, participate extensively in teamwork and innovative activities, learn about new approaches, technologies and products from diverse meetings, networks and highly-skilled workers, and effectively use different approaches to protect their product and process innovations (Webster, 2004).

Table 4: Overview of different aspects of innovation, their main characteristics and supporting literature

	Main characteristics	**Supporting literature**
Motives for stimulating innovation	Process optimisation, improved cost-efficiency, higher output and production quality, faster decision making, increased human capital and agility.	Birkinshaw, Hamel and Mol, (2008) Webster (2004) De Faria, Lima and Santos (2010) Carpinetti, Gerolamo and Galdámez (2007) He and Chen (2014) Lawson and Samson (2001)
Innovation outcomes important for companies	New products/services, more customers, decentralisation, creative climate, flexible management, economies of scale, spread of risk and cost-sharing.	Birkinshaw, Hamel and Mol, (2008) Webster (2004) De Faria, Lima and Santos (2010) Carpinetti, Gerolamo and Galdámez (2007) He and Chen (2014) Lawson and Samson (2001) Cole (2002)
Obstacles hampering innovation activities	Lack of information regarding technology, lack of information regarding markets, absence of qualified human resources, absence of cooperation and innovative partners, the emergence of new technologies, new markets, new political rules, changes in market sentiment or behaviour and depletion of innovation options.	Sipos, Bizoi, and Ionescu (2014) Tidd and Bessant (2018)

Source: Own work.

Because employee creativity is one of the main factors influencing the success of innovation, many researchers have focused on methods that help stimulate employee creativity. Importantly, deliberate creative energy and effort from individuals are required to foster efficiently and effectively creativity (Adams, 2006; Heslin, 2009; Hollanders, 2009; Hollanders & Van Cruysen, 2009; Ortega, 2001; Sears & Baba, 2011; Sipos, Bizoi & Ionescu, 2014). The drivers of creativity are learning and exploration. Thus, a persistent learning mechanism is of great value for effective knowledge creation and accumulation (Cole, 2002). To foster innovation in all respects and to use it efficiently and effectively to reduce production costs, optimise production and deliver higher quality products and processes, employees as a driving force and source of knowledge creation capabilities required for a company to thrive should be provided good incentive systems that combine different motivational stimuli, such as recognition, work freedom, flexibility, teamwork, challenges, defined career path, participation in decision making and a good compensation system (Carpinetti, Gerolamo & Galdámez, 2007; He & Chen, 2014; Lawson & Samson, 2001).

Webster (2004) concluded that the innovation orientation of companies is positively influenced by their spending, not only on human capital, but also on physical capital (e.g. machinery, new technologies, software and information technology). For this reason, cooperation with other companies and institutions is also extremely important in the organisation of research and innovation processes, as it provides opportunities for companies to gain access to technologies and specific knowledge that their internal sources cannot deliver. These complementary resources help companies to grow faster, spread risk and achieve economies of scale, and are also a great mechanism for cost-sharing (De Faria, Lima & Santos, 2010).

Because innovation is also a source of demand-side advantages for companies, Webster (2004) investigated which external factors and driving forces make some companies engage in more innovative activities and projects than others. She found locally owned companies, companies with fewer employees and companies with a wholesale business model have higher levels of innovation (greater agility and faster decision-making). Similarly, companies dealing with volatile product markets and companies operating in industries with a higher level of knowledge spill-over are more innovative.

In contrast to other literature, Sipos, Bizoi, and Ionescu (2014) focused their research on factors that hinder the innovation performance of companies. They found that the factors most at risk for innovation are a lack of information regarding technology, a lack of information regarding markets, a lack of skilled human resources, and a lack of cooperation and innovative partners. Sometimes, even changes that are external to a company can cause the discontinuation of innovation because companies struggle to adapt to them. These triggers/sources include the emergence of new technologies, new markets or new policy rules, changes in market sentiment or behaviour, or simply running out of innovation options, which is specific for mature industries (Tidd & Bessant, 2018). In addition, innovation is not always desirable or even appropriate for companies due to the associated risk and specific internal capabilities, the operating environment, external pressures and constraints (Webster, 2004).

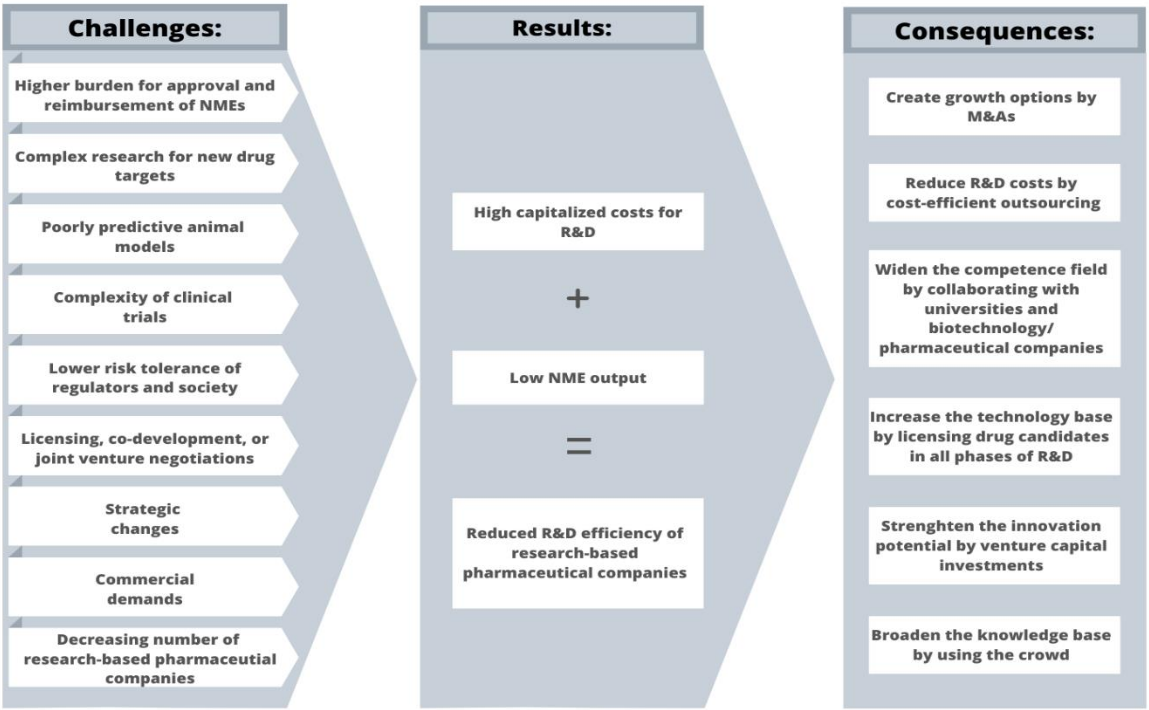
3.2 Innovation specifics in the pharmaceutical industry

Pharma has a unique approach to R&D relative to other industries. As previously mentioned, this industry is driven by R&D, is highly regulated and is facing a trend of increasing product complexity and quality requirements (Grabowski, 2004). According to the EFPIA (2014), the successful development of a new blockbuster drug and obtaining market approval generally take more than ten years and require at least $1 billion (and sometimes in excess of $10 billion). Development is not only characterised by long time requirements and long testing cycles, but also by uncertain prospects for commercial success (Song & Han, 2016).

The pharmaceutical industry is the top investor in R&D. Moreover, expenditure by pharma companies on R&D activities is a clear signal of its importance for individual companies and for the industry as a whole. Although R&D expenditure is rising, the sector is not discovering enough new molecular entities (NMEs) that would be necessary to achieve product innovation-based growth objectives. As a result, companies are not achieving investors' expectations about the return on their investments. On average, only 4% of projects are successful and they must generate enough revenue to compensate for investments in the remaining 96% of failed projects. It is thus important to discuss the efficiency parameters of R&D in the industry and the consequences of low output rates (Schuhmacher, Gassmann & Hinder, 2016).

Low R&D efficiency has been triggering alarming signals, and companies have been reacting accordingly, making changes to their R&D ecosystems. Kruse, Slomiany, Bitar, Jeffers, and Hassan (2014) conducted research on the leading research-based pharma companies and determined that 73% of the companies they studied were making changes to their R&D process. These changes are summarised in Figure 10.

Figure 10: Challenges and consequences of low R&D efficiency



Source: Schuhmacher, Gassmann & Hinder (2016).

Today, all major pharma companies are trying to access external innovation by exploiting opportunities along the entire R&D value chain, either in the form of partnerships and traditional collaborations or by applying more modern forms, including open innovation models such as virtual R&D, crowdsourcing, innovation centres and open-source innovations (Schuhmacher, Gassmann & Hinder, 2016). In the past, it was common for pharma companies to collaborate with third parties with specific know-how (Tralau-Stewart, Wyatt, Kleyn & Ayad, 2009). However, significantly increased levels of R&D complexity in the industry have led to collaborations that provide an enlarged set of skills and technologies. For example, GSK is investing almost half of its funds earmarked for R&D in collaborations with partners from the biotechnology industry and academia, which supply the company with ideas that boost its innovation potential (Regalado, 2012). In some areas of research, companies have even moved their technology to a large number of external institutional and academic premises, thereby increasing their flexibility and reaping the benefits of governmental funding (Ekins, Waller, Bradley, Clark & Williams, 2013). By working with academics, companies are striving to translate their basic academic research into novelty drugs.

In order to provide a clearer overview, the specific innovation strategies of pharmaceutical companies are separated into three categories based on the perspectives of the areas of interest that are most impacted: financial perspective, knowledge generation perspective and strategic perspective. Table 5 presents an overview of which strategies support each of the three perspectives. The perspectives are also explained in sections 3.2.1 to 3.2.3.

Table 5: Overview of the three innovation perspectives, and the supporting strategies and aims thereof

Perspective	Strategy	Aim
Financial	Virtual R&D model	Reduce capital requirements, overhead costs, infrastructure costs, financial risks and gain flexibility
Knowledge generation	Open-source innovation	Providing the best solution for a particular challenge
	Crowdsourcing	Providing companies with access to expert know-how
	Prevention strategy	Evergreening
Strategic	Innovation strategy	Outpacing competition with a business model or product innovations
	Extraction strategy	Full exploitation of a company’s existing market position without additional investments in product innovation
	Adaption strategy	Innovator companies aim to retain their existing customer base by becoming active players on generic markets
	M&A	Developing new core competencies or filling R&D pipeline gaps with external sources
	Project portfolio management	Increasing R&D efficiency
	Outsourcing	Long-term relationships with a limited number of partners
	Innovation centres	Facilitate drug discovery alliances and the filling of product/project pipelines

Source: Own work.

3.2.1 Financial perspective

The aim of the financial perspective is to reduce capital requirements, overhead costs, infrastructure costs and financial risks, and to achieve flexibility. Thus, a handful (five) of companies have succeeded in establishing a **virtual R&D model**, which is a smaller organisation with a small number of employees who, for the purpose of developing their selected R&D projects, use external technologies and resources, and facilities on demand (Schuhmacher, Gassmann & Hinder, 2016). This model has proven to be highly efficient. For example, the productivity of Chorus (an entity owned by Eli Lilly) has been three 3 to 10 times higher than the productivity of Eli Lilly's traditional R&D model (Longman, 2007).

Shire (part of Takeda Pharmaceutical Company Ltd) is the first organisation in the pharmaceutical industry to combine several open innovation aspects into one coherent unit and implement the radical concept of knowledge leverage, an open R&D organisation that operates virtually. The top innovators in the industry typically follow the models of knowledge creators or knowledge integrators, which represent two of the four open innovation models identified by Schuhmacher, Germann, Trill, and Gassmann (2013). Knowledge integrators are companies that work on externally generated R&D projects with a combination of their in-house expertise in R&D management (Schuhmacher, Germann, Trill & Gassmann, 2013). Their team focuses on the acquisition of outside innovation, i.e. ideas, know-how and technology, to discover and develop new drugs (Schuhmacher, Gassmann & Hinder, 2016), whereas knowledge creators are of an open type, and implement inbound innovation management and apply it to a preferably internally generated project portfolio.

3.2.2 Knowledge generation perspective

Although it is not typical for the sector, some companies are also exploring **open-source innovation**, which is a strategy within the knowledge generation perspective. Open-source innovation is primarily based on transparency, and is also accompanied by access to results and products for everyone, freedom to operate, no financial rewards for contributors, collaborative improvements and merely recognition for providing the best solutions to identified challenges. For example, the Pool for Open Innovation against neglected tropical diseases (NTDs) formed by GSK, the Massachusetts Institute of Technology (MIT) and Alnylam Pharmaceuticals provides open access to 2,300 patents in order to stimulate the development of medicines to treat tropical diseases (Schuhmacher, Gassmann & Hinder, 2016). GSK has already started applying this model to other therapeutic areas.

Crowdsourcing is yet another novel innovation-supporting infrastructure in the pharmaceutical industry, with Eli Lilly being the pioneer and also the leader of crowdsourcing in the industry, as it has launched multiple crowdsourcing initiatives (e.g. YourEncore and Innocentive). YourEncore is a network of experts working on various challenges in the technology industry and providing companies with access to expert know-how. This organisation supports multiple fields from pharma (e.g. preclinical and clinical development and regulatory affairs, currently serving 24 out of the top 30 pharma companies) and other industries (YourEncore, 2020). On the other hand, Innocentive is an open innovation marketplace where companies, i.e. solution seekers (e.g. the National Aeronautics and Space Administration; hereinafter: NASA, and

AstraZeneca), present their challenges to the Innocentive network of over 400,000 non-competitive expert challenge solvers within and outside the industry, where the company only awards solutions that meet its needs as payment (Innocentive, 2020).

Patent cliffs and patent protection expirations are also the drivers of innovation strategies in different areas that pharmaceutical companies pursue. Song and Han (2016) discussed four innovator strategies companies pursue when facing patent expirations. Although these are not typical product innovation strategies, they are encouraging innovation in other areas, as well. The first one is the **prevention strategy**, which involves legally exploiting possibilities to extend market exclusivity. Thus, over time, companies have become very creative doing so and are today actively creating so-called "patent clusters" as solid patent portfolios made of patents that protect the main active drug ingredient (the primary patent may be split into several patents) and secondary patents that cover other features of a drug (e.g. methods of formulation or use and crystalline forms of the original compound) and/or subsequent improvements of the primary drug (Burdon & Sloper, 2003). For example, a patent cluster of secondary patents for a drug named ritonavir (a human immunodeficiency virus or HIV medication) could delay market entry by generic competitors for 12 years after the expiry of patent protection of the medicine's base compound (Amin & Kesselheim, 2012). The industry's ratio of primary to secondary patents is 1:7 (Song & Han, 2016). These secondary patent extensions of market monopoly with secondary patenting beyond the known patent life of a drug are also known as "evergreening" (Dwivedi, Hallihosur & Rangan, 2010).

3.2.3 Strategic perspective

Another strategy is called the **innovation strategy,** and its primary goal is to avoid competition by outpacing it with a business model or product innovations. The hallmark of successfully outpacing others are active provocations of the industry's evolution and continuous innovations (Gilbert & Strebel, 1987). The main role in product innovation is played by product-line extensions (variations and improvements of existing products, either of the drug itself or the manufacturing procedure) (Dubey & Dubey, 2009), the introduction of follow-on products, new indication approval or switching a prescription drug to an OTC drug, where all of these elements build the knowledge and structural assets of a company (Song & Han, 2016).

Product line extensions help with reasonable revenue generation, despite new generic versions of a product on the market (Hong, Shepherd, Scoones & Wan, 2005). New indication approval refers to the identification of novel ways to use a medication that were not identified during clinical studies, and a company was thus not aware of them at the time of registration. When the reformulation of new indications is approved, a company has the possibility of gaining at least three additional years of market exclusivity (Bhat, 2005). Multiple-indication medications have a better base and thus a higher chance of competing on different markets. They also send a message regarding the superiority of the modified drug to several price-insensitive customers. The introduction of a follow-on product that is technologically or therapeutically advanced and delivers significant improvements in patient outcomes is the most promising of innovation strategies, but is also the most difficult to implement. If an attempt is successful, it transfers the brand reputation to the new drug, but if the drug does not deliver expected improvements, it becomes the subject of sharp criticisms from funding bodies and may face substantial regulatory drawbacks.

The relationship between two products is also of great importance. If the follow-on product is a substitute, it often has a cannibalising effect on sales of the predecessor drug, whilst a parallel, complementary offering may generate carry-over revenue. Companies must thus adapt such market releases according to the relationship between the two drugs. By switching a prescription drug to an OTC drug, a company expands the customer segment it serves (change in legal status and business strategy), which provides a new stream for sustained revenue and allows the producer to exploit the value of the brand, despite patent expiry. However, this switch cannot always be executed, as the process is highly regulated and scientifically rigorous. OTC business is also characterised by low prices and heavy marketing efforts. A business model innovation strategy involves changing and adapting a company's core logic and, by specifying the value chain, creating and capturing new value. Many companies fail despite their product innovation capabilities. This is frequently due to failing to adjust their business model to the turbulent changes in the environment. Song and Han (2016) state: "Business model-related strategy comprises the realignment of structure and governance of transactions designed to create and capture value through an interrelated set of decision variables."

As previously discussed, the prevailing blockbuster business model is becoming significantly out of sync with changing social demands and technical discontinuities. Instead, the focus of research is being redirected towards personalised medicine, patient-centred practices, therapies for stratified groups and outcome-based reimbursements (Mittra & Tait, 2012). For homogenising the industry as a whole, however, company-level strategic differences are becoming an unfit factor that may create the opposite state, i.e. diversification (Mittra, 2007). The fact is that diversity in the strategic profile and innovation processes are increasing, but each company has their own preferred balance between value gain and value provision, depending on a company's specific situational context. For this reason, it is possible that a company with a vertically integrated value chain might transform into a product platform or even a service-oriented business model (Bigliardi, Nosella & Verbano, 2005).

The third generic strategy is the **extraction strategy**, which aims to fully exploit a company's existing market position without additional investments in product innovation. There are two different strategic approaches through which a company can achieve this. The first involves stimulating product turnover through marketing campaigns and different pricing strategies, and by lowering product-related expenses before generic competition enters the market (Song & Han, 2016). By decreasing prices, originator companies compete directly with generics, yet sometimes tend to pursue the opposite strategy and attempt to reach the segment of price-insensitive customers by increasing prices (Chandon, 2004; Grabowski & Vernon, 2000) and thus maximise short-term profit as inevitable generic competition is about to release substitutes.

On the other hand, these strategies only have a temporary effect and must be abandoned sooner rather than later (Ching, 2010). An alternative approach is licensing or selling a trademark and patent rights to produce a product to a generic company before market exclusivity expires. By doing so, an innovator company may also benefit from complementary technologies possessed by licensees (Somaya, 2003). Chong and Sullivan (2007) argue that out-licensing may contribute to the discovery of new indications, and has proven that the repurposing of old drugs successfully results in new therapies.

Song and Han (2016) concluded their list with the **adaption strategy**, where innovator companies strive to retain their existing customer base by becoming active players on the generic market and introducing their own branded generic products under another brand, also known as a “fighter brand”. There are two ways companies can approach this strategy. They can either develop a low-cost alternative through a separate wholly-owned subsidiary that operates outside of the main company (e.g. Sandoz from Novartis Group) (Gilbert & Strebel, 1987), or offer a generic product through the originator company itself (Agrawal & Thakkar, 1997). Today, companies with generic subsidiaries split their generic divisions from branded divisions in order to gain flexibility and better adapt to changing market dynamics (Song & Han, 2016). The rationale behind this strategy lies in segmentation and targeting based on the price sensitivity of customers and higher profit margins that derive from cost advantages and brand reputation based on the manufacturing learning curve (Raasch, 2008). Although this strategy may be very appealing, it also comes with significant critical issues that must be addressed. The marketing of low-price products is frequently not aligned with a company's corporate image, business model and culture. If a discounted drug serves as a substitute for a branded drug, it can easily create a cannibalising effect on the high-priced branded product. A company must thus be careful with timing and should introduce its generic drug soon after patent expiration and before any other generic competitor proactively engages in pricing behaviour and aggressively markets their product to drug prescribers (Song & Han, 2016).

M&As have become increasingly important as they help companies to develop new core competencies or fill their R&D pipeline gaps by accessing drug candidates and research projects from external sources (e.g. the biopharmaceutical sector) and thus improve their prospects in product innovation. Today, external sources are powering around 50% of R&D pipelines at multinational pharma players (Schuhmacher, Germann, Trill & Gassmann, 2013).

Project portfolio management is another approach to increase R&D efficiency. It results in optimisation by focusing more on project return-on-investment (hereinafter: ROI) and project-related costs. It has, for example, helped companies to decrease the average time from the start of a project to its abandonment in subsequent clinical trials from 4.7 years to 3.3 years (30%), thereby reducing R&D costs through earlier decision-making (DiMasi, Kim & Getz, 2014). Modern value-based portfolio management argues that the failure of individual projects can be compensated for by a large portfolio of robust projects and thus provide the ROI investors expect. The bigger the portfolio, the easier it is to compensate for failed projects. Due to this phenomena, the top pharma companies are now including more than 150 projects in development phases in their corporate R&D pipelines. For example, Pfizer had 205 projects, Novartis 223 projects, Roche 248 projects and GSK 261 projects in 2013 (Citeline, as cited in Schuhmacher, Gassmann & Hinder, 2016).

Some companies are reducing their R&D costs by cutting the number of R&D personnel and **outsourcing** some activities to service providers, which is currently a standard collaboration strategy in the industry. It is not uncommon to outsource R&D, manufacturing and marketing activities (Clark, 2011; Mehta & Peters, 2003). It has been predicted that outsourcing to multiple external service providers will develop into an integrated model of long-term relationships with a limited number of partners in the future (Levy, 2013).

It is undeniable that the driving force of innovation and creativity lies in **innovation centres**, where internal and external experts and know-how are brought together to solve R&D challenges and facilitate drug discovery alliances (Schuhmacher, Gassmann & Hinder, 2016). GSK established its Centre of Excellence for External Drug Discovery (hereinafter: CEEDD), which combines the principles of virtual organisation with a biotech alliance where partners contribute their technologies, and GSK provides its expertise and services related to drug discovery and development. This is fuelling 50% of GSK's early-stage pipeline (GlaxoSmithKline plc, n.d.). Similarly, Pfizer developed its Global Centers for Therapeutic Innovation (hereinafter: CTIs), where academic medical partners bring their hypotheses and Pfizer provides personnel, funding and technologies to test them, a process in which decisions are made collectively (Ratner, 2011).

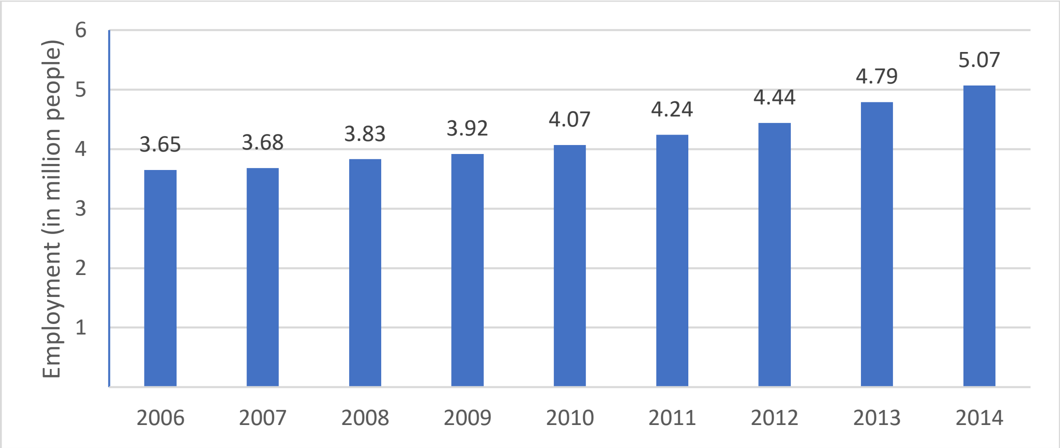
The total contract research organisation market generated revenue of $28,882 million in 2015 and is expected to grow to $40,400 million in 2020. Data for 2018 show that, according to research function, almost 74% of the aforementioned market was accounted for by the category of Clinical Development and Other, 14% by Preclinical/Prehuman Development and Safety, 9% by the Discovery phase and the rest by the Central Lab function (C.S. & Evaluate, 2016).

3.3 Investments in human resources

Investing in human resources is crucial in the pharmaceutical industry, as it is one of the most human-capital intensive industries. Companies in the industry require employees with higher levels of education, expertise and skills, and thus employ a higher percentage of employees with a college education than other industries (Wang, 2009). As seen in Figure 11, global employment in the pharmaceutical industry has increased by nearly 1.5 million employees in less than ten years. The main source of this growth lies in the overall development of the industry as a whole which is constantly creating new job opportunities for highly skilled jobs in both developed and developing countries.

The pharmaceutical industry represents one of the top-performing high-tech sectors in Europe and is thus a key asset in the European economy. The European Federation of Pharmaceutical Industries and Associations (hereinafter: EFPIA) represents more than 1,900 EU pharma companies in Europe. For this reason, it also represents the whole European pharmaceutical industry (EFPIA, 2020). For the purpose of this research, data reported by the EFPIA will be taken as an approximation for the whole European pharmaceutical industry. Table 6 presents total R&D expenditure, employment and R&D employment for the EFPIA. Here we can observe how R&D expenditure is rising, while the absolute and relative numbers of R&D employees are not experiencing a similar upward trend. This data confirms the problem of diminishing R&D productivity, increasing drug complexity and resulting long drug development periods, which are accompanied by rising costs of R&D due to the high number of failed attempts and significant investments in modern equipment.

Figure 11: Global employment in the pharmaceutical industry from 2006 to 2014 (in million people)



Source: International Federation of Pharmaceutical Manufacturers & Associations (2017).

Table 6: Expenditure (in million €) and employment statistics (in units or percentage) for EFPIA for 2000, 2010, 2017 and 2018 (estimated)

Industry (EFPIA total)	**2000**	**2010**	**2017**	**2018**
R&D expenditure (in million €)	17,849.00	27,920.00	35,318.00	36,500.00
Employment (units)	554,186.00	670,088.00	760,795.00	765,000.00
R&D employment (units)	88,397.00	117,035.00	114,655.00	115,000.00
Percentage of R&D employees	15.95	17.47	15.07	15.03

Note. Data are summarised for the EU-27, where data for Switzerland and Norway are from 2005 on, data for Serbia and Croatia are from 2010 on, data for Turkey are from 2011 on and data for Russia are from 2013 on.

Source: EFPIA (2019c).

In 2017, Germany was the largest employer of workerss in pharma with 117,013 employees, followed by France and Italy with 98,786 and 65,400 employees respectively, while Slovenia employed almost 10,000 workers. Table 7 presents employment in all EFPIA countries for 2017. However, data are not current for all countries (see note).

In 2013, pharmaceuticals and medicines were one of the three largest industry groups in terms of domestic R&D employment in the US, with 18.8% of employees in the sector being employed in R&D, while the average of all industries was 7.5% (Shackelford & Moris, 2016). The US average of R&D employees in pharmaceuticals and medicines was 16% (out of a total of 1,010 employers in the industry) in 2016. The total R&D headcount was 161 thousand employees, of which 107 thousand (66%) were researchers (of that amount, 28 thousand (26%) were researchers with a PhD), 22 thousand (14%) were R&D technicians and equivalent staff and 32 thousand (20%) were other R&D support staff. A total of 83 thousand (52%) were male and the rest were female (48% or 78 thousand). Pharmaceuticals and medicines were thus among the industry groups in the US with the highest representation of women in their R&D workforce (the average across all industries is 25%). A total of 76% of these R&D employees were domestic and 24% foreign. Of all domestic employees, 99% were full-time and full-time equivalents (hereinafter: FTEs), which is also above average.

Table 7: Total number of employees in the pharmaceutical industry by EFPIA country in 2017

Country	Number of employees	Country	Number of employees
Russia	n.a.	Austria	14,860
Germany	117,013	Bulgaria	11,500
France	98,786	Sweden	11,012
Italy	65,400	The Czech Republic	10,083
United Kingdom	63,250	Slovenia	9,954
Switzerland	46,503	Portugal	7,700
Spain	42,687	Croatia	5,474
Belgium	35,711	Finland	4,722
Romania	30,000	Norway	3,800
Poland	29,873	Slovakia	2,287
Ireland	29,766	Latvia	2,154
Hungary	29,400	Lithuania	1,220
Denmark	26,963	Cyprus	1,140
Turkey	20,000	Malta	1,057
Greece	19,700	Iceland	500
Netherlands	17,900	Estonia	380

Note. Due to the unavailability of current data, numbers for Turkey are from 2016, while data for Sweden are from 2014. The numbers reported for Lithuania and Cyprus are from 2013 and 2007, respectively.

Source: EFPIA (2019c).

It is interesting to note that the R&D cost per R&D employee in this sector averaged $463 thousand, with a large gap between R&D costs per domestic and foreign employee, with cost per domestic employee totalling $527 thousand and costs per foreign employee amounting to $257 thousand. It can be observed that the difference here was $270 thousand per employee, while the average gap for all industries was $131 thousand (National Science Foundation, National Center for Science and Engineering Statistics, 2019). Shackelford and Moris (2016) reported that in 2013, the sector of pharmaceuticals and medicines in the US had the highest

R&D employee compensation per domestic FTE, of $251,000. These data further support previous claims regarding the industry's R&D intensity and also indicate the intensity of human capital needed to perform R&D activities. They also indicate the importance of a good employee incentive system.

In addition, companies that foster an employee-friendly environment have been found to outperform their rivals in productivity, value creation and profitability (Faleye & Trahan, 2011). An employee-friendly environment could also help reduce lawsuits by employees, which result in high direct and indirect costs for companies, impede innovation activity and lower employee morale. Such lawsuits should thus be avoided. Nevertheless, lawsuits are one of the not-so-typical challenges that companies are facing to an increasing extent in relations with their employees (Rayfield & Unsal, 2019).

4 CHARACTERISTICS OF RESEARCH, DEVELOPMENT AND INNOVATION IN THE PHARMACEUTICAL INDUSTRY

Research, development and innovation are the research topics in this section. They are thus explained first in order to avoid misunderstanding. The Frascati Manual is a document referred to herein for its definitions, as it provides internationally accepted definitions of R&D and the components thereof as a common language for R&D. It is thus globally recognised. It was first issued in June 1963 at an OECD meeting. On the basis of experience and collective work, the sixth edition was published in 2002, with an increasing focus on R&D and innovation being the key elements in a knowledge-based economy. Because comparable statistics and indicators must be monitored and reliable, the 2002 edition focused on strengthening methodological recommendations and guidelines (OECD, 2002). These R&D definitions and guidelines have become an integral part of OECD member countries striving to improve their understanding of the role played by science and technology. This is accomplished through innovation analysis. The seventh edition from 2015 is considered the most significant revision since the first issue of the manual, where further emphasis was placed on enriching the macro picture of R&D in order to improve understanding of micro-data, and the associated dynamics and links (OECD, 2015).

In the Frascati Manual, R&D is understood as creative and systematic work that is supposed to increase the stock of knowledge from humankind to culture and society, and to enable new knowledge applications. R&D strives for new findings, regardless of specificity or generality, with uncertainty about the final outcome. An R&D activity must meet five criteria to be deemed such, i.e. it must be novel, uncertain, systematic and transferable or reproducible. R&D is divided into the following types (OECD, 2015):

- **Basic research** is undertaken to acquire new knowledge regarding phenomena and observable facts related to experimental or theoretical work of general interest. No specific view of use is envisaged, since the researcher is not aware of all the potential applications of the research. Moreover, basic research is mostly published in scientific articles rather than sold.

- **Applied research**, in contrast to basic research, is aimed at acquiring new knowledge with a specific, practical goal or objective. Existing knowledge is therefore taken and extended in order to solve real problems and be applied to actual products, operations, methods or systems. These applications can be protected by intellectual property instruments.
- **Experimental development** involves systematically building upon research and practical experience in order to produce additional knowledge valuable for further product and process improvement.

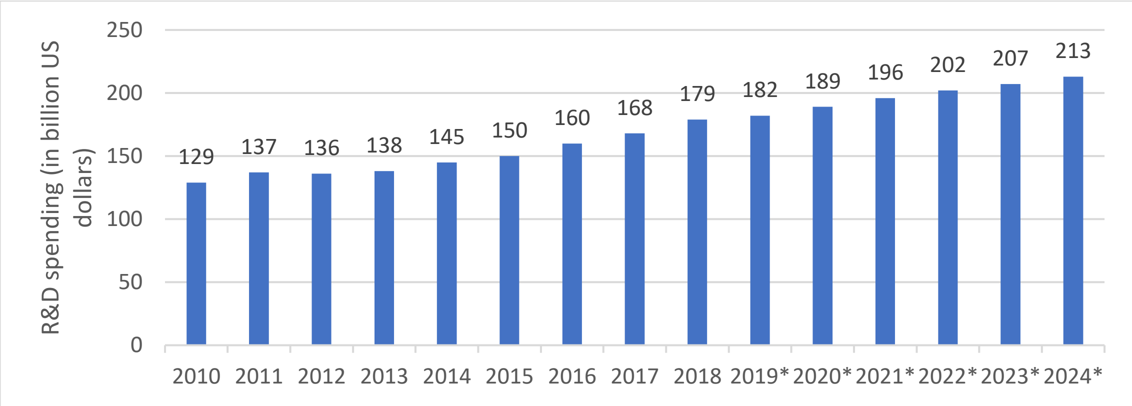
Innovation was described in detail in section 3. For the purpose of conclusiveness, however, some crucial observations are also emphasised here. Innovation refers to the introduction of new or significantly improved products on the market, or to improving processes and methods for the introduction of products to the market. Innovation activities range from R&D to the acquisition of existing knowledge, machinery, equipment, training, marketing, design and software development. In addition, innovation activities can be carried out by a company itself or by external partners (OECD, 2015).

4.1 Overview and analysis of R&D expenditure

The primary research interest of pharmaceutical companies is the identification and development of components used to develop new medications. Because the research projects that these companies undertake are enormous in scale, it is not surprising that the pharmaceutical industry earmarks the highest percentage of its spending for investments in R&D among all industries (Pharmaceutical Executive, 2019). Figure 12 shows historical numbers and forecasts of global pharma R&D spending, where a positive trend is present in all years but one year (from 2011 to 2012). From the beginning to the end of the observed time period, investments in R&D are projected to almost double, illustrating the importance and the scale of R&D activities in the industry. Although the forecasts point to positive growth, that growth is expected to slow in the coming years, falling from as high as 6.7% in 2016, 5.1% in 2017 and 6.5% in 2018, to as low as 1.6% in 2019, then rising to 4% in 2020 and gradually decreasing to 2.7% in 2024 (Evaluate, 2019a). Not surprisingly, the largest companies are those with the most intensive investments in their R&D (in absolute amounts). Figure 13 presents R&D investments of the top 15 global companies according to their sales.

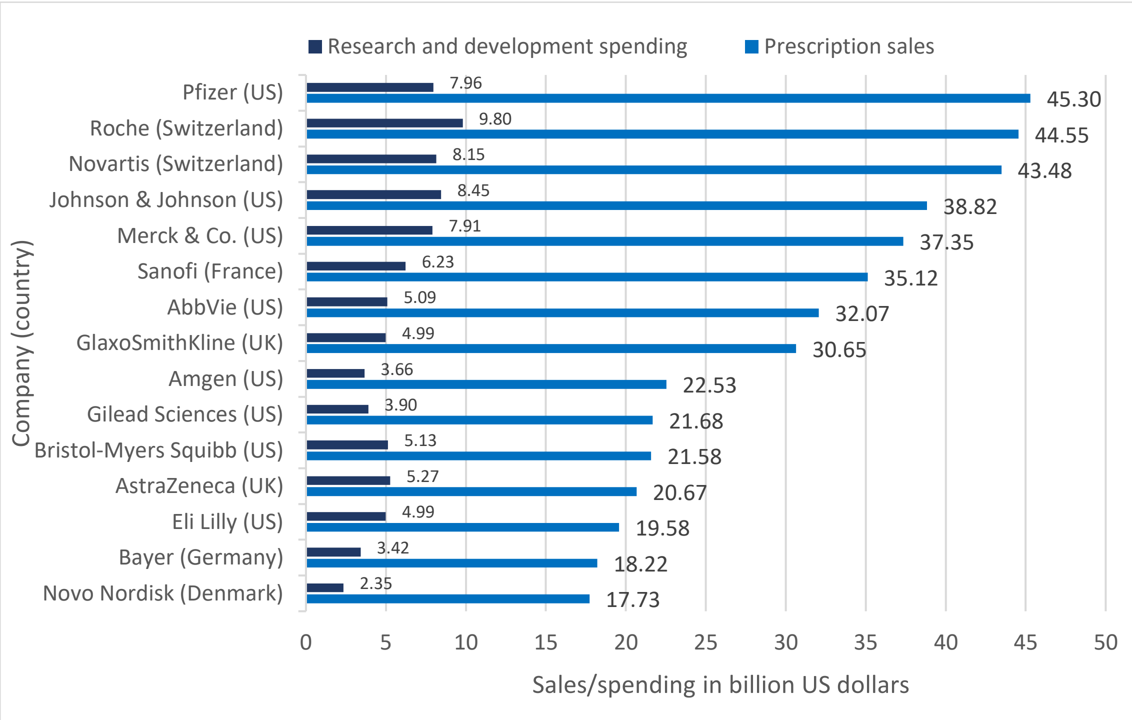
In addition, the steady growth in R&D investment has turned into growth in the number of drugs in the R&D pipelines of companies. In 2019, there were more than 4,000 pharmaceutical companies with active R&D pipelines worldwide, which is almost four times more than in 2001. A total of 46% of these companies are located in the US, 26% in Europe, 23% in Asia and 1% in Latin America and Africa combined. Worldwide figures show that all efforts to discover new medicines helped to almost triple the number of drugs in R&D pipelines over the last 19 years, raising the number of drugs in pipelines from 5,995 in 2001 to more than 10,000 (10,452) for the first time in 2012, and settling at approximately 16,181 (estimated) in 2019 (Pharma Intelligence, 2019).

Figure 12: Total global pharmaceutical R&D spending from 2010 to 2024 (in billion US dollars)



Source: Evaluate (2019a).

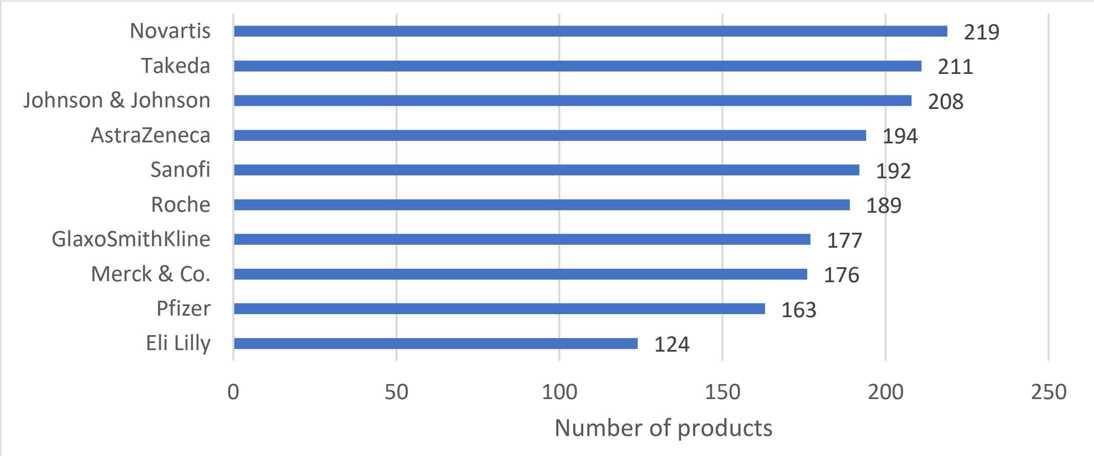
Figure 13: Top 15 global pharmaceutical companies by prescription sales and R&D spending in 2018 (in billion US dollars)



Source: Executive (2019b).

Nevertheless, due to its complex nature, the size of R&D spending does not directly translate into the number of products a company has in its R&D pipeline. Thus, the list of the top 10 companies based on their R&D pipelines (Figure 14) differs from the list of the top R&D investors (Figure 13). Nevertheless, all of them are major players in the industry.

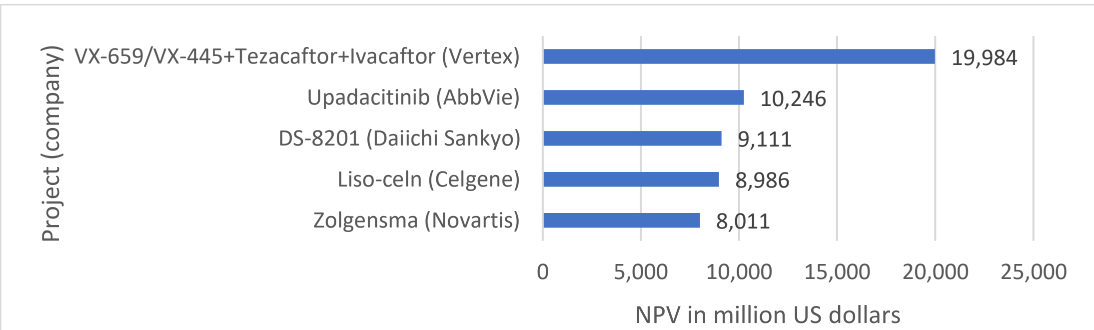
Figure 14: Top 10 pharmaceutical companies worldwide by number of products in their R&D pipelines in 2019



Source: Pharma Intelligence (2019).

Although the largest companies may invest the most in R&D, their primary focus in this regard is on fundamental research, which consumes a great deal of time and resources, while profitability is not guaranteed. Hence, the net present value (hereinafter: NPV) of their projects is not necessarily the highest. Figure 15 shows the top five pharmaceutical projects based on their NPV in May 2019, along with the company that is implementing those projects and their total NPV. It is surprising that three out of those projects are being implemented by companies that have not yet been mentioned in this overview, namely, Vertex, Daiichi Sankyo and Celgene. Vertex's project claimed an NPV of almost $20 billion (Figure 15), which is more than twice as much as the total 2018 R&D expenditure of Pfizer (Figure 13).

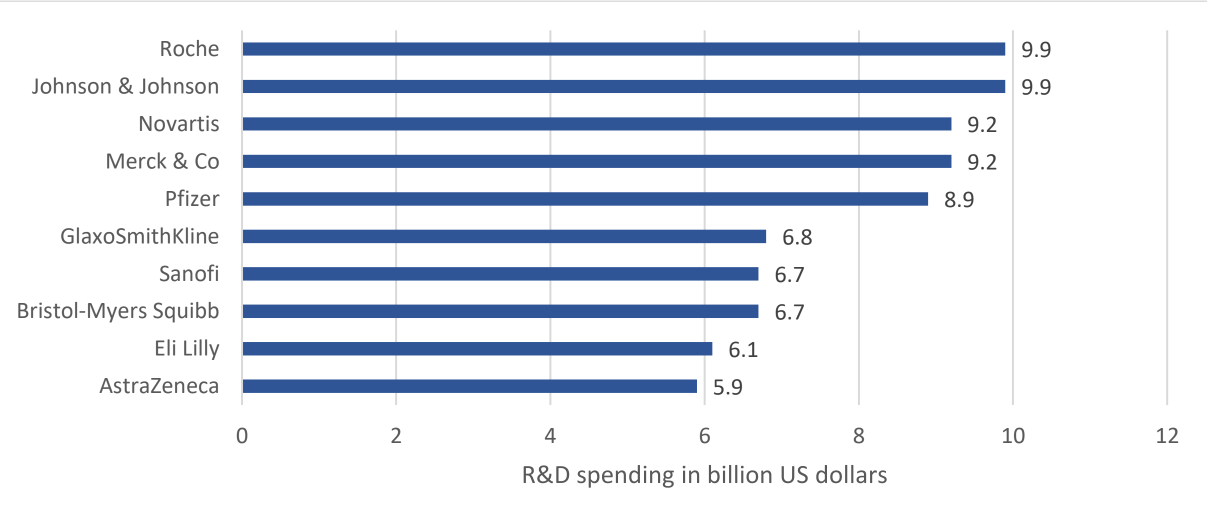
Figure 15: Selected top pharmaceutical R&D projects based on NPV by company in May 2019 (in million US dollars)



Source: Evaluate (2019f).

Due to the turbulent environment and stiff market competition, pharmaceutical companies tend to increase their investments in R&D to keep up with their competitors and secure their market position. Figure 16 shows a projection of R&D spending by major industry players for 2024. It can be observed that the market positions of leading companies based on R&D investments are expected to change compared to their position in 2018 (Figure 13). As previously discussed, Europe lags behind the US in terms of the development of new substances. Although there was a large lag in the annual growth rate of R&D spending between the European (3.8%) and US (8.6%) pharma industry (EFPIA, 2019a) in the period 2014 to 2018, it has been positive ever since 1990 (EFPIA, 2019d). Figure 17 shows the 11 leading European pharma companies by R&D spending in 2018.

Figure 16: Global top 10 pharmaceutical companies based on projected R&D spending in 2024 (in billion US dollars)



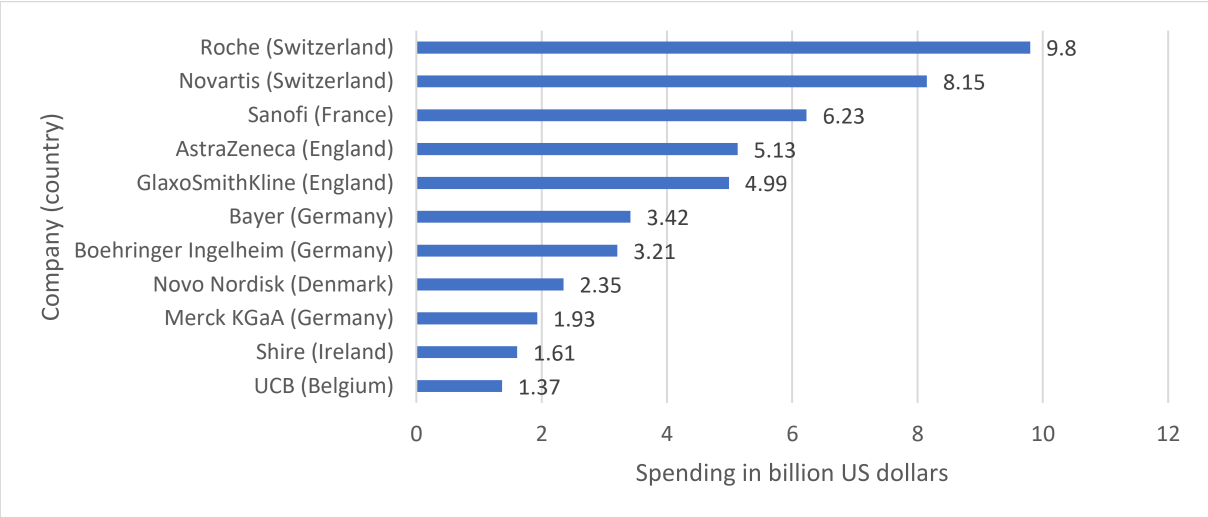
Source: Evaluate (2019c).

Roche and Novartis are the two leading companies in terms of R&D spending, and were also among the top two according to retail sales in 2018, generating $44.5 billion and $43.5 billion, respectively. Sanofi ranked third with $30.6 billion in sales. The list of the top five is completed by AstraZeneca and GlaxoSmithKline. It is interesting to note that although GSK generated $5 billion more in sales than AstraZeneca, it invested slightly less than the latter during the same year (Evaluate, 2019b). This discrepancy between revenue generation and R&D investment can be due to various reasons, ranging from owning patented blockbuster drugs to company policy.

4.2 Patent expiration and its effect on innovation intensity

Pharmaceutical companies continuously adapt their business models towards the development of a single drug that cures a wide spectrum of medical conditions and, therefore, targets a broader population. However, as multiple companies try to create a breakthrough in similar indication areas, they tend to file a patent application for a newly discovered drug candidate as soon as possible, making patent expiration earlier than would be optimal. This, in turn, significantly shortens the effective market life of medications (Hemphill & Sampat, 2012). To ensure that new medications are effective and safe, regulatory requirements for the qualification of drug candidates have become very complex over time. This has resulted in a significant increase in the time and cost requirements of new drug discovery, which is later reflected in the market price of a substance, resulting in higher overall healthcare costs (Aitken, Berndt & Cutler, 2009; Fischer, 1999). After companies file for patent protection, it usually takes from 12 to 13 years and around $1 billion for all necessary R&D activities to be completed. Because it takes some time from the initial patent filing to the regulatory approval of a new medication, the effective time of market exclusivity gets reduced to between seven and eight years (EFPIA, 2014). Figure 18 and Figure 19 show the process of developing a new drug in detail by phases and the costs that are allocated to each of the phases.

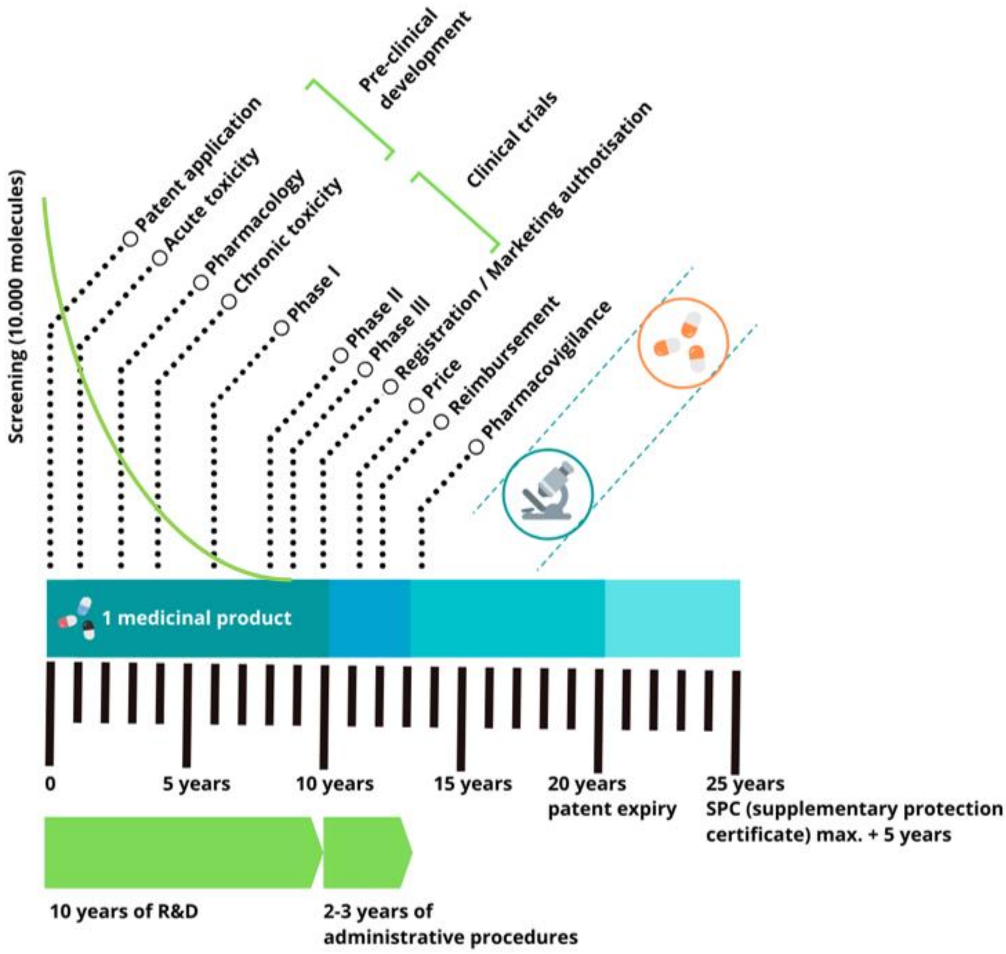
Figure 17: Leading European pharmaceutical companies by spending on R&D in 2018 (in billion US dollars)



Source: Evaluate (2019d).

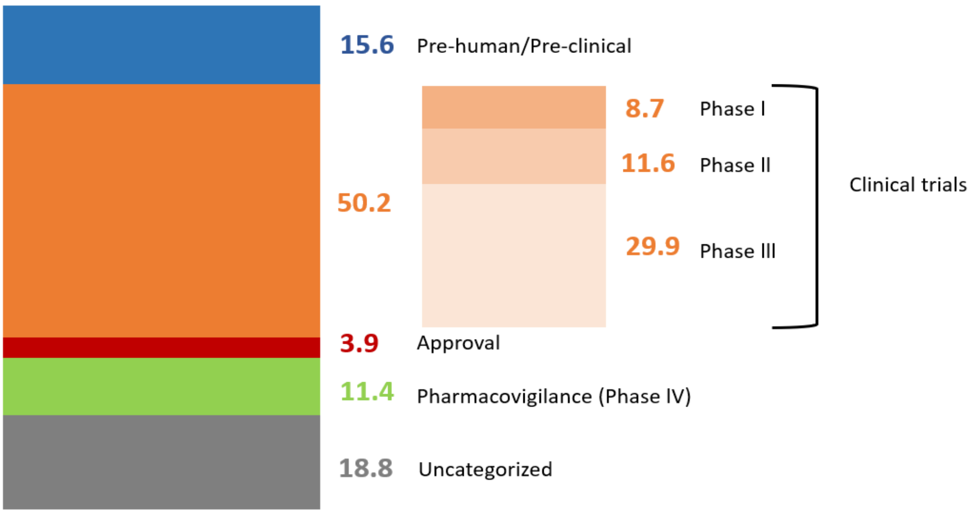
A shortened exclusivity period prevents innovators from earning a positive return on their investment (Grabowski & Moe, 2008). Innovator companies are also at risk of losing their patents due to their own mistakes, such as poor patent claims, double patenting or nondisclosure of best practices (Dubey & Dubey, 2010). Figure 20 illustrates the typical market life cash flows of a blockbuster drug. The growing cash flow stream from the period between one and five years reflects market acceptance of the drug due to aggressive promotion with the aim of getting an increasing number of physicians to adopt it (Dubey & Dubey, 2010).

Figure 18: Phases of new drug development R&D process, by time span



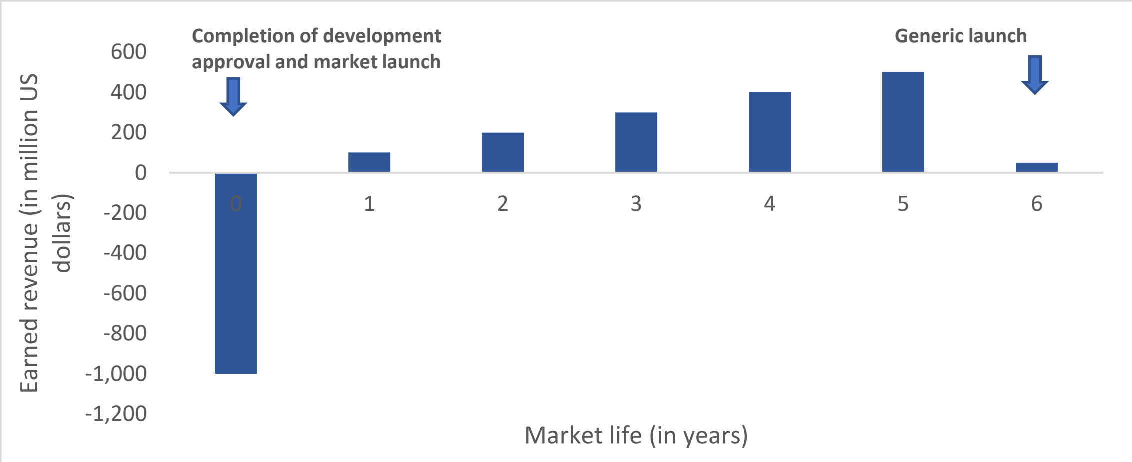
Source: EFPIA (2019e).

Figure 19: Allocation of R&D investments by function (in %)



Source: EFPIA (2019e).

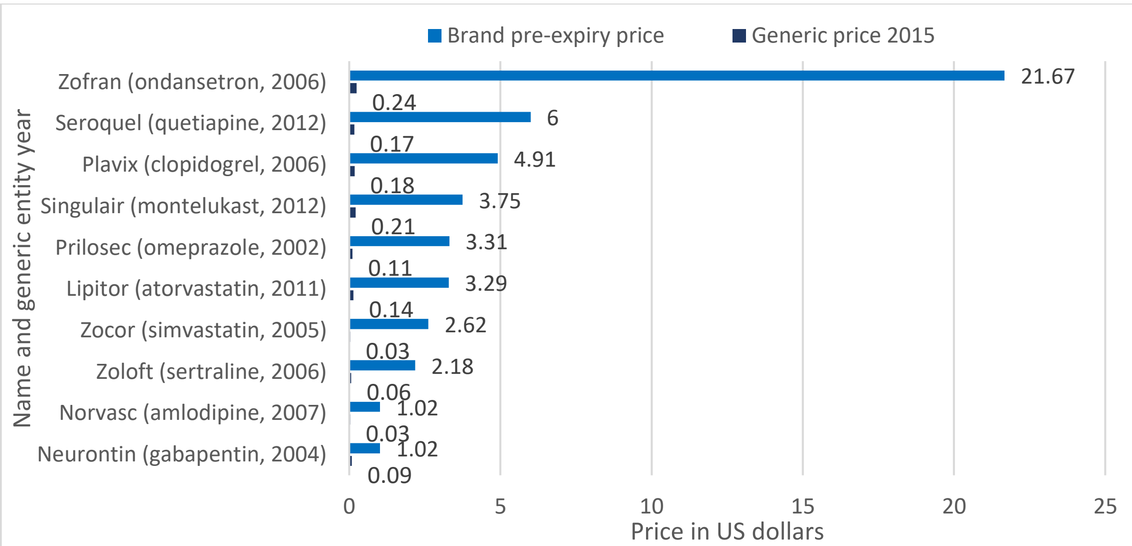
Figure 20: Typical market life (in years) of an approved drug product before and after approval of generic products in terms of revenue earned (in million US dollars)



Source: Dubey & Dubey (2010).

Patent expiration presents challenges for innovator companies due to the drastically declining revenue they face. The current "blockbuster business model" results in the loss of an innovator company's core business portfolio every 10 to 12 years. The loss of protection is expected to cause a drop in sales of more than $100 billion in the coming years, leaving a "financial vacuum" for the affected company (Vollerbregt & Denoon, 2010). For example, Plavix (made by Bristol-Myers Squibb Company) was originally sold for an average of $2 per dose, but once its protection expired, a generic company in India produced and sold it for 3 cents per dose (ProText Knowledge Services, 2010). Figure 21 further illustrates the extreme difference in patented drug price and its generic price (data for prices in the US).

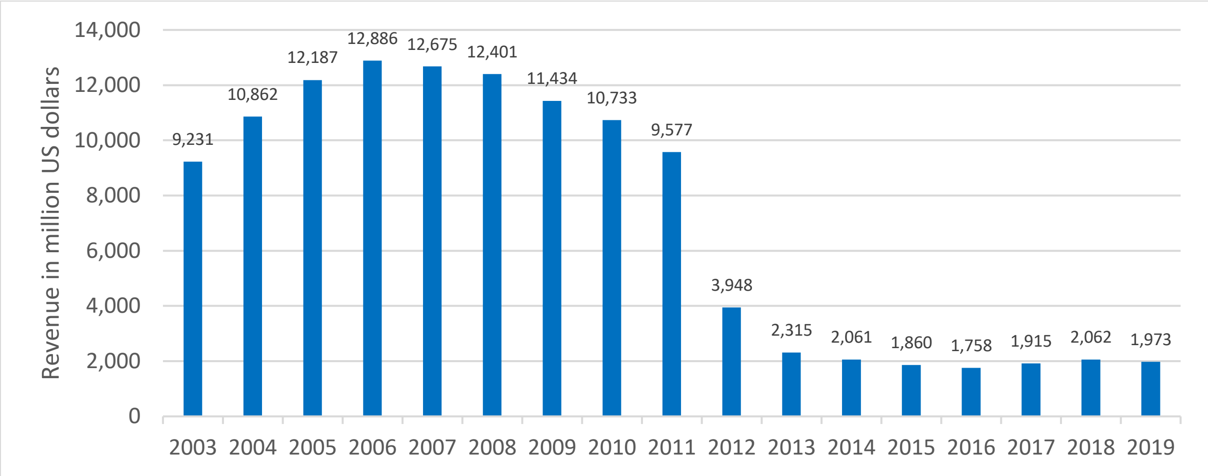
Figure 21: Comparison of brand pre-expiry price and generic price of selected drugs in the US as of 2015 (in US dollars)



Source: GPhA (2016).

Lipitor (by Pfizer) listed its patent protection in November 2011 and by 2014, generic versions of the drug had already accounted for more than 97% of sales. Once a medication faces a patent cliff, the first generic to market a copy of the drug is granted a 180-day exclusivity period (Indxx, 2016). Figure 22 shows the sales dynamics of Lipitor, which was a historically best-selling prescription drug from Pfizer. Once its period of market exclusivity expired in 2011, a dramatic drop in sales is visible between 2011 and 2012.

Figure 22: Worldwide revenue of Pfizer's Lipitor from 2003 to 2019 (in million US dollars)

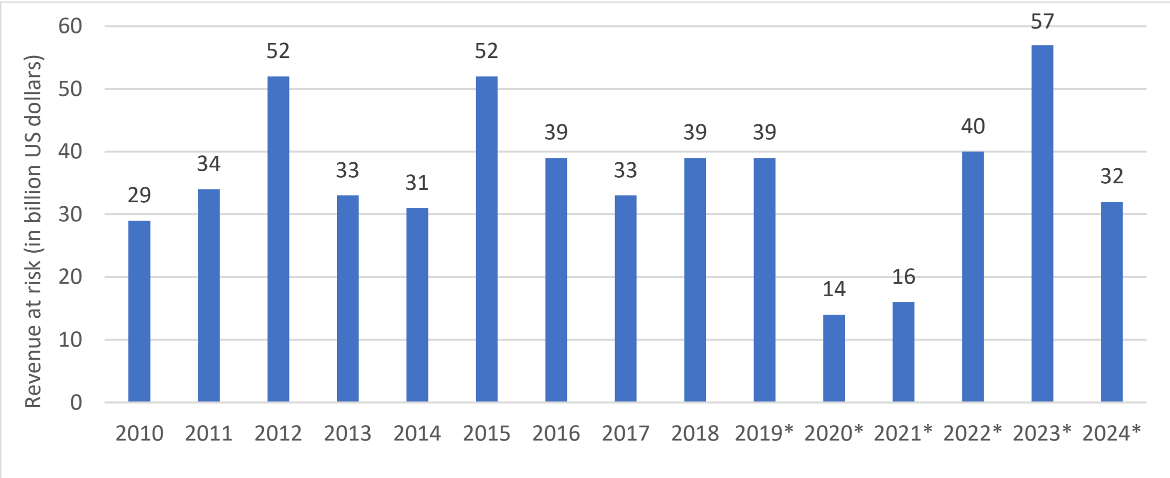


Source: Pfizer (2020).

This fall in revenue immediately after the expiration of patent protection, as seen in Figure 22, is commonly referred to as a "patent cliff" (Jimenez, 2012). The dynamic forces driving patent cliffs are the increasing competition of generic companies and shortcomings in regulatory frameworks. Because blockbuster drugs account for a large percentage of a company's turnover, this entails the dependence of innovator companies on repeated R&D successes, with an uneven spread of risk throughout the sector (Song & Han, 2016). A number of drugs have lost their patent protection in the past few years, while another large wave of patent expiration is expected to occur in the coming years. Figure 23 shows the alarming amount of revenue at risk due to patent expirations. It is evident that the figures are not small and mean the loss of billions of dollars for innovator companies. The next big wave that is expected in 2022 and 2023 is expected to erode almost $100 billion in revenue.

These losses are forcing big pharma to look for new revenue streams and sometimes force them to participate in M&As (Mittra, 2007). Companies appear to have learned valuable lessons from their competitors' patent cliffs, which left deep scars on their operating results and financial position, and now seem to be better prepared to face the future. There is no "one-size-fits-all" solution to strategically address the question of sustaining the competitiveness of branded products beyond the end of their market exclusivity. However, research-driven pharma companies have a range of strategies at their disposal that can extend their patent protection on pharmaceutical composition or therapeutically active substances, and thus maximise the commercial value of their product and retain their market share (Prajapati, Tripathy & Dureja, 2013; Song & Han, 2016). One strategy is to develop an isomer or an active metabolite of an existing drug, i.e. a drug that a company has under active patent protection. They also frequently launch a controlled-release version of a drug or a combination of a product and the identification of new treatment usages, and thus gain further market exclusivity by additionally patenting these new products (Dubey & Dubey, 2010).

Figure 23: Worldwide total prescription drug revenue at risk from patent expiration from 2010 to 2024 (in billion US dollars)

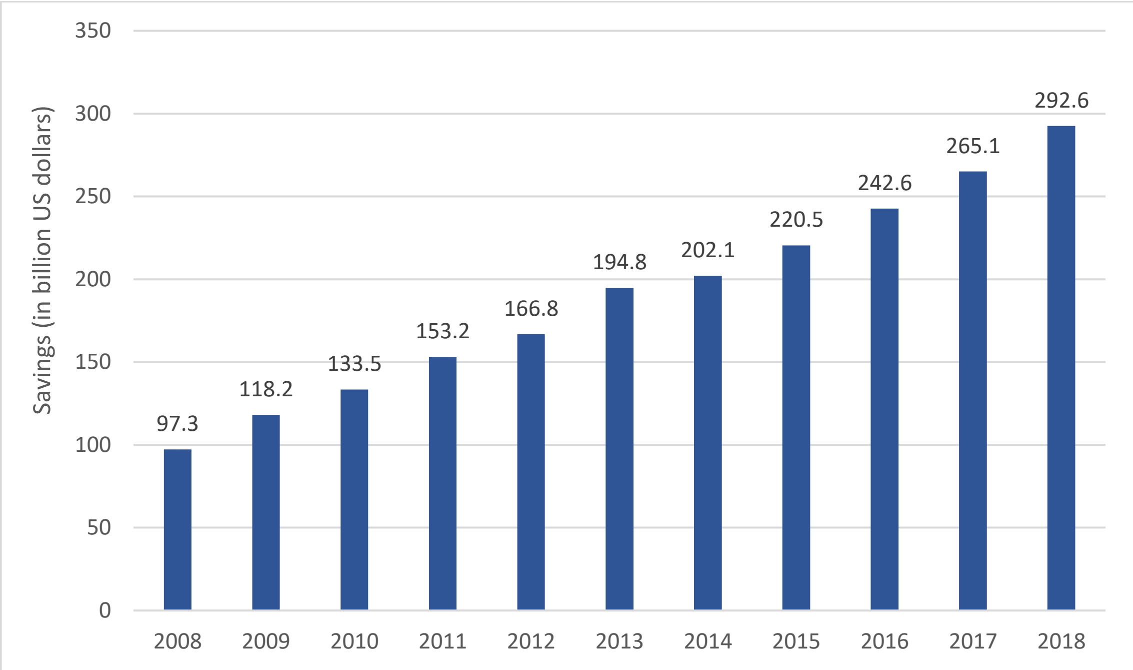


Source: Evaluate (2019g).

Although a generic's copycat launches dry up an innovator's revenue streams, these products create incentives for additional research, help to ease pressure on public health budgets and increase consumer welfare (Song & Han, 2016). Savings of $97.3 billion were recorded in 2008 due to the use of generic drugs in the US. This number rose quickly and settled at around $300 billion in 2018 (Figure 24). In 2018, the largest savings were achieved in expenditure on generic drug usage by older adults (age group between 40 and 64), in the amount of $128.7 billion, followed by $105.3 dollars for the age group of seniors (above 65 years). Savings in the groups of young adults (between 20 and 39 years) and children (between 0 and 19 years) were $38 billion and $20.6 billion, respectively (IQVIA, 2019b).

Patent expirations have generated enough financial resources for generics to rise from fringe players into the "New Big Pharma", and move into new exciting areas of duplicating more complex products, which will allow them to charge higher prices with higher profit margins and protect them from the competition. For example, biosimilars are a biologics class of drugs, which are far more complex than traditional drugs (both in terms of molecular structure and production). It is thus much more complicated to duplicate them, which allows the generics of these products to charge higher prices (Indxx, 2016). Some generic companies have already started investing their money in fundamental research and are beginning to pursue the business model of innovator companies. On the contrary, innovator companies are investing in generic drugs, with Novartis as an excellent example in that regard. Based on their generated revenue in 2018, the top five manufacturers of generic drugs were Mylan ($11.26 billion), Sandoz ($9.85 billion), Teva ($9.67 billion), Sun Pharmaceutical ($4.11 billion) and Lupin with $2.27 billion in revenue (Pharmaceutical Technology, 2019).

Figure 24: Savings through generic drug usage from 2008 to 2018 in the United States (in billion US dollars)



Source: IQVIA (2019a).

In order to survive on the market, it is necessary for innovator companies to protect their revenue stream by implementing different approaches rather than unjustifiably abusing their intellectual property rights at the expense of public welfare and competition (Glasgow, 2001). For this reason, they are strongly encouraged to pursue R&D in so-called "niche busters", which are specialty medications with very low substitution potential (Dolgin, 2010; Kakkar & Dahiya, 2014). By focusing on niche products, companies can focus on enhancing their core competencies, avoid dealing with assets that are unimportant for competing on a global scale and thus free up more resources (Song & Han, 2016). Another area of potential research is "orphan drugs", which are developed to treat extremely rare diseases. Due to their rarity, however, they are not very attractive for companies, as their profitability is very low or even non-existent. Nevertheless, these drugs are given special incentives and receive special benefits from governments and international organisations.

The business environment has changed dramatically in recent years. Pharmaceutical companies have thus given a great deal of thought to developing new business models and evaluating legislative practice (Rusu, Kuokkanen & Heier, 2011). PricewaterhouseCoopers (2009) argues that a business model that is based on marketing and sales will not be efficient in the future, as most medicines will likely be priced and bought on the basis of the results they deliver, and companies will have to engage in “profiting together” strategies rather than “profiting alone” by moving into health management and research areas beyond medicine.

5 EMPIRICAL ANALYSIS OF INNOVATION IN THE PHARMACEUTICAL INDUSTRY

With this section, the analysis shifts from a theoretical to an empirical point of view. Four countries were considered for the purpose of analysis: Germany, France, Italy and Slovenia. The following abbreviations were used for the studied countries: GE = Germany, France = FR, ITA = Italy, SI = Slovenia.

Two research questions were addressed. The Community Innovation Survey (hereinafter: CIS) was reviewed in order to identify the characteristics of innovation in the studied countries, where focus was placed on the competitiveness of Slovenia relative to the other three countries, deemed the leading European countries in terms of innovation investments and strategies. In addition, innovation and value-added in the pharmaceutical sector were examined to determine how value-added per employee relates to investments in R&D.

5.1 Analysis of R&D and innovation in the pharmaceutical sector using CIS data

The CIS is a survey conducted by Eurostat, the statistical office of the EU, in EU member states, and in some EFTA and EU candidate countries on a regular basis since 1993. Its aim is to collect information regarding innovation activities at the enterprise level, grouped by industry for all participating countries. Its structure is designed in a way that the results provide information regarding the innovativeness of different sectors by type of enterprise, different types of innovation, expenditure for innovation activities, their objectives and effects, types of cooperation and many other aspects. It relates to all enterprises with at least ten employees, although if treated separately, companies with less than ten employees can also be included. The statistical units are therefore enterprises (the data are anonymous), which are categorised by country, economic activity, type of innovation activity and size (Damijan, Kostevc & Rojec, 2014; Eurostat, 2020; Eurostat, 2019).

At least three size categories are considered: small (between 10 and 49 employees), medium-sized (between 50 and 249 employees) and large (more than 250 employees). Enterprises from different economic activities are included in the survey. The basic Nomenclature of Economic Activities (hereinafter: NACE) coverage takes into account:

- mining and quarrying (NACE 10-14),
- manufacturing (NACE 12-37),
- electricity, gas and water supply (NACE 40-41),
- wholesale trade (NACE 51),

- transport, storage and communication (NACE 60-64),
- financial intermediation (NACE 65-67),
- computer and related activities (NACE 72),
- research and development (NACE 73),
- architectural and engineering activities (NACE 74.2), and
- technical testing and analysis (NACE 74.3).

Additional coverage is added on a voluntary basis (Eurostat, 2020; Eurostat, 2019; Damijan, Kostevc & Rojec, 2014).

For the purpose of this analysis, the following two NACE codes were considered:

- "NACE C21 – Manufacture of basic pharmaceutical products and pharmaceutical preparations" was used as the representative classification for the pharmaceutical industry.
- "NACE B-M73_INN – Innovation core activities (Com. Reg. 995/2012)" was used as the representative classification for a general picture of the economy, comprising all industries.

The CIS is carried out biannually. The interval between the first four reports was four years. However, reporting frequency was then increased, with reports published every two years since 2005. Although important microdata are gathered via this survey, it also comes with some limitations. First, because the questionnaire is constantly adapting and changing, not all indicators are available for all reported years. Second, due to the voluntary nature of the survey, the sample of participating countries changes from wave to wave. Third, the original survey is distributed to the national statistical institutes (hereinafter: NSIs) of all countries that participate in the survey. However, NSIs may modify the survey to some extent. They are not required to collect all variables, but should report data at the enterprise level in order to produce internationally comparable statistics. There are three categories of questions in the original survey, with the first category being obligatory under Regulation (EU) 995/2012, the second category comprising questions that are not obligatory, but perceived as very important, and the last category comprising questions that are also not obligatory, but deemed important. Finally, the reference periods are not the same for all indicators. Most are based on a three-year reference period, while some are based on a one-year period (Eurostat, 2020; Eurostat, 2019; Damijan, Kostevc & Rojec, 2014).

The CIS provides information regarding the characteristics of innovation activity at the enterprise level. It allows Europe's progress to be monitored in the area of innovation, creating a better understanding of the innovation process, with an analysis of the objectives and the effects of innovation. These results can also be linked to variables related to competitiveness, employment and economic growth. The concepts are in line with those recommended by the Oslo Manual (2nd edition, 1997 and 3rd edition, 2005), which is the internationally recognised standard methodology for collecting innovation statistics (OECD & Eurostat, 2018).

In this research, data were collected and analysed for the time period 2012 to 2016 (three reports). Due to the crisis in 2008, data from reports in 2008 and 2010 may not be representative of how the pharmaceutical industry differs from other sectors. For this reason, they were not analysed. It is a well-known fact that pharma is a perfect textbook example of a non-cyclical industry that, because it produces essential goods, performs well during economic downturns. In addition, the CIS covers four broad types of innovations. These are product, process, organisational and marketing innovations. This analysis focused on product and process innovation due to the industry's specific marketing nature, which is not widely comparable to other sectors' efforts (marketing to final consumers only represents a small proportion of all marketing efforts).

The CIS is based on the following definitions, which are also referred to in this research (Eurostat, 2020b):

- **Innovation** means the implementation of a product that is either new or significantly improved. Besides a product, it can also refer to a process, new marketing methods or newly organised business, workplace or external relations.
- **Product innovative enterprises** represent enterprises introducing new or significantly improved goods and/or services, where aestheticism or the resale of newly purchased goods and services from other enterprises are not categorised as such. Changes could be one or a combination of the following: capabilities, user-friendliness, components, sub-systems.
- **Process innovative enterprises** refer to a new or significantly improved production process, distribution method or supply activity.
- **Organisational innovative enterprises** are enterprises that introduce a new organisational method in business or workplace practices or external relations.
- **Marketing innovative enterprises** implement a new or significantly improved marketing concept or strategy (e.g. significantly altered product design or packaging, product placement, product promotion or pricing). Seasonal, regular and other routine changes in marketing concepts are not categorised as such.
- **Innovative enterprises** engage in one or more types of the innovations described above, where enterprises with on-going and abandoned activities are also included. In addition, an innovation could have been actually implemented, reviewed only or not implemented at all.
- **Non-innovative enterprises** do not engage in any of the innovations described above.

Two aspects of innovation are considered: innovation related to core activities and innovation related to basic pharmaceutical products and pharmaceutical preparations. The focus of core innovation types is on product and process innovation. An increasing number of enterprises are meeting the basic requirements to be characterised as “innovative”. Merely being aware of innovativeness itself, however, is not enough; how and which types of innovation are implemented is of additional interest (Eurostat, 2020b).

In the analysis, the EU-27, EU-28 or EU-15 was compared with four counties: Germany, France, Italy and Slovenia. Germany, France and Italy were mentioned as the leading European pharmaceutical markets. The EU-15 comprises 15 countries that were Members States between 1995 and 2004, the EU-27 comprises 25 countries that were Members States between 2007 and

2013 and the EU-28 comprises 28 countries that were Members States between 2013 and 2020. The analysis is divided into the following sections (Eurostat, n.d.-a):

- Basic economic information regarding enterprises.
- General information regarding enterprises.
- Enterprises by main types of innovation.
- Enterprises by specific types of innovation.
- Product and process innovative enterprises.
- Innovation activities and expenditure by enterprises.
- Public funding at enterprises.
- Types of cooperation of enterprises.
- Organisational and marketing innovation at product and process innovative enterprises.
- Intellectual property rights and licensing at enterprises.
- Importance of reasons for failure to innovate and of the barriers to innovation at enterprises.

All of these sections are analysed in section 5.1.1. A review of innovation related to core activities and innovation related to basic pharmaceutical products and pharmaceutical preparations is presented for each section. In addition, corresponding comparisons are also made, either between enterprises or the EU.

Table 8 presents the number of enterprises from the pharmaceutical industry for the countries that were included in the analysis. Those enterprises are categorised as manufacturers of basic pharmaceutical products and pharmaceutical preparations. Germany has the highest number of enterprises, regardless of the year, followed by Italy, France and Slovenia, despite the fact that France is the largest country in terms of geographic area (World Bank Group, n.d.) and second largest in terms of population (Eurostat, n.d.-b). More than 70% of enterprises are innovative, depending on the country, with more than 90% of enterprises deemed innovative enterprises in Germany. Among innovative enterprises, more than 30% of German and Italian enterprises in 2016 were also product and/or process innovative enterprises, while 16.82% of French enterprises could be categorised in the same. For comparison, also non-innovative enterprises are included in the table. Because the numbers are complementary to the number of innovative enterprises, Germany is again the top-listed country.

Insufficient data for the EU and Slovenia are available to draw any relevant conclusions. Moreover, nothing could be concluded regarding the size of enterprises, as the analysis did not group them in terms of the number of employees for the manufacture of basic pharmaceutical products and pharmaceutical preparations.

Table 8: Number of enterprises in terms of innovativeness by country and innovative enterprises as a proportion of all enterprises for the manufacture of basic pharmaceutical products and pharmaceutical preparations for 2012, 2014 and 2016

	Year		GE	FR	ITA	SI
Total enterprises	2012	Number	324	230	304	6
	2014	Number	326	233	290	n.a.
	2016	Number	346	220	294	5
Innovative enterprises *	2012	Number	298	192	272	n.a.
		Percent	92	83	89	n.a.
	2014	Number	304	206	254	4
		Percent	93	88	88	n.a.
	2016	Number	315	172	232	n.a.
		Percent	91	78	79	n.a.
Product and/or process innovative enterprises only *	2012	Number	69	32	74	n.a.
		Percent	21	14	24	n.a.
	2014	Number	58	30	87	0
		Percent	18	13	30	n.a.
	2016	Number	107	37	91	0
		Percent	31	17	31	n.a.
Non-innovative enterprises	2012	Number	26	38	32	0
		Percent	8	17	11	0
	2014	Number	22	27	36	n.a.
		Percent	7	12	12	n.a.
	2016	Number	31	48	62	n.a.
		Percent	9	22	21	n.a.

Note. * = Including enterprises with abandoned/suspended or on-going innovation activities.

Source: Eurostat (2020).

5.1.1 CIS data analysis

The paragraphs below provide an analysis of available data according to the sections outlined above, where tables and figures are used for better presentation. In addition, relevant explanations are given and a summary made at the end of the section.

Basic economic information regarding enterprises. At enterprises categorised as innovative in terms of their core activities, growth was observed in both the total number of employees and in total turnover in Germany and France. Conversely, Italy and Slovenia recorded a negative trend in the total number of employees and total turnover, which was more significant in Slovenia than in Italy. Table 9 presents this numerically. In addition, employees in Germany in 2014 accounted for around one-third of all employees in the EU-15 and one-fourth of all employees in the EU-28. The proportions of enterprises, employees and turnover accounted for by Germany decreased when comparing the EU-15 to the EU-28, which is consistent with the increased number of Member States in the EU. However, the proportions of enterprises and employees decreased disproportionately more than the proportion of turnover, an indication of the strength and/or size of German enterprises. Slovenia's total number of employees and enterprises represented 1.65% and 1.95% of those same totals for Germany, respectively, while the Slovenia's total turnover represented 0.73% of the turnover generated by Germany. Slovenia accounted for 0.22% and 0.44% of turnover and the total number of enterprises in the EU-28, respectively.

Table 9: Total turnover (in thousand €), number of employees and enterprises for innovation core activities by country from 2010 to 2016

	2010	**2012**	**2014**	**2016**
Total turnover				
GE	4,083,248,000	4,287,731,000	4,306,870,000	4,500,296,260
FR	1,664,009,177	1,883,521,835	1,936,518,043	2,039,491,266
ITA	1,378,243,142	1,654,964,825	1,527,369,764	1,625,344,482
SI	33,544,786	36,970,577	34,734,641	33,073,243
Total number of employees				
GE	10,357,616	10,354,374	10,624,085	10,813,218
FR	4,356,155	4,533,882	4,678,007	n.a.
ITA	4,033,961	4,000,122	3,777,209	3,955,708
SI	208,599	199,077	185,826	178,394
Total number of enterprises				
GE	n.a.	90,395	91,120	91,192
FR	n.a.	37,924	39,672	41,611
ITA	n.a.	65,481	54,458	61,952
SI	n.a.	1,959	1,906	1,767

Source: Eurostat (2020).

Table 10 offers a relative comparison of the same data, where total turnover per employee is presented. It is evident that Germany has the highest turnover per employee in all years, except 2014, when France ranked first. In 2016, the three larger countries (Germany, France and Italy) were closely grouped, while Slovenia generated less than half of their turnover per employee (Table 10).

Table 10: Turnover per employee for innovation core activities by country from 2010 to 2016 (in thousand €)

	2010	**2012**	**2014**	**2016**
GE	394.23	414.10	405.39	416.18
FR	381.99	415.43	413.96	n.a.
ITA	341.66	413.73	404.36	410.89
SI	160.81	185.71	186.92	185.39

Source: Eurostat (2020).

In terms of innovation related to basic pharmaceutical products and pharmaceutical preparations, no data were available for Slovenia. A review of the other three countries was thus made. A decline in the number of employees was observed for Germany and Italy, while the number of employees increased in France during the observed period. Conversely, Italy recorded growth in total turnover from 2010 to 2016, while Germany and France recorded a decline, with turnover decreasing more than the number of employees. The total number of enterprises decreased in Italy and France, while Germany recorded growth.

Because the studied countries are of different sizes, a relative comparison should also be considered. Thus, turnover per employee was calculated for innovation related to core activities. Germany, France and Italy recorded turnover per employee of more than €400 thousand, while Slovenia recorded approximately half of that number. According to turnover per enterprise, German and French enterprises have the highest turnover per enterprise, although not much growth or decline was seen in any country.

Taking into account growth rates for total turnover, total number of enterprises and total number of employees, total turnover recorded the lowest growth rates, meaning that more enterprises on the market and more employees at those enterprises create disproportionately lower value or, stated differently, more enterprises and more employees would be expected to contribute to higher total turnover, but they do not. This is summarised in Table 11. It should be emphasised, however, that not necessarily the same enterprises are included in all three analyses, i.e. for 2012, 2014 and 2016. Nevertheless, these are presented anyway for the purpose of a rough understanding.

Table 11: Growth rates for total turnover (in %), total number of enterprises and total number of employees for innovation related to core activities by country, for different time intervals from 2010 to 2016

Country	Growth (in %)
Total turnover (2014 vs 2010)	
GE	2.57
FR	7.39
ITA	-6.36
SI	-10.92
Total number of enterprises (2016 vs 2012)	
GE	10.21
FR	22.56
ITA	17.93
SI	-1.41
Total number of employees (2014 vs 2010)	
GE	5.48
FR	16.38
ITA	10.82
SI	3.55

Source: Eurostat (2020).

A relative comparison of turnover per employee and turnover per enterprise for innovation related to basic pharmaceutical products and pharmaceutical preparations showed the following results. In 2014, France and Italy recorded turnover per employee in excess of €450 thousand and €400 thousand, respectively, with Germany only slightly above €350 thousand, which is the only studied indicator where Germany performs relatively worse compared to other studied countries. Because the values of turnover per employee for innovation related to core activities were close to each other for Germany, France and Italy, it can be concluded that Germany is stronger in innovation related to core activities than in innovation related to basic pharmaceutical products and pharmaceutical preparations. Nonetheless, turnover per employee is decreasing in all three countries. Next, the highest turnover per enterprise was identified in France, followed by Germany and Italy, with all three countries recording a downward trend.

Taking into account the growth rates for total turnover, total number of enterprises and total number of employees, growth rates for total turnover were lowest in Germany and France, and highest in Italy. Despite the growing number of enterprises in Germany, those enterprises are not able to create more turnover. In France, the same holds true for the total number of employees. Conversely, Italy recorded growth in total turnover, although the number of both enterprises and employees decreased. Thus, enterprises on the market and employees at those enterprises create more value. This is summarised in Table 12.

Table 12: Growth rates (in %) for total turnover (in thousand €), total number of enterprises and total number of employees for innovation related to basic pharmaceutical products and pharmaceutical preparations by country from 2010 to 2016

Country	2010	2012	2014	2016	Growth (in %)
Total turnover (growth: 2016 vs 2010)					
GE	55,422,000	49,731,000	47,717,000	49,290,838	-11.06
FR	37,367,722	35,781,250	33,859,969	30,559,527	-18.22
ITA	22,251,078	n.a.	24,325,424	24,356,717	9.46
Total number of enterprises (growth: 2016 vs 2012)					
GE	n.a.	298	304	315	5.70
FR	n.a.	192	206	172	-10.42
ITA	n.a.	272	254	232	-14.71
Total number of employees (growth: 2014 vs 2010)					
GE	141,131	138,275	132,563	127,651	-6.07
FR	67,958	67,247	69,938	n.a.	2.91
ITA	54,967	56,424	52,908	55,630	-3.75

Source: Eurostat (2020).

From here until the end of the section, the focus of the analysis is on product and/or process innovative enterprises only, as innovation is of primary interest in this research and those enterprises are the most important for further industry development.

A declining trend for total turnover is evident for product and/or process innovative enterprises, which is the opposite of the total turnover for the industry as a whole, where not only product and/or process innovative enterprises were considered. The exception is Slovenia, where the total turnover of product and/or process innovative enterprises is increasing, despite the fact that the total turnover of all enterprises is decreasing. It can thus be concluded that product and/process innovative enterprises are doing relatively better than the industry as a whole in Slovenia. The opposite holds true for the other three studied countries. The total number of enterprises and total number of employees are recording a negative trend in Germany, meaning that all three indicators for product and/or process innovative enterprises signifies negative growth rates.

General information regarding enterprises. Enterprises that sell goods and/or services on the national market account for the highest proportion of enterprises in terms of innovation core activities in Germany, regardless of the year. In France, Italy and Slovenia enterprises that sell goods and/or services on the local or regional markets are the most significantly represented. Besides these, enterprises that are part of an enterprise group, enterprises for which the largest market in terms of turnover is the national market, enterprises that sell goods and/or services in other EU, EFTA or EU-candidate countries, and enterprises that sell goods and/or services in any other country than EU countries, EFTA or EU-candidate countries are highly represented in the studied countries. Table 13 summarises the number of enterprises in terms of these categories for 2016. Slovenian enterprises represent 0.80% and 4.13% in most of the studied indicators, except enterprises for which the largest market in terms of turnover is other EU, EFTA and/or EU-candidate countries, where the number of enterprises is relatively higher. With regard to enterprises categorised as manufacturers of basic pharmaceutical products and pharmaceutical preparations, Germany and Italy accounted for the highest proportion of enterprises that sell goods and/or services on the national market from 2012 to 2016, with an increasing trend. Due to deficient data for Slovenia, no comparison can be made from that perspective.

Enterprises by specific types of innovation. Considering enterprises with product and/or process innovation only, their innovation can be viewed from the following aspects: goods innovation, service innovation and process innovation. Due to a lack of data, only the four countries were taken into account for the analysis, as no data for the EU is available. Germany and France recorded a positive trend from 2012 to 2016 in the indicators measuring innovation related to core activities. The highest proportion of enterprises' innovation is attributed to goods innovation, followed by process innovation through the improvement of manufacturing or production methods. Conversely, Slovenia recorded a negative trend during the same period, while the proportion of innovation was again the highest in goods innovation. Italy's innovation decreased from 2012 to 2014, but has either returned to its initial level or even exceeded it in 2016. In all studied countries, the fewest enterprises have developed process innovation by improving logistics, delivery or distribution methods and supporting activities for processes. A relative comparison between Germany and Slovenia shows that the proportions of Slovenia enterprises that developed any kind of innovation were between 1.62% and 2.01% in 2016.

With regard to the manufacturing of basic pharmaceutical products and pharmaceutical preparations, the number of enterprises in Germany that developed goods innovation, service innovation and process innovation by improving logistics, delivery or distribution methods, and manufacturing or production methods increased, with the only decrease in the number of enterprises that developed supporting activities for processes. In France, the number of enterprises that innovated in goods and processes by improving methods manufacturing or production methods decreased, while other indicators increased. In Italy, a decrease can be observed in goods and service innovation, while process innovation in all three categories increased. An insufficient amount of data for Slovenia is available to draw any conclusions. Overall, there is a significantly higher number of enterprises that developed any kind of product- or process-related innovation related to core activities than basic pharmaceutical products and preparations. The numbers are summarised in Table 14 for both innovation core activities (hereinafter: I) and the manufacture of basic pharmaceutical products and pharmaceutical preparations (hereinafter: M) by countries for the latest available year, i.e. 2016.

Table 13: Number of enterprises in terms of business expansion and target market by country in 2016

	GE	FR	ITA	SI
Enterprises that have merged with/taken over another enterprise	1,655	658	1,109	30
Enterprises that have sold/closed/outsourced tasks or functions	1,698	399	643	19
Enterprises that are part of an enterprise group	5,917	3,683	3,017	175
Enterprises that are part of an enterprise group and have a foreign head office	1,471	3,683	626	52
Enterprises for which the largest market in terms of turnover is the other EU, EFTA and/or EU-candidate countries	1,520	692	2,518	178
Enterprises for which the largest market in terms of turnover is the local or the regional market	8,268	3,096	7,282	156
Enterprises for which the largest market in terms of turnover is the national market	12,276	3,883	5,378	139
Enterprises for which the largest market in terms of turnover is all other countries than EU countries, EFTA or EU-candidate countries	1,964	418	1,227	31
Enterprises that sell goods and/or services in other EU, EFTA or EU-candidate countries	12,643	4,765	10,779	430
Enterprises that sell goods and/or services on the local or regional markets	14,872	6,946	15,378	461
Enterprises that sell goods and/or services on the national market	17,884	6,686	14,362	371
Enterprises that sell goods and/or services in any other country than EU countries, EFTA or EU-candidate countries	7,889	3,704	8,196	258

Source: Eurostat (2020).

Innovation activities and expenditure, and product and process innovative enterprises. Innovation can be either internal or external. In all four countries, the highest expenditure for innovation core activities is related to the acquisition of machinery, equipment or software, external knowledge, and external as well as internal R&D for both innovation core activities and the manufacture of basic pharmaceutical products and pharmaceutical preparations. For the indicators where expenditure for the EU-27 are available, it is evident that Germany's expenditure accounts for between 20% and 25% of all expenditure in the EU-27. Slovenian enterprises invest between 0.46% and 5.52% of what their German counterparts invest. This data is evident from Table 15. Enterprises in the studied countries are the most heavily engaged in developing products and/or services by themselves, or via R&D service providers if innovation core activities are considered. No data is available for the EU and Germany. In France, Italy and Slovenia, the number of enterprises for this indicator increased from 2012 to 2016. The number of enterprises does not differ much between Italy and France, while the number of Slovenian enterprises is between 0.50% and 7.90% of the other countries' of enterprises.

Table 14: Number of enterprises by specific types of innovation for innovation core activities (I) and the manufacture of basic pharmaceutical products and pharmaceutical preparations (M) by country in 2016

	GE		**FR**		**ITA**		**SI**	
	I	M	I	M	I	M	I	M
Enterprises that developed goods innovation	38,051	217	14,611	101	29,549	119	766	n.a.
Enterprises that developed service innovation	25,425	58	11,968	49	17,586	39	414	0
Enterprises that developed process innovation by improving logistics, delivery or distribution methods	18,542	75	8,510	31	13,547	39	300	n.a.
Enterprises that developed process innovation by improving manufacturing or production methods	30,449	131	15,586	114	23,489	113	542	n.a.
Enterprises that developed process innovation by supporting activities for processes	28,442	96	11,157	62	23,691	114	525	n.a.

Source: Eurostat (2020).

Public funding in enterprises. In terms of funding, enterprises receive financial assistance from the EU, the central government, local or regional authorities, other public funding or the 7^{th} Framework Programme. Considering either innovation core activities or the manufacturer of basic pharmaceutical products and pharmaceutical preparations, most enterprises in all four countries received other types of public funding and funding from the central government. A comparison between Germany and Slovenia is presented in Table 16. A further comparison of Slovenia and Germany indicates that a relatively higher proportion of enterprises in Slovenia receive funding.

Table 15: Number of enterprises by innovation activity and expenditure (in thousand €) for the EU-27, Germany and Slovenia for innovation core activities in 2016

	EU-27	GE		SI	
	Number	Number	% of EU-27	Number	% of EU-27
Enterprises, engaged continuously in in-house R&D activities	n.a.	22,885	n.a.	509	n.a.
Enterprises, engaged occasionally in in-house R&D activities	n.a.	12,536	n.a.	561	n.a.
Enterprises, engaged in design activities to improve or change the shape of the appearance of goods or services	n.a.	16,314	n.a.	582	n.a.
Enterprises, engaged in acquisition of machinery, equipment and software	171,257	43,550	25.43	1,040	0.61
Expenditure on the acquisition of machinery, equipment and software	n.a.	38,314,904	n.a.	240,645	n.a.
Enterprises, engaged in the market introduction of innovations	n.a.	17,433	n.a.	590	n.a.
Enterprises, engaged in acquisition of other external knowledge	53,590	13,445	25.09	499	0.93
Expenditure on the acquisition of external knowledge	n.a.	2,459,015	n.a.	14,244	n.a.
Enterprises, engaged in other innovation activities	n.a.	27,038	n.a.	506	n.a.
Enterprises, engaged in external R&D activities	57,613	11,032	19.15	609	1.06
Expenditure on external R&D	n.a.	14,711,911	n.a.	88,209	n.a.
Enterprises, engaged in in-house R&D activities	140,361	35,421	25.24	1,069	0.76
Expenditure on in-house R&D	n.a.	73,640,282	n.a.	416,327	n.a.
Enterprises, engaged in training for innovation activities	n.a.	32,787	n.a.	611	n.a.

Note. Expenditure in thousand €.

Source: Eurostat (2020).

Type of cooperation of enterprises. As a part of their cooperation strategy, enterprises engage in the following types of cooperation: with other enterprises within an enterprise group, with competitors or other enterprises of the same sector, with clients or customers from the private or public sector, with suppliers of equipment, materials, components or software, with universities or other higher education institutions, with government, public or private research institutes, or in any type of innovation cooperation with partners from different geographic areas. Most German enterprises cooperate with universities or other higher education institutions, while most French and Italian enterprises cooperate with suppliers of equipment, materials, components or software. In Germany and Italy, the trends are moving in different directions, depending on the type of cooperation; in France all trends are upwards moving, meaning that more and more enterprises engage in cooperation. In Slovenia, the highest number of enterprises in 2016 cooperated with government, public or private research institutes, followed by cooperation with suppliers of equipment, materials, components or software, and clients or customers from the private sector. Slovenian trends are moving downward for most indicators, meaning that fewer enterprises are engaging in cooperation. This is evident in Table 17. German enterprises account for between 8.4% and 20.8% of the EU-28. A comparison of the number of Slovenian enterprises with the number of German enterprises shows that Slovenian enterprises accounted for between 4% and 10% of German enterprises in terms of cooperation when innovation core activities are considered. In terms of the manufacture of basic pharmaceutical products and pharmaceutical preparations, German and French enterprises mostly cooperate with universities or other higher education institutions, while Italian enterprises cooperate with government, public or private research institutes. No data for Slovenia is available.

Table 16: Number of enterprises that received public funding in Germany and Slovenia for innovation core activities (I) or manufacture of basic pharmaceutical products and pharmaceutical preparations (M) in 2016

	GE		**SI**		
	I	**M**	**I**	**M**	**% of Germany**
Enterprises that received funding from the European Union	3,702	93	174	n.a.	4.70
Enterprises that received funding from the central government (including central government agencies or ministries)	10,358	113	283	n.a.	2.73
Enterprises that received funding from local or regional authorities	3,714	44	39	0	1.05
Enterprises that received any public funding	14,823	158	361	n.a.	2.44
Enterprises that received funding from the 7th Framework Programme	1,951	59	77	n.a.	3.95

Source: Eurostat (2020).

Organisational and marketing innovation at product and process innovative enterprises. In an analysis of organisational and marketing innovation at product and process innovative enterprises, it was noted that France was the only country with an upward trend for all indicators, i.e. enterprises introducing significant changes to aesthetic design or packaging, new methods for product placement, new media or techniques for product promotion, new methods of pricing goods or services, new business practices for organising procedures, new methods of organising external relations, and new methods of organising work responsibilities and decision making. In Italy, the number of enterprises decreased from 2012 to 2014 and increased from 2014 to 2016. However, the number did not exceed the number of enterprises in 2016. A negative trend can be observed in Slovenia, while in Germany, an increasing number of enterprises are introducing new business practices for organising procedures, and new methods of organising work responsibilities and decision making. Conversely, the number of enterprises introducing other changes is decreasing. French enterprises in the manufacture of basic pharmaceutical products and pharmaceutical preparations recorded a downward trend in all indicators. More Italian enterprises introduced new methods of organising external relations and new methods of organising work responsibilities and decision making, while more German enterprises introduced significant changes to aesthetic design or packaging, new methods for product placement and new media or techniques for product promotion. The data for the latest available year (i.e. 2016) for these three countries are summarised in Table 18. An insufficient amount of data for Slovenia and the EU is available for drawing any relevant conclusions.

Table 17: Number of enterprises by type of cooperation for innovation core activities in Slovenia in 2012, 2014 and 2016

	2012	**2014**	**2016**
Enterprises cooperating with other enterprises within an enterprise group	283	212	251
Enterprises cooperating with competitors or other enterprises of the same sector	355	181	368
Enterprises cooperating with clients or customers from the private sector	488	271	415
Enterprises cooperating with clients or customers from the public sector	239	124	223
Enterprises cooperating with suppliers of equipment, materials, components or software	524	432	515
Enterprises cooperating with universities or other higher education institutions	350	273	312
Enterprises cooperating with Government, public or private research institutes	n.a.	197	793

Source: Eurostat (2020).

Table 18: Number of enterprises related to organisational and marketing innovation for innovation core activities (I) or the manufacture of basic pharmaceutical products and pharmaceutical preparations (M) by country in 2016

	GE		**FR**		**ITA**		**SI**	
	I	M	I	M	I	M	I	M
Enterprises that introduced significant changes to aesthetic design or packaging	15,451	16.2	8,214	28.9	13,068	36	376	n.a.
Enterprises that introduced new methods for product placement	18,606	18.0	5,659	15.0	7,621	30	330	n.a.
Enterprises that introduced new media or techniques for product promotion	16,624	21.1	10,341	26.8	13,165	43	448	n.a.
Enterprises that introduced new methods of pricing goods or services	11,860	15.0	7,087	n.a.	8,625	14	343	n.a.
Enterprises that introduced new business practices for organising procedures	26,993	34.6	14,866	47.6	15,962	74	490	n.a.
Enterprises that introduced new methods of organising external relations	13,558	28.9	8,353	38.3	7,846	45	310	n.a.
Enterprises that introduced new methods of organising work responsibilities and decision making	26,080	36.8	16,280	n.a.	20,417	76	525	n.a.

Source: Eurostat (2020).

Intellectual property rights and licensing at enterprises. Pharmaceutical enterprises included in the analysis held several different intellectual property rights (hereinafter: IPRs) and licensing, including patents, trademarks, utility models, industrial design, trade secrets and copyrights. Due to low data availability, only 2016 is considered to give an overall impression. In core innovation activities, trade secrets were held by almost half of all enterprises in Germany, followed by trademarks at 20.7% and patents at 19.9%. The highest number of enterprises in France and Italy held trademarks, as well, at 21.1% and 19.5%, respectively. The majority of German enterprises categorised as manufacturers of basic pharmaceutical products and pharmaceutical preparations held trade secrets (88.7%), while around half held patents (55.3%) and/or trademarks (46.6%). In Italy, one-third of enterprises held patents (32.7%) and/or trademarks (31.7%). An insufficient amount of data for France is provided in the analysis.

Importance of the reasons for failure to innovate and of the barriers to innovation at enterprises. The CIS analysis in 2014 did not include innovative enterprises. In addition, the data for a limited number of countries are available. However, due to the importance of the reasons and barriers for not innovating, these are included herein, as raising awareness regarding reasons and barriers is the first step for overcoming them. French and Italian enterprises in core innovation activities listed a "no compelling barrier" as the most important reason to not innovate, at 90.3% and 79.6%, respectively. From a substantive point of view, low market demand was stated most frequently, at 18.6% in France and 26.3% in Italy. In addition, all manufacturers of basic pharmaceutical products and pharmaceutical preparations in France found "no compelling barrier" as the most problematic, while more than 60% of Italian manufacturers listed "excessive barriers". In 2016, the highest number of enterprises categorised as core activities innovators in Germany, Italy and Slovenia stated low market demand as the reason to not innovate while in France, the most common reason was lack of internal financing.

5.1.2 Discussion

Throughout most of the analysis, Germany was the country with the highest numbers for the studied indicators, followed by France, Italy and Slovenia, which is consistent with the population size and geographic area of the countries. A total of 91% of all German enterprises were deemed innovative enterprises, while 31% of them were product and/or process innovative in 2016. Despite France and Italy having a similar proportion of innovative enterprises (78% and 79%, respectively), 31% Italian enterprises were product and/or process innovative while the same held true for only 17% of French enterprises. In the segment of innovation core activities, pharma mostly recorded a positive trendline in terms of total turnover, total number of enterprises and employees, with Slovenia being the exception. Although global employment in pharma grew by 9% from 2010 to 2012 and by 14% from 2012 to 2014 (International Federation of Pharmaceutical Manufacturers & Associations, 2017), the growth rates in studied countries are not that high. Taking into account the manufacturers of basic pharmaceutical products and pharmaceutical preparations, the trends in terms of total turnover, total number of enterprises and employees were negative in all studied countries, meaning that industry as a whole is doing relatively better than that specific sector.

As the pharmaceutical industry was forced to make changes to its operating models in the last two decades according to the four trends described in section 2.1, it is of little surprise that a significant proportion of enterprises introduced process-related innovation. The proportion of enterprises grouped as innovation core activities in the studied countries mostly exceeded 60% of enterprises, while the proportions of enterprises grouped as manufacturers of basic pharmaceutical products and pharmaceutical preparations were on average higher by indicator.

Given the characterisation of innovation as an enabler for enterprises and countries to survive (Fleury, Fleury & Borini, 2013), this is an important area for exploration. In terms of innovation activities, more than 60% of product and/or process innovative enterprises in innovation core activities engaged in the acquisition of machinery, equipment and software. In addition, in-house R&D activities have proven to be more popular than external R&D activities. Half of German and Italian enterprises engaged in in-house R&D activities, while that figure was 66% and 77% for French and Slovenian enterprises, respectively. Slovenia had the highest proportions of enterprises in terms of R&D activities, notwithstanding the studied indicator. Besides R&D investments, enterprises also exploited the synergies arising from cooperation. Relatively more enterprises from Slovenia engaged in any type of cooperation compared to the other three countries, which could be due to the small size of the economy, as 38% of enterprises engaged in any type of innovation cooperation with a partner from the EU, EFTA or EU candidates. Although M&As are an increasingly employed strategy, CIS data does not support that finding. In 2014, around 10% of French enterprises merged with or took over another enterprise compared with 6 to 7% of Italian and Slovenian enterprises, and 3% of German enterprises. In 2016, the proportion of such enterprises fell to 1% or less for all four countries.

In terms of organisational and marketing innovation, most German enterprises introduced new organisational business practices, while enterprises in the other three countries focused more on new methods of work responsibilities and decision-making organisation. According to the data, French enterprises appear to be the most innovative from that perspective, followed by Slovenian enterprises. On the other hand, enterprises in innovation core activities in all four countries reported low market demand, a lack of external financing, high costs, high competition and previous innovations as the most compelling reason not to innovate, none of which were cited as obstacles to innovation activities from the literature referred to in section 2.2. However, the proportion of the enterprises did not exceed 20% for any barrier on the list. Moreover, data availability for this section was too low to make any generalised conclusions, but should be prioritised due to low R&D efficiency (Schuhmacher, Gassmann & Hinder, 2016).

In all four countries, funding from the central government proved to be the most important in both innovation core activities and the manufacture of basic pharmaceutical products and pharmaceutical preparations, when public funding is concerned. A total of 43% of French enterprises received central government funding compared to 15 to 20% of enterprises in the other three countries.

5.2 Analysis of innovation and value-added in the pharmaceutical industry

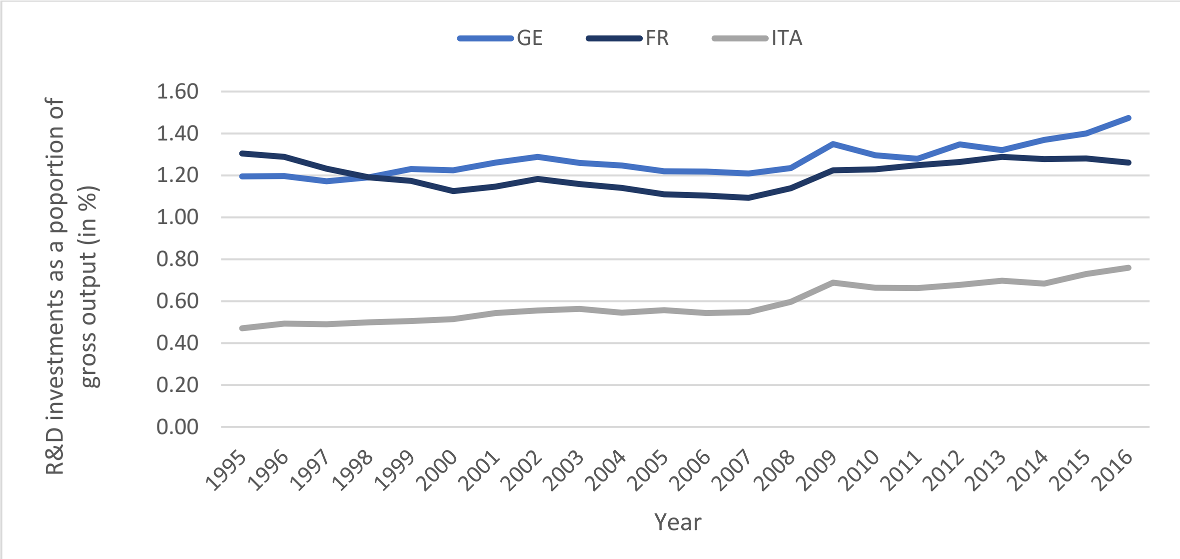
As the pharmaceutical industry has been highlighted as a growth-enhancing industry, this section reviews the data of the pharmaceutical industry against other industries. It is an industry that is often mentioned as being innovative, as well as one with high value-added. This section examines the comparative performance of the pharmaceutical industry in terms of value-added and innovation at the aggregate level. As a continuation of the CIS analysis, the innovation characteristics of the pharmaceutical industry are analysed further.

The analysis relies on the EU KLEMS database and aims to demonstrate the importance of innovation, especially in the pharmaceutical industry. EU KLEMS is a database that provides data on capital formation and technological change, economic growth, employment creation and productivity at the industry level for EU Member States starting from 1970. The database is managed by the Vienna Institute for International Economic Studies (hereinafter: the WIIW) (The Vienna Institute for International Economic Studies, 2019c). There are two databases available: statistical and analytical. For the purpose of our analysis, three variables were selected in order to examine the relationship between value-added per employee and R&D investment, which will be discussed later in this section. Germany, France and Italy were considered as units of analysis, as they are the leading European pharmaceutical markets, while a comparison with Slovenia was limited due to the low availability of data (Vienna Institute for International Economic Studies, 2019c, 2019d). The aforementioned analysis is presented below. In order to understand where the pharmaceutical industry is positioned, i.e. whether it is similar to, below or above the economy as a whole, the analysis is divided into two parts. First, an overview of investment and R&D is provided for the entire economy for the studied countries. Second, an overview of investment and R&D is provided for the pharmaceutical industry, specifically for the studied countries. The same applies to value-added.

5.2.1 Investment and R&D intensity at the aggregate level

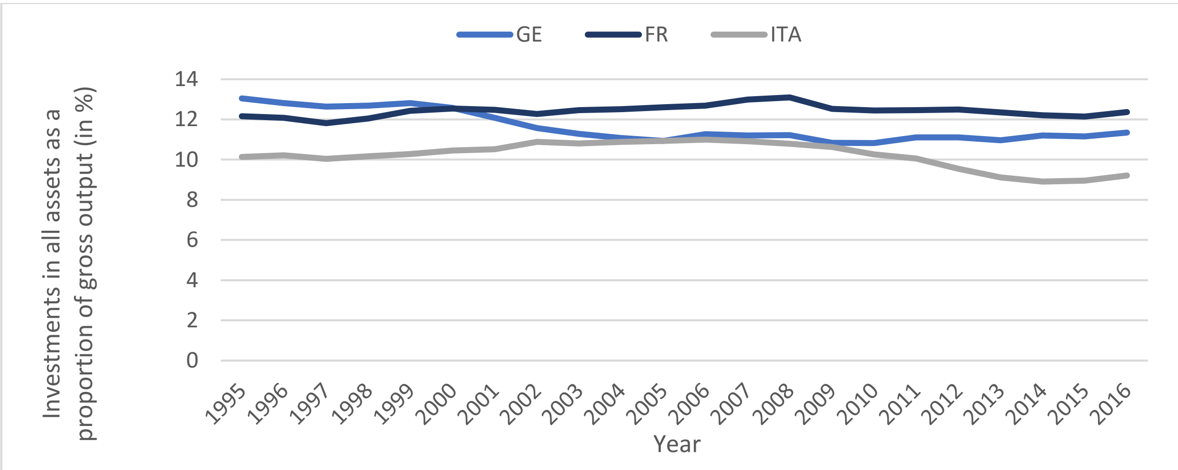
Investment in all assets (an expression from the original EU KLEMS database that is used herein as a synonym for total investment) in Germany accounted for 11.35% of gross output in 2016, while R&D accounted for 1.47%. While the proportion of all assets in gross output has been steadily declining from 13.05% in 1995, the proportion of R&D has been moving in the opposite direction, starting at 1.2% in 1995. The same trends have been observed in Italy. All assets accounted for 10.13% of gross output in 1995 and decreased to 9.21% in 2016. The proportion of R&D started at 0.47% in 1995 and increased by almost two thirds to 0.76% in 2016. In contrast, French investment in R&D as a proportion of gross output decreased from 1.30% in 1995 to 1.26% in 2016, reaching its lowest level in 2007 (at 1.09%). Investment in all assets as a proportion of gross output fluctuated up and down over the entire period, starting at 12.16% in 1995 and increasing to 12.36% in 2016. Detailed statistics are depicted in Figure 25 and Figure 26, and numerically summarised in Appendix 2.

Figure 25: R&D investments as a proportion of gross output from 1995 to 2016 by country (in %)



Source: Vienna Institute for International Economic Studies (2019b).

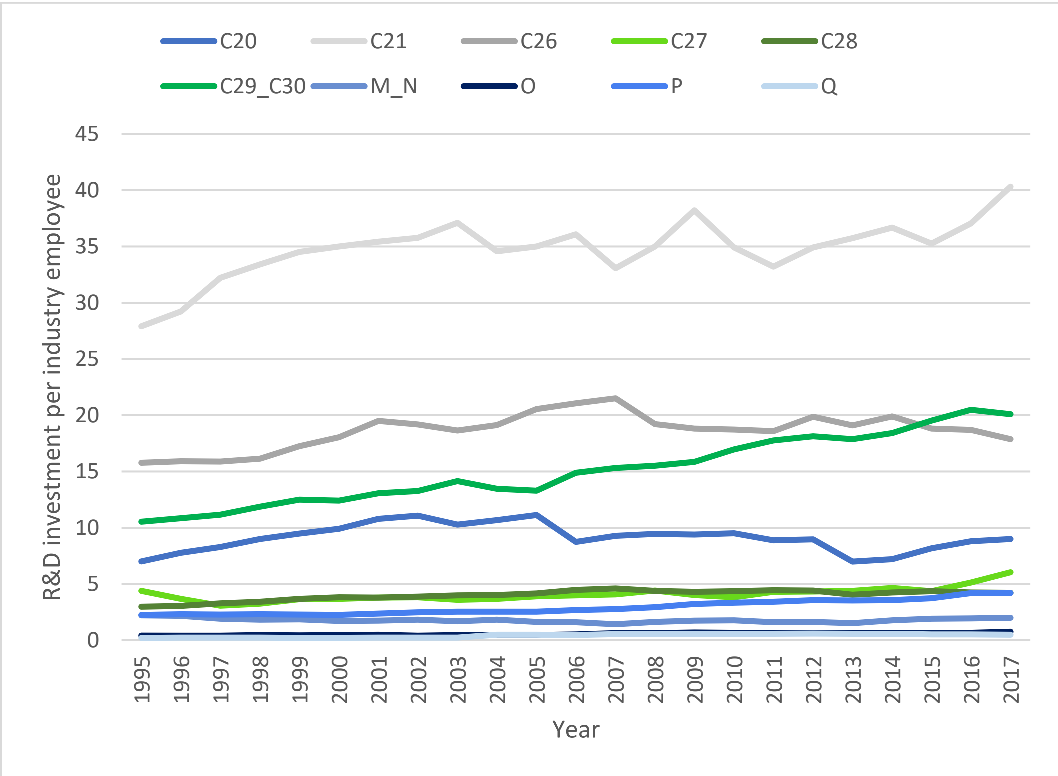
Figure 26: Investments in all assets as a proportion of gross output from 1995 to 2016 by country (in %)



Source: Vienna Institute for International Economic Studies (2019b).

Germany recorded the highest growth in R&D investment in the total economy (35.09%) followed by Slovenia (29.60%), France (25.78%) and Italy (20.63%) from 2005 to 2015. In Germany and France, the pharmaceutical industry has grown less than the total economy (18.03% and 14.45%, respectively). In Italy, the pharmaceutical industry has grown two times faster than the total economy, i.e. 42.28%. A detailed breakdown by industry is not available for Slovenia. As is evident from Appendix 3, where a summary of R&D investments by industry for the studied countries is provided, the pharmaceutical industry (C21) ranked in the top 10 out of 40 industries in terms of R&D investment in Germany, France and Italy in 2015. Among the industries that score higher than the pharmaceutical industry, notwithstanding the country, are as follows: Computer, electronic and optical products (C26), Transport equipment (C29_C30) and Professional, scientific, technical, administrative and support service activities (M_N). Besides those, there are some certain other industries with higher R&D investment in a specific country. Figure 27 shows the top 10 German industries in terms of R&D investment per industry employee from 1995 to 2017.

Figure 27: Top 10 industries by NACE code in terms of R&D investment per industry employee in Germany from 2005 to 2015 (in million €)



Note. For industry code explanation, see List of NACE codes.

Source: Vienna Institute for International Economic Studies (2019b).

A comparison of R&D investment between the total economy and the pharmaceutical industry by country in 2005, 2010 and 2015 (Table 19) shows that the proportion of the total economy's R&D accounted for by the R&D of the pharmaceutical industry decreased in all three countries, although the figure was higher in 2015 in absolute terms than in 2005. This indicates that R&D in other industries is increasing more significantly, which might be related to the fact that R&D in the pharmaceutical industry is already among the highest over a longer period, while the importance of R&D in other industries has only recently risen significantly.

Table 19: R&D investment (in million €) in the total economy and pharmaceutical industry (in million € and as a percentage of the total economy) by country in 2005, 2010 and 2015

		2005		2010		2015	
		Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
GE	Economy	53,525	n.a.	61,926	n.a.	72,304	n.a.
	C21	3,884	7.26	4,120	6.65	4,585	6.34
FR	Economy	37,917	n.a.	43,525	n.a.	47,690	n.a.
	C21	2,462	6.49	3,392	7.79	2,818	5.91
ITA	Economy	17,903	n.a.	20,722	n.a.	21,596	n.a.
	C21	453	2.53	861	4.16	645	2.99

Note. Economy = Total economy, C21 = Basic pharmaceutical products and pharmaceutical preparations.

Source: Vienna Institute for International Economic Studies (2019b).

5.2.2 Value-added and investment

The pharmaceutical industry ranks among the top industries in terms of investment. It is therefore of interest to investigate whether this investment results in higher added value. Appendix 4 provides a detailed overview of value-added by industry in the studied countries. It is evident that the pharmaceutical industry (C21) ranked among the top 10 out of 40 industries in terms of value-added in Germany, France and Italy in 2015. Conversely, it is ranked only among the top 25 in Slovenia. Slovenian C21 also lags behind the other three countries taking into account growth in value-added, as the latter grew by around 65% in Slovenia compared to around 250% in Germany, 600% in France and 590% in Italy from 2005 to 2015. Among the industries that score higher than the pharmaceutical industry in Germany, France and Italy are the following: Transport equipment (C29_C30), Computer, electronic and optical products (C26), and Professional, scientific, technical, administrative and support service activities (M_N). In Slovenia, these are different, where a higher number of industries record higher value-added.

A comparison of value-added between the total economy and pharmaceutical industry (Table 20) by country in 2005, 2010 and 2015 shows that the proportion of the total economy's R&D accounted for by the R&D of the pharmaceutical industry is growing in France, Italy and Slovenia, while it is virtually unchanged in Germany. Slovenia recorded the highest growth from 2005 to 2015. Moreover, the proportion of the total economy's value-added accounted for by C21 in Slovenia is significantly higher than the other three countries (14.07% in 2015 compared to less than 1% for Germany, France and Italy). This indicates that the pharmaceutical industry is an important contributor to value-added in the Slovenian economy. The proportion of of the total economy accounted for by C21 grew steadily from 1.27% in 1995 to 15.16% in 2017, while it was about the same in other three countries notwithstanding the year.

In order to understand the correlations between value-added and investment by type, investment in all assets as a proportion of value-added was first calculated. It is evident from Figure 28 that investment in all assets in C21 accounts for higher proportions of value-added in three studied countries (i.e. Germany, France and Italy) than in the total economy of the same countries. No detailed data by industry was available for Slovenia. For this reason, a comparison between the total economy and C21 could not be made. Although in Italy the proportion of investment in all assets in C21 was lower than in the total economy in some years, it reached similar levels to Germany in 2017. In Germany, that proportion has fluctuated up and down, but was not much different in 2017 than it was in 1995. Conversely, the proportion of investment in all assets decreased slightly from 1995 to 2017 in France. Nevertheless, the proportion of investment in all assets in C21 was still slightly higher than in the total economy in 2017.

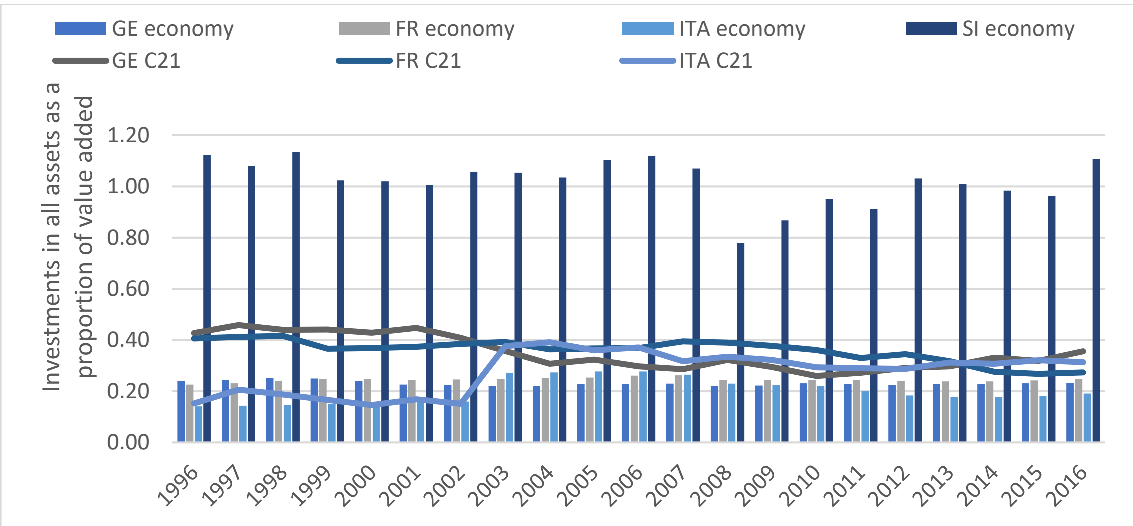
Table 20: Value-added (in million €) in the total economy and pharmaceutical industry (in million € and as a percentage of the total economy) by country in 2005, 2010 and 2015

		2005		2010		2015	
		Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
GE	Economy	2,176,017	n.a.	2,321,695	n.a.	2,522,362	n.a.
	C21	19,366	0.89	20,850	0.90	21,568	0.86
FR	Economy	1,717,865	n.a.	1,797,790	n.a.	1,897,524	n.a.
	C21	9,914	0.58	11,776	0.66	13,155	0.69
ITA	Economy	1,462,478	n.a.	1,443,247	n.a.	1,410,389	n.a.
	C21	7,547	0.52	8,361	0.58	9,460	0.67
SI	Economy	8,365	n.a.	8,913	n.a.	6,978	n.a.
	C21	534	6.38	782	8.77	982	14.07

Note. Economy = Total economy, C21 = Basic pharmaceutical products and pharmaceutical preparations.

Source: Vienna Institute for International Economic Studies (2019b).

Figure 28: Investments in all assets as a proportion of value-added for the total economy and C21 in Germany, France, Italy and Slovenia from 1996 to 2017



Note. Due to the unavailability of detailed industry data for Slovenia, SI C21 is not included in the figure.

Source: Vienna Institute for International Economic Studies (2019b).

5.2.3 Relationship between value-added per employee and investment by type

Value-added per employee varies between the studied countries, both in terms of size and the proportion of the total economy's value-added accounted for by the pharmaceutical industry (C21). Italy was the only country to record a declining trend in value-added per employee in the total economy, while the other countries, regardless of the year, recorded growth in the total economy and C21. Similarly, in the same three countries, value-added per employee in C21 almost doubled compared to the economy as a whole in 1995 and almost tripled in 2017. In Italy, value-added per employee in the total economy was only higher than in C21 in 1995. That trend reversed in 2017, when value-added per employee in C21 was twice as high as in the economy as a whole. Despite Germany recording the highest values in most of the indicators throughout the analysis, value-added per employee was the highest in France in the total economy and C21, followed by Italy, Germany and Slovenia. Slovenian values are close to one-half lower than the other three countries. Appendix 5 includes a summary of value-added per employee for the total economy and pharmaceutical industry (C21).

In terms of investment, the following categories were taken as variables in the analysis:

- Computer equipment (Iq_IT).
- Communications equipment (Iq_CT).
- Computer software and databases (Iq_Soft_DB).
- Transport equipment (Iq_TraEq).
- Other machinery and equipment (Iq_OMach).
- Total non-residential investment (Iq_OCon).
- Residential structures (Iq_RStruc).
- Cultivated assets (Iq_Cult).
- Research and development (Iq_RD).
- Other IPP assets (Iq_OIPP).
- All assets (Iq_GFCF).

These variables were correlated with value-added per employee that was calculated from gross value-added (VA_Q) and number of employees (EMPE) in order to see whether there were any correlations between value-added per employee (VA_Q/EMPE) and specific types of investment. Bivariate correlations were performed for both the total economy and C21, and are presented in Table 22 and 21. The analysis showed several correlations between a specific type of investment and value-added per employee. Taking into account the total economy, computer equipment, transport equipment and total non-residential investment proved to be significant in all four countries (Table 22), which means that investment in communications equipment, transport equipment and total non-residential investment correlated with value-added per employee. Most of the relationships were positive, indicating that higher investment had a positive effect on value-added per employee, i.e. the higher the investment, the higher the value-added per employee. The data showed that transport equipment is almost perfectly correlated with value-added per employee in Germany (0.953), while the correlation in Slovenia is 0.743.

On the other hand, investment in other machinery and equipment was negatively correlated with value-added per employee (-0.829) in Germany, indicating that the latter decreased with higher investment in this type of investment. In Italy, this is the case with investment in communications equipment.

Table 21: Bivariate correlation between value-added per employee and investment type variables for basic pharmaceutical products and pharmaceutical preparations (C21) in Germany, France and Italy from 1995 to 2017

	GE		FR		ITA		
	VA_Q/EMPE		VA_Q/EMPE		VA_Q/EMPE		
	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)	N
Iq_IT	-0.220	0.313	*-.521	0.011	**.747	0.000	23
Iq_CTt	-0.400	0.058	-0.324	0.131	-0.013	0.953	23
IQ_Soft_ DB	**.866	0.000	**.984	0.000	**.622	0.002	23
IQ_TraEq	**.765	0.000	**.560	0.005	**-.644	0.001	23
Iq_OMach	**.698	0.000	-0.025	0.909	**.552	0.006	23
Iq_OCon	0.155	0.480	*-.470	0.024	0.122	0.580	23
Iq_RStruc	b	c	b	c	c	c	23
Iq_Cult	b	c	b	c	b	c	23
Iq_RD	**.660	0.001	**.807	0.000	0.295	0.172	23
Iq_OIDP	b	c	b	c	b	c	23
Iq_GFCF	**.758	0.000	**.744	0.000	**.685	0.000	23

Note: * = Correlation is significant at a value of 0.05 (2-tailed), ** = Correlation is significant at a value of 0.01 (2-tailed), b = Cannot be computed because at least one of the variables is constant, c = Cannot be computed.

Source: Own work.

Taking C21 as only one industry of the total economy, three variables proved to be significant in three studied countries (excluding Slovenia), i.e. computer software and databases, transport equipment and all assets (Table 22). Here, all but one significant relationship is positive. More investment in computer software and databases, transport equipment and generally all assets correlated with value-added per employee. The higher the value of these types of investment, the higher the value-added per employee. The opposite is true for a correlation between investment in transport equipment and value-added per employee in Italy.

Considering that a significant correlation also exists between investment in all assets and value-added per employee, this may indicate that investment in general and overall is highly important, especially in the pharmaceutical industry, which has been characterised as an industry driven by investment as one of the factors that puts it in such a successful position in terms of business results. However, further analysis is needed to prove this causality.

Table 22: Bivariate correlation between value-added per employee and investment type variables for the total economy in Germany, France, Italy and Slovenia from 1995 to 2017

	GE		**FR**		**ITA**		**SI**		
	VA_Q/EMPE		**VA_Q/EMPE**		**VA_Q/EMPE**		**VA_Q/EMPE**		
	Pearson Correlation	**Sig. (2-tailed)**	**Pearson Correlation**	**Sig. (2-tailed)**	**Pearson Correlation**	**Sig. (2-tailed)**	**Pearson Correlation**	**Sig. (2-tailed)**	**N**
Iq_IT	*0.484	0.019	**0.901	0.000	-0.108	0.623	**0.763	0.000	23
Iq_CT	**0.684	0.000	**0.819	0.000	**-0.648	0.001	**0.776	0.000	23
Iq_Soft_DB	**0.942	0.000	**0.976	0.000	-0.256	0.239	*0.463	0.026	23
Iq_TraEq	**0.953	0.000	**0.813	0.000	**0.602	0.002	**0.743	0.000	23
Iq_OMach	**0.942	0.000	**0.743	0.000	0.272	0.209	**0.844	0.000	23
Iq_OCon	**-0.829	0.000	**0.725	0.000	**0.697	0.000	**0.834	0.000	23
Iq_RStruc	*-0.445	0.033	**0.756	0.000	0.359	0.093	**0.791	0.000	23
Iq_Cult	-0.204	0.350	*-0.520	0.011	**0.725	0.000	*-0.450	0.031	23
Iq_RD	**0.836	0.000	**0.967	0.000	**-0.767	0.000	0.161	0.463	23
Iq_OIDP	**0.676	0.000	**0.923	0.000	-0.255	0.241	-0.219	0.315	23
Iq_GFCF	**0.796	0.000	**0.906	0.000	*0.440	0.035	**0.980	0.000	23

Note: * = Correlation is significant at a value of 0.05 (2-tailed), ** = Correlation is significant at a value 0.01 (2-tailed).

Source: Own work.

CONCLUSION

The pharmaceutical industry or pharma has grown rapidly growing over the last two decades, and settled at around $1.2 trillion in revenue in 2018, which is almost triple the revenue generated in 2001. The top markets in 2018 were the US ($460 billion), Europe ($196 billion) and the ROW ($110 billion). While currently leading markets are expected to settle in terms of growth until 2030, India, China and Indonesia are expected to grow the most, which is one of the trends affecting pharma development. On the European market, Germany (€40,141 million), France (€29,007 million) and Italy (€26,004 million) are among the leading pharmaceutical markets, with Slovenia ranking 8th in Central and Eastern Europe in 2018 (€587 million). The goal of this thesis was to provide a systematic review of the industry, particularly in terms of innovation. Another aim was to review trends and, based on empirical analysis, provide a comparison between Slovenia and three leading European markets, i.e. Germany, France and Italy.

Over the decades, two large segments have formed within the pharmaceutical industry: prescription medicines and OTC. The two differ in terms of growth rates, R&D investments, margins, VAT rates and consumer loyalty. In section 2, some other trends were also outlined, including the transition from massive to lean, from hubs to hotspots and from primary to specialty. Because 2012, 2014 and 2016 were taken into account in the CIS analysis, this limits the ability to draw any empirical conclusions regarding trends. It would therefore make sense to carry out a longitudinal study covering a longer period of data from 2002 onwards to determine the direction of trends and to forecast future trends. Nevertheless, literature finds that these trends will also be valid in the coming years. It is also becoming increasingly important to make healthcare access affordable and sustainable for patients, governments and healthcare companies. Moreover, strategies should find ways to include IT in healthcare, and thus benefit from apps and wearable devices. Pharma is also faced with an ageing population and has recently encountered the COVID-19 situation, and other potential pandemic/epidemic diseases. In the case of the latter, developing a vaccine is challenging, requires time and is not necessarily successful. The otherwise low success rate of pharmaceutical projects forces companies to diversify portfolios, and combine primary care and specialty units.

In recent years, the collaboration of pharmaceutical companies with third parties has intensified, and is shifting in particular from specific know-how collaboration to collaboration with a focus on an enlarged set of skills and technologies across the whole R&D value chain, which is the result of increased R&D. The CIS data analysis provided similar conclusions. Upward trending in terms of cooperation was observed for many indicators in Germany, France, Italy and Slovenia. In particular, cooperation with non-European countries has intensified, indicating that not only are companies from the East gaining in importance, but also current, global-leading companies are increasingly aware of Eastern competitors and therefore seek to cooperate with them rather than being outrivalled by them. It is evident that the proportion of Slovenian companies engaging in cooperation exceeds the proportion in the other three countries and the EU average for most indicators.

In terms of innovation perspectives, literature describes financial, knowledge generation and strategic perspectives, each of which brings different strategies and aims that were presented in section 3. The CIS data analysis has showed that product innovation is the most popular type of innovation among companies, as it is used by more than 70% of companies, regardless of country. Moreover, product and/or process innovation is most frequently carried out together with other enterprises or institutions/R&D service providers. Neither the proportions of product innovation companies nor organisational and marketing innovative enterprises differ significantly between the countries.

The fifth section empirically compared the pharmaceutical industry, the economy as a whole and other industries. The EU KLEMS database showed that R&D investment and the level of innovation are greater in the pharmaceutical industry than in the total economy. Pharma is ranked among top 10 economic sectors in Germany, France and Italy. The German pharmaceutical industry invests the most in R&D, followed by France and Italy. This is reflected in value-added, where the same order can be observed. Interestingly, the proportion of the total economy’s value-added accounted for by the pharmaceutical industry is significantly higher in Slovenia than in the other three countries, which might be due to the small size of the economy and would be a worthwhile focus for future research.

While Italian value-added per employee has recorded a declining trend, other countries have recorded growth in both the total economy and the pharmaceutical industry specifically, regardless of the year. Despite Germany recording the highest values in most of the indicators throughout the analysis, value-added per employee was the highest in France in both the total economy and C21, followed by Italy, Germany and Slovenia. Slovenian value-added figures are about one-half lower than the other three countries. In addition, an analysis of bivariate correlation between value-added per employee and specific types of investment showed several significant correlations in all four countries, i.e. computer equipment, transport equipment and total non-residential investment. Transport equipment is almost perfectly correlated with value-added per employee in Germany (0.953, $p = 0.01$), while the correlation in Slovenia is 0.743 ($p = 0.01$). On the other hand, investment in other machinery and equipment was negatively correlated with value-added per employee in Germany (-0.829, $p = 0.829$), while it was 0.834 ($p = 0.01$) in Slovenia. Taking into account C21, significant correlations in the three studied countries (excluding Slovenia due to incomplete data) exist between value-added per employee and the following investment types: computer software and databases, transport equipment and all assets. All but one significant relationship is positive.

The correlations vary by direction and country. It could be that less productive industries in terms of value-added are using more traditional forms of capital and assets, while more productive industries in terms of value-added are using more knowledge-intense capital.

Human capital could also be categorised among the latter. The pharmaceutical industry is known as one of the most human-capital intensive industries, requiring employees with higher levels of education, expertise and skills. Knowledge capital could be an accelerating factor in value-added creation. However, no precise conclusions could be drawn based on this research. A related focus for further research is to delve deeper into these correlations and explore the causality between them.

Limitation of this research lies in low data availability. The nature of data is sensitive and mostly internal to the companies, thus it was not available for all indicators and all countries observed. Due to this fact, the structure of analysis in terms of richness of comparisons of different factors between countries is not consistent. Limited data resulted in limited depth of the analysis itself, however, the best efforts were put into extracting as much meaningful information from the available data.

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APPENDICES

Appendix 1: Povzetek (Summary in the Slovene language)

Farmacevtska panoga ali farmacija vključuje aktivnosti odkrivanja, razvoja, proizvodnje in prodaje zdravil s strani javnih in zasebnih podjetij (Kitsis, 2011). Leta 2018 se je njena vrednost ustalila pri približno 1,2 bilijona ameriških dolarjev prihodkov, kar je skoraj trikrat več kot v primerjavi z letom 2001. Neprestano in hitro rast poganja staranje prebivalstva in novosti, ki zdravijo redka bolezenska stanja. Največji trgi v letu 2018 so bili ZDA (460 milijard ameriških dolarjev), Evropa (196 milijard ameriških dolarjev) in ROW (110 milijard ameriških dolarjev). Na evropskem trgu so bile v letu 2018 med državami kot vodilnimi farmacevtskimi trgi Nemčija (40,141 milijona €), Francija (29,007 milijona EUR) in Italija (26,004 milijona EUR), Slovenija pa je na območju srednje in vzhodne Evrope zasedla 8. mesto (587 milijonov €). Omenjene štiri države so bile zajete tudi v empirično analizo.

Medtem, ko naj bi se rast trenutno vodilnih trgov do leta 2030 ustalila, je pričakovati največjo rast v azijskih državah, in sicer, v Indiji, na Kitajskem in v Indoneziji, kar je eden od trendov, ki vplivajo na razvoj farmacije. Poleg tega je farmacija v zadnjih desetletjih doživela več prehodov, zaradi česar je morala spremeniti svoj poslovni model in družbeni vpliv (Pan & Gautam, 2016). Skladno s prehodi in spremembami sta bila oblikovana dva velika segmenta, tj. zdravila na recept in zdravila brez recepta. Razlikujeta se v stopnjah rasti, naložbah v raziskave in razvoj, maržah, stopnjah davka na dodano vrednost in zvestobi potrošnikov. Akademiki kot ključne razvojne trende opisujejo še sledeče strateške spremembe v organizaciji dela: prehod od množičnih do vitkih, od baz do vročih točk in od primarnih do specializiranih. Aktualnost določenih trendov se pričakuje tudi v prihodnjih letih, hkrati pa bo na pomembnosti pridobila cenovna dostopnost in trajnost zdravstvenega varstva za bolnike, vladne organizacije in zdravstvena podjetja. Nove strategije bodo morale najti načine, kako v zdravstvo vključiti informacijsko tehnologijo in izkoriščati aplikacije ter nosljive naprave za izboljšanje zdravstva. Nedavni pojav koronavirusa (COVID-19) pa je pokazal tudi, da je potrebno okrepiti pristope k ravnanju v času pandemije/epidemije, ki zahteva dolgotrajne, drage in ne nujno uspešne procese razvoja cepiva. Tudi sicer v farmacevtskih projektih velja nizka stopnja uspeha novih projektov, ki podjetja sili v raznolike portfelje z združevanjem primarne zdravstvene oskrbe in posebnih enot.

Pregled značilnosti in trendov farmacevtske industrije sta bili dve raziskovalni vprašanji, ki jih pokriva to magistrsko delo. Hkrati pa se magistrsko delo osredotoča na primerjavo slovenske farmacevtske industrije s panogo v drugih državah in pomen raziskav in razvoja na dodano vrednost. Skladno s tem je cilj magistrskega dela sistematično in strukturirano predstaviti podatke o farmacevtski industriji, ki bodo omogočili globlje razumevanje inoviranja v panogi, po drugi strani pa drugim panogam ponudili vpogled v spreminjanje in prilagajanje poslovnih modelov za povečanje inovativnega doprinosa ter zasledovanja ustreznih strategij. Magistrsko delo odgovarja na naslednja raziskovalna vprašanja:

- V1: Katere so glavne značilnosti farmacevtske industrije in njenih inovacij?

- V2: Kateri trendi so oblikovali panogo v zadnjih desetletjih, kakšni trendi naj bi se pojavljali v prihodnosti in kako bodo oblikovali poslovne modele farmacevtskih podjetij ter celotne industrije?
- V3: Kako je slovenska farmacevtska industrija primerljiva z vodilnimi evropskimi državami glede naložb v inovativnost in glede strategij, ki jih zasleduje?
- V4: Kako je dodana vrednost na zaposlenega povezana z naložbami v raziskave in razvoj?

Pristop farmacevtske panoge k raziskavam in razvoju je edinstven, kar ji omogoča doseganje poslovnih rezultatov in večjo uspešnost v primerjavi z drugimi panogami. Po drugi strani so podjetja prisiljena zadostiti visoki regulaciji ter zahtevam po kakovosti izdelkov, soočena pa so tudi z dolgotrajnimi postopki razvoja zdravil, visokimi finančnimi vložki in patenti. Slednji jim sicer omogočajo ekskluzivnost na trgu (Grabowski, 2004), a njihov potek lahko povzroči veliko izgubo prihodkov. Omenjene značilnosti so farmacevtska podjetja vodile k sklepanju partnerstev, tradicionalnih sodelovanj, virtualnega raziskovanja in razvoja, množičnega trženja, ustanavljanja inovacijskih centrov in odprtokodnih inovacij. Čeprav je analiza CIS podatkov pokazala, da je inoviranje izdelkov najbolj priljubljena vrsta inovacij med 70% podjetji v štirih analiziranih državah, so se podjetja prisiljena osredotočiti tudi na druge vrste inovacij, če želijo ostati konkurenčna (npr. inovacije v upravljanju, inovacije v poslovnih modelih in inovacije v zvezi z zaščito izdelkov) (Song & Han, 2016).

V zadnjih letih je opaziti okrepljeno sodelovanje farmacevtskih podjetij s tretjimi osebami, pri čemer se le-to ne osredotoča več toliko na specifično znanje in izkušnje, ampak poudarek preusmerja na razširjen nabor znanj in tehnologij v celotni vrednostni verigi raziskav in razvoja. Analiza podatkov CIS je prinesla podobne ugotovitve. Naraščajoči trendi v sodelovanju so bili opaženi za številne kazalnike v Nemčiji, Franciji, Italiji in Sloveniji. Zlasti se je okrepilo sodelovanje z neevropskimi državami, kar ne kaže samo na to, da so podjetja z vzhoda vedno bolj pomembna, ampak da se tudi trenutno vodilna svetovna podjetja vse bolj zavedajo vzhodnih konkurentov, zato si prizadevajo za sodelovanje z njimi, kar je zanje bolj optimalno kot da bi jih le-ta v razvoju prehitela. Podatki kažejo, da je delež slovenskih podjetij, ki aktivno sodelujejo z drugimi, višji od deležev v ostalih treh državah in nad povprečjem EU za večino kazalcev sodelovanja z zunanjimi partnerji.

Za empirično primerjavo farmacevtske industrije, gospodarstva kot celoto in drugih panog je bila uporabljena podatkovna baza EU KLEMS, ki je pokazala, da so naložbe v raziskave in razvoj ter stopnja inovativnosti v farmacevtski industriji višje kot v primerjavi s celotnim gospodarstvom. V Nemčiji, Franciji in Italiji se farmacevtska industrija uvršča med 10 najuspešnejših gospodarskih panog. V raziskave in razvoj največ investira nemška farmacevtska industrija, sledita ji Francija in Italija. To se odraža v dodani vrednosti, kjer je mogoče opaziti isti vrstni red. Zanimiva je ugotovitev, da je delež slovenske farmacevtske dodane vrednosti v celotnem gospodarstvu bistveno večji kot v ostalih treh državah, kar bi lahko bila posledica majhnosti gospodarstva, hkrati pa to predstavlja pomembno iztočnico za prihodnje raziskave.

Medtem ko je v italijanski dodani vrednosti na zaposlenega v farmaciji opaziti upadanje, druge države ne glede na leto beležijo rast dodane vrednosti tako v celotnem gospodarstvu kot v farmacevtski industriji. Za razliko od ostalih preučevanih dejavnikov, kjer je prednjačila Nemčija, je bila dodana vrednost na zaposlenega najvišja v Franciji tako v celotnem gospodarstvu kot tudi v C21, sledile pa so ji Italija, Nemčija in Slovenija. Slovenske vrednosti dodanih vrednosti so za približno polovico nižje v primerjavi z ostalimi tremi državami.

Analiza bivariativnih korelacij med dodano vrednostjo na zaposlenega in posameznimi vrstami investicij je pokazala več statistično pomembnih korelacij v gospodarstvih vseh štirih državah, tj. pri računalniški opremi, transportni opremi in skupnih nestanovanjskih investicijah. Transportna oprema je v Nemčiji skoraj popolnoma korelirana z dodano vrednostjo na zaposlenega (0,953, p = 0,01), medtem ko je ta korelacija v Sloveniji 0,743 (p = 0,01). Investicije v druge stroje in opremo pa so bile v Nemčiji negativno korelirane z dodano vrednostjo na zaposlenega (-0,829, p = 0,829), medtem ko je bila v Sloveniji ta korelacija 0,834 (p = 0,01). Tudi upoštevajoč zgolj farmacevtsko panogo obstajajo pomembne korelacije v treh raziskanih državah (brez analize za Slovenije zaradi nepopolnih podatkov) med dodano vrednostjo na zaposlenega in naslednjimi vrstami naložb: računalniška programska oprema in baze podatkov, transportna oprema in vsa sredstva. Vse, razen ene korelacije od vseh statistično značilnih, so pozitivne.

Korelacije se razlikujejo glede na smer in državo. Možno je, da manj produktivne panoge glede na dodano vrednostjo uporabljajo več klasičnega kapitala in sredstev, medtem ko bolj produktivne panoge glede na dodano vrednostjo uporabljajo več intelektualnega kapitala. Med slednje bi lahko uvrstili tudi človeški kapital. Farmacevtska industrija je znana kot ena najbolj intenzivnih panog kar zadeva človeške vire, ki zahteva zaposlene z višjo stopnjo izobrazbe, več strokovnega znanja in veščin. Intelektualni oz. človeški kapital bi lahko bil dejavnik pospeševanja ustvarjanja dodane vrednosti. Kljub vsemu na podlagi te raziskave o tem ni bilo mogoče natančno sklepati, zato bi bilo smiselno z nadaljnjimi raziskavami poglobiti področje korelacij in raziskati vzročnost med njimi.

Omejitev te raziskave je v nizki razpoložljivosti podatkov. Narava podatkov je občutljiva in je večinoma interna za podjetja, zato te niso bili na voljo za vse kazalnike in vse opazovane države. Zaradi tega dejstva struktura analize v smislu količine primerjav različnih dejavnikov med državami ni usklajena pri vseh točkah. Omejeni podatki so povzročili omejeno globino same analize, zato je bilo veliko truda vloženega v pridobivanje čim več pomembnih informacij iz razpoložljivih podatkov.

Appendix 2: R&D investment and investment in all assets as a proportion of gross output from 1995 to 2016 by country (in %)

Table 1: R&D investment and investment in all assets as a proportion of gross output from 1995 to 2016 by country (in %)

	R&D in gross output (total economy, in %)			All assets in gross output (in %)		
	GE	**FR**	**ITA**	**GE**	**FR**	**ITA**
1995	1.20	1.30	0.47	13.05	12.16	10.13
1996	1.20	1.29	0.49	12.81	12.08	10.22
1997	1.17	1.23	0.49	12.64	11.81	10.05
1998	1.19	1.19	0.50	12.69	12.04	10.17
1999	1.23	1.17	0.51	12.82	12.42	10.28
2000	1.22	1.13	0.51	12.58	12.54	10.46
2001	1.26	1.15	0.54	12.07	12.48	10.51
2002	1.29	1.18	0.56	11.56	12.26	10.88
2003	1.26	1.16	0.56	11.29	12.46	10.81
2004	1.25	1.14	0.54	11.07	12.52	10.88
2005	1.22	1.11	0.56	10.93	12.60	10.93
2006	1.22	1.10	0.54	11.26	12.68	11.00
2007	1.21	1.09	0.55	11.21	12.99	10.91
2008	1.24	1.14	0.60	11.22	13.09	10.78
2009	1.35	1.22	0.69	10.84	12.53	10.62
2010	1.30	1.23	0.66	10.82	12.45	10.26
2011	1.28	1.25	0.66	11.11	12.46	10.05
2012	1.35	1.26	0.68	11.11	12.49	9.55
2013	1.32	1.29	0.70	10.96	12.35	9.12
2014	1.37	1.28	0.68	11.20	12.20	8.91
2015	1.40	1.28	0.73	11.15	12.15	8.96
2016	1.47	1.26	0.76	11.35	12.36	9.21

Source: Vienna Institute for International Economic Studies (2019b).

Appendix 3: R&D investment by industry and country in 2005, 2010 and 2015 (in million €)

Table 2: R&D investment by industry and country in 2005, 2010 and 2015 (in million €)

	2005				2010				2015			
	GE	FR	ITA	SI	GE	FR	ITA	SI	GE	FR	ITA	SI
Total economy	53,525	37,917	17,903	502	61,926	43,525	20,722	686	72,304	47,690	21,596	651
Total industries	53,525	37,905	17,903	503	61,926	43,525	20,722	686	72,304	47,698	21,597	651
Market economy	45,432	33,836	9,964	428	50,720	39,576	12,316	590	59,777	43,688	13,818	571
A	106	208	0	n.a.	167	272	7	1	203	523	0	0
B	38	239	37	4	18	149	226	6	19	287	99	3
C	37,436	17,815	6,675	303	39,689	21,746	8,752	403	45,704	23,135	10,473	386
C10-C12	599	326	144	n.a.	595	527	263	n.a.	576	581	324	n.a.
C13-C15	175	131	117	n.a.	172	164	552	n.a.	157	124	680	n.a.
C16-C18	389	62	63	n.a.	443	80	112	n.a.	473	100	113	n.a.
C19	31	93	2	n.a.	105	101	6	n.a.	122	275	15	n.a.
C20	3,637	1,186	721	n.a.	3,075	1,530	477	n.a.	2,807	1,825	404	n.a.
C21	3,884	2,462	453	n.a.	4,120	3,392	861	n.a.	4,585	2,818	645	n.a.
C22_C23	1,061	904	224	n.a.	1,069	1,019	333	n.a.	1,158	1,175	498	n.a.
C24_C25	1,390	811	165	n.a.	1,445	1,012	393	n.a.	1,378	1,167	409	n.a.
C26	6,408	4,042	895	n.a.	5,709	4,052	1,199	n.a.	6,378	4,302	1,473	n.a.
C27	1,926	615	373	n.a.	1,843	895	536	n.a.	2,131	1,023	603	n.a.
C28	4,021	732	739	n.a.	4,440	963	1,321	n.a.	4,870	1,073	1,586	n.a.
C29_C30	12,736	6,186	1,959	n.a.	15,205	7,628	2,400	n.a.	19,563	8,289	3,448	n.a.
C31-C33	1,179	267	818	n.a.	1,470	383	298	n.a.	1,508	385	275	n.a.
D	69	2,335	73	1	112	469	77	5	158	554	30	3
E	6	194	9	1	6	109	68	1	7	74	25	1

(continues)

(continued)

	2005				2010				2015			
	GE	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**
F	28	96	78	0	61	137	62	2	26	86	95	2
G	219	0	449	14	261	0	243	8	1,205	0	373	11
G45	36	n.a.	10	n.a.	41	n.a.	6	n.a.	149	n.a.	7	n.a.
G46	96	n.a.	407	n.a.	119	n.a.	219	n.a.	700	n.a.	246	n.a.
G47	87	n.a.	32	n.a.	101	n.a.	18	n.a.	357	n.a.	41	n.a.
H	78	29	80	0	58	46	60	2	89	186	84	0
H49	18	n.a.	32	n.a.	17	n.a.	30	n.a.	22	n.a.	2	n.a.
H50	2	n.a.	0	n.a.	2	n.a.	0	n.a.	3	n.a.	3	n.a.
H51	8	n.a.	0	n.a.	6	n.a.	0	n.a.	7	n.a.	0	n.a.
H52	41	n.a.	47	n.a.	25	n.a.	30	n.a.	44	n.a.	24	n.a.
H53	9	n.a.	0	n.a.	8	n.a.	0	n.a.	13	n.a.	11	n.a.
I	0	0	19	0	0	0	5	0	0	0	4	0
J	1,223	2,238	674	8	2,067	3,374	1,258	29	2,408	4,194	1,166	19
J58-J60	608	517	7	n.a.	930	852	84	n.a.	972	1,172	56	n.a.
J61	161	684	273	n.a.	298	823	851	n.a.	286	898	625	n.a.
J62_J63	454	1,039	394	n.a.	839	1,699	324	n.a.	1,149	2,123	485	n.a.
K	196	0	746	1	302	0	530	1	264	0	343	1
L	0	0	21	0	0	0	10	0	0	0	1	0
M_N	5,856	10,652	582	95	7,743	13,233	619	132	9,445	14,583	730	142
O-Q	8,109	4,078	7,918	74	11,206	3,949	8,396	96	12,522	4,008	7,777	79
O	1,288	3,322	6,848	2	1,809	3,497	7,023	1	1,648	3,801	5,416	1
P	4,894	78	511	63	7,055	33	549	82	8,218	36	1,545	68
Q	1,932	673	559	9	2,342	419	824	12	2,663	172	816	11

(continues)

(continued)

	2005				2010				2015			
	GE	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**
R_S	181	38	543	2	236	41	411	2	294	73	397	2
R	181	37	305	2	236	39	315	2	294	45	279	2
S	0	1	238	n.a.	0	2	96	0	0	28	118	0
T	0	0	0	0	0	0	0	0	0	0	0	0
U	0	0	0	0	0	0	0	0	0	0	0	0

Note. For industry code explanation, see List of NACE codes.

Source: Vienna Institute for International Economic Studies (2019b).

Appendix 4: Value-added by industry and country in 2005, 2010 and 2015 (in million €)

Table 3: Value-added by industry and country in 2005, 2010 and 2015 (in million €)

	2005				**2010**				**2015**			
	GE	**FR**	**IT**	**SI**	**GE**	**FR**	**IT**	**SI**	**GE**	**FR**	**IT**	**SI**
Total economy	2,176,017	1,717,865	1,462,478	8,365	2,321,695	1,797,790	1,443,247	8,913	2,522,362	1,897,524	1,410,389	6,978
Total industries	2,169,425	1,713,993	1,445,566	28,803	2,315,128	1,793,799	1,425,240	31,557	2,516,026	1,894,148	1,391,673	32,515
Market economy	1,539,772	1,122,753	1,004,381	21,316	1,633,498	1,163,091	983,626	23,408	1,800,151	1,230,455	949,552	24,238
A	16,109	29,940	28,574	647	16,700	32,005	28,417	626	15,243	34,336	29,221	746
B	4,626	2,550	6,057	129	5,301	2,250	4,597	139	4,500	1,787	5,925	127
C	485,843	211,023	244,341	6,084	515,175	206,056	228,279	6,367	590,495	218,514	228,672	6,786
C10-C12	40,741	37,409	25,867	506	38,110	37,047	24,801	464	48,118	39,842	26,757	515
C13-C15	7,643	6,502	25,114	401	6,958	4,936	22,075	249	6,531	5,179	22,567	180
C16-C18	24,383	11,068	17,032	508	24,207	10,943	15,415	490	25,061	11,751	13,994	474
C19	7,128	3,894	3,890	1	5,503	1,845	2,164	1	4,688	3,090	843	1
C20	38,139	15,581	10,476	298	40,987	14,521	9,894	331	41,254	18,438	10,630	326
C21	**19,366**	**9,914**	**7,547**	**534**	**20,850**	**11,776**	**8,361**	**782**	**21,568**	**13,155**	**9,460**	**982**
C22_C23	35,914	20,450	24,480	782	37,702	18,053	21,828	687	41,742	18,624	20,335	615
C24_C25	63,762	24,485	39,400	1,004	62,513	25,268	36,296	1,079	71,763	26,290	37,815	1,172
C26	20,324	8,262	9,260	208	30,508	11,460	8,164	246	43,086	14,114	7,492	258
C27	37,490	8,461	11,208	531	39,750	7,077	11,297	619	38,014	6,298	10,130	627
C28	80,953	13,248	29,023	363	77,102	11,275	30,336	423	83,244	11,645	31,389	469
C29_C30	82,166	29,384	19,246	447	96,645	25,716	17,528	562	129,380	24,297	18,474	617
C31-C33	33,486	25,854	22,023	558	34,340	26,140	20,123	435	35,479	25,241	17,901	566
D	50,459	33,578	27,462	743	56,033	25,720	25,238	835	49,552	28,146	19,745	855

(continues)

(continued)

	2005				2010				2015			
	GE	**FR**	**IT**	**SI**	**GE**	**FR**	**IT**	**SI**	**GE**	**FR**	**IT**	**SI**
E	23,833	13,302	12,588	264	23,930	13,934	12,465	309	30,303	12,414	9,212	285
F	96,790	111,508	92,122	2,013	99,843	108,114	81,207	2,015	103,493	97,921	63,627	1,660
G	228,713	187,159	169,925	3,644	229,376	189,615	160,670	3,863	257,938	211,614	170,064	4,082
G45	41,250	28,293	19,459	445	39,978	27,724	16,777	474	44,356	25,782	15,435	503
G46	113,215	94,141	76,143	1,670	107,362	85,373	73,620	1,743	125,978	92,823	77,354	1,905
G47	74,162	66,668	74,581	1,527	82,036	76,518	70,273	1,646	87,262	93,079	77,211	1,674
H	95,911	77,345	80,747	1,411	107,850	83,049	77,902	1,747	110,077	81,463	68,776	1,844
H49	37,962	36,077	43,849	741	41,692	38,321	43,282	862	44,972	39,593	37,185	918
H50	4,418	1,740	4,069	112	7,780	2,355	2,942	75	4,108	5,778	2,095	38
H51	5,357	4,252	1,767	24	6,408	5,849	1,618	33	3,766	5,994	808	17
H52	38,445	25,336	26,689	370	39,216	27,942	25,619	575	42,258	26,320	24,166	677
H53	12,115	9,680	4,549	179	12,754	8,583	4,440	203	14,225	6,339	3,662	172
I	35,726	44,384	48,850	724	33,271	47,223	51,656	689	36,888	49,246	51,583	732
J	79,184	78,212	54,897	978	103,345	92,297	62,264	1,286	132,813	110,500	60,490	1,449
J58-J60	27,648	21,016	11,049	246	28,447	21,306	11,700	248	28,205	21,942	7,740	220
J61	20,551	24,364	20,900	387	27,472	30,227	25,488	531	31,828	41,173	24,941	524
J62_J63	32,286	33,298	23,242	349	47,426	40,764	25,076	508	72,982	48,013	27,717	709
K	108,939	71,449	65,284	1,333	106,292	81,573	75,910	1,697	110,602	90,280	75,627	1,458
L	247,725	211,786	187,002	2,202	267,279	227,561	188,746	2,537	279,083	239,121	194,167	2,579
M_N	237,888	217,523	140,167	2,460	246,332	230,391	135,963	2,990	266,878	246,484	130,897	3,330
O-Q	383,767	380,027	254,308	5,327	414,351	403,147	252,869	5,611	436,960	424,403	247,855	5,678
O	138,112	140,062	103,614	1,839	146,718	147,073	103,094	2,083	150,340	150,861	98,553	2,005
P	105,964	99,263	64,051	1,921	103,667	97,151	63,723	1,881	103,655	100,494	62,627	1,924

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(continued)

	2005				2010				2015			
	GE	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**	**GE**	**FR**	**ITA**	**SI**
Q	140,518	141,136	86,681	1,574	163,966	158,923	86,052	1,647	183,087	173,062	86,613	1,748
R_S	88,195	45,481	36,102	892	90,050	50,864	39,058	844	90,261	49,736	37,593	857
R	29,215	21,305	14,476	536	30,552	24,309	16,621	504	33,370	25,021	15,775	493
S	58,985	24,169	21,593	356	59,498	26,555	22,438	340	56,880	24,698	21,827	363
T	6,591	3,857	16,837	24	6,567	3,990	18,006	26	6,361	3,374	18,730	26
U	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

Note. For industry code explanation, see List of NACE codes.

Source: Vienna Institute for International Economic Studies (2019b).

Appendix 5: Value-added per employee in total economy and C21 (in million €)

Table 4: Value-added per employee in total economy and C21 (in million €)

	Value-added per employee (total economy)				**Value-added per employee (C21)**			
	GE	**FR**	**IT**	**SI**	**GE**	**FR**	**IT**	**SI**
1995	55	65	80	26	99	116	70	45
1996	56	65	81	28	99	117	75	47
1997	57	66	82	30	106	125	78	54
1998	58	67	82	30	107	126	81	57
1999	58	67	82	31	112	136	85	61
2000	58	68	84	32	119	165	88	69
2001	60	68	83	33	126	176	95	72
2002	60	69	82	34	123	179	98	78
2003	61	69	81	35	139	179	97	101
2004	62	71	82	36	149	173	101	97
2005	62	72	81	37	174	184	103	98
2006	64	73	81	39	178	214	110	122
2007	65	73	81	40	185	219	111	129
2008	65	73	80	40	196	221	120	128
2009	61	72	76	38	177	227	116	121
2010	64	74	79	40	177	240	130	125
2011	65	75	79	41	188	266	139	129
2012	64	76	77	41	188	274	135	126
2013	64	76	77	41	183	260	143	129
2014	65	77	77	43	182	268	149	131
2015	65	77	77	43	166	286	158	127
2016	66	78	76	43	178	298	154	116
2017	66	78	76	44	177	307	160	120

Source: Vienna Institute for International Economic Studies (2019b).