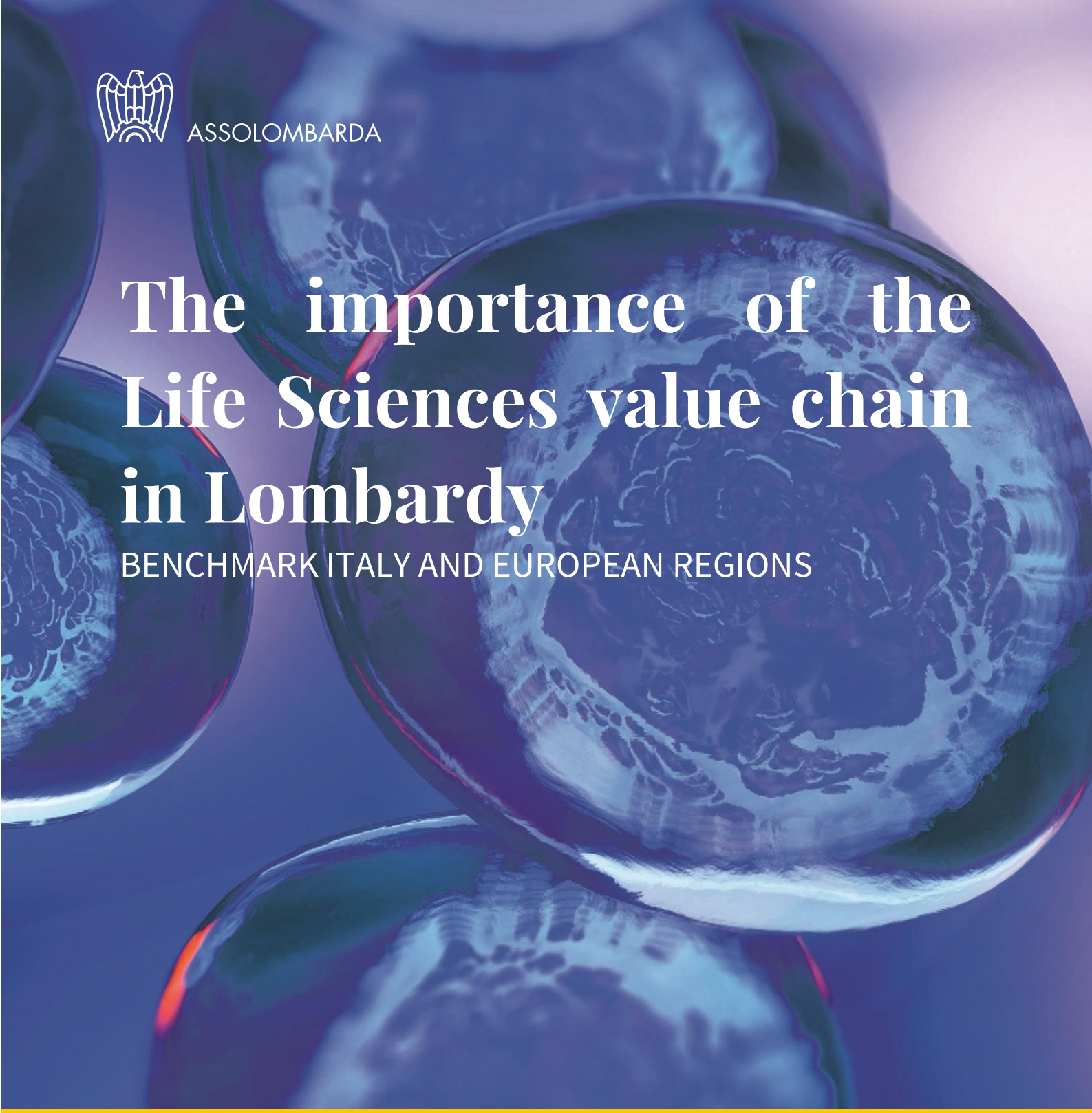

ASSOLOMBARDA

The importance of the Life Sciences value chain in Lombardy

BENCHMARK ITALY AND EUROPEAN REGIONS

Report n° 7/2022

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Introduction

1.1 FOREWORD

Since 2017, the Report on the Life Sciences value chain in Lombardy has been a communication, policy and work tool for Assolombarda, its member companies and policy makers.
It is a repeated and up-to-date analysis of the economic value generated by the players in the value chain and of their competitive positioning at international level, with the aim of overcoming the fragmentation of data and information about individual sectors to provide the reader with an overview of this 'ecosystem'. The work is based on the successful cooperation between Assolombarda and the Associations operating in the Life Sciences at national level, for the purpose of jointly promoting the development of optimal conditions for the growth and competitiveness of the value chain.

In this perspective, the Report is now in its fourth edition in 2022, fitting synergistically into the 'Life Sciences Hub' project of Assolombarda. The latter is a project aimed at increasing the competitiveness and internationalisation of the Life Sciences value chain and of the Regional Health System (SSR) of Lombardy.

In particular, the Life Sciences Hub project, coordinated by the Assolombarda Vice-President responsible for Life Sciences, promotes dialogue and collaboration between the public and private sectors by focusing on the following strategic actions:

- Promotion of the value of the value chain and the SSR in Italy and abroad through events and business missions;
- Definition of proposals and guidelines for the development of the sector, in cooperation with regional and national institutions;
- Development and performance analysis for the research and clinical trial sector to increase its competitiveness;
- Creation of projects linking business and academia to align the demand and supply of skills;
- Facilitation of relations between companies and institutions from different territories and countries, to promote the development of collaborations and partnerships;
- Providing guidance to companies and institutions towards funding opportunities for research and development, both at national and european level.

1.2 OBJECTIVES

The report aims to evaluate and analyse in economic terms the whole Life Sciences value chain, starting upstream from industry (production of pharmaceutical intermediates and active ingredients, drugs, medical devices, medical gases and biotech research services), including commercial activities (wholesale and retail trade of pharmaceuticals, medical devices and health care articles), up to the provision of health care services. The document also highlights the central role of Life Sciences in research and innovation as well as the significant transformations and opportunities associated with the digital revolution.

The analysis compares Lombardy with Italy and with primary benchmark regions, i.e. Baden-Württemberg, Cataluña and Île de France, which have similar economic structures, are important players in the economy of their countries and, most importantly, together with Lombardy are the most developed areas in Europe in the area of Life Sciences.

1.3 CREDITS

The report was edited by: Felice Lopane and Stefania Saini (Assolombarda). The authors would like to thank Laura Giudice, Luigi Maria Preti, Alberto Ricci (CERGAS-SDA Bocconi) for their scientific support. Furthermore, special thanks to the following contributors: Ettore Russo for Anitec-Assinform, Angelo Cassoni for AIOP, Fabrizio Cannioto for Confindustria Dispositivi Medici, Riccardo Pareschi and Carlo Riccini for Farmindustria, Juliette Vitaloni for Federchimica, Elvira Marchianò for Assobiotec, Vera Codazzi for the Lombardy Life Sciences Cluster, Cristian Ferraris and Valeria Negri for Assolombarda.

2

Main Results

The main results of this edition confirm the importance of the Life Sciences value chain for the economic development of the Italian and Lombard system, the primary role of Lombardy in the national context and its competitive positioning among the most advanced European regions in the Life Sciences, and the consolidated specialisation of the region in the health care industry and services.

The first outstanding point is that in 2020 and 2021 neither the pandemic nor the critical issues that have emerged in global supply and production chains have halted the growth of the Life Sciences, both in Lombardy and in Italy. According to our analyses based on the data available to date, in 2021 in Italy the turnover in the Life Sciences value chain reached 250 billion Euros, increasing by +6.9% vs. 2020 and by +10.1% vs. 2019, and the value added exceeded 105 billion (+3.4% vs. 2020, +4.8% vs. 2019). Likewise, in Lombardy the value of production in the value chain rose to over 74.5 billion Euros (+5.4% vs. 2020, +5.5% vs. 2019) and added value increased to almost 27 billion (+3.5% vs 2020, +5.8% vs. 2019). Considering both the direct contribution of the Life Sciences value chain sectors and the satellite industries activated in other economic sectors, in 2021 the value added of the Life Sciences value chain thus corresponds to 10.6% of GDP in Italy, while the incidence in Lombardy is even higher and amounts to 13% of the regional GDP, with an overall direct and satellite value added of more than 51.5 billion Euros.

The second aspect is the primary contribution of the life Sciences from Lombardy to the overall economic value of the national value chain, which is reaffirmed by the 2021 snapshot: Lombardy, where one sixth of the national population resides, accounts for as much as 20% of the workforce, 26% of the value added and 30% of the turnover of the Italian value chain.

The third piece of evidence is related to industry, whose robustness is a distinctive feature of Lombardy. In Lombardy, the industry alone generates 44% of the turnover (32.6 billion Euros) and 36% of the value added (9.7 billion Euros) of the whole Life Sciences value chain, which is higher than the figures reported for Italy. The Life Sciences industry in Lombardy also represents half of the whole sector at national level in both the economic variables under consideration. It should also be emphasised that, even in a year of severe economic downturn such as 2020, the Life Sciences industry in Lombardy has experienced a sustained growth and the increase between 2021 and 2019 amounts to +9.7% in terms of turnover and +10.2% in terms of value added (this performance, however, is slightly lower than the national overall figure). Finally, in Europe, Lombardy continues to stand out as one of the top pharmaceutical regions together with Cataluña, Baden-Württemberg and Île de France thanks, in particular, to a value added per capita equal to 618 Euros (2020 figures), a figure higher than the benchmarks. The positioning on international markets is also significant (in 2021, pharmaceutical exports from Lombardy amount to 7.7 billion Euros), showing a very strong growth in the last decade (+80%), even if in the pandemic years it has been much lower in comparison to Baden-Württemberg, the top performer (+0.7% in 2021-2019 vs. +23.1%).

The fourth interesting aspect is the activity carried out by industrial enterprises. Among the 74 largest companies in Lombardy (turnover above 100 million Euros), approximately 60% carry out production activities in the region and an equally large percentage are involved in clinical trials, while a still important but smaller share, 40%, has a corporate research centre.

The fifth point regards the strategic relevance of health care services, strongly reaffirmed in the response to the health emergency that between 2020 and 2021 saw Lombardy among the most intensely affected areas in the world. Health care services represent 55% of the value added and 34% of the turnover of the whole value chain in Lombardy and the sector is characterised by the positive dynamics of its variables between 2021 and 2019: +7.9% for turnover and +1.2% for value added. This growth, which is especially significant for the first variable, is driven by an acceleration in the funding of the public health system, which experienced unprecedented increases in the two-year period of the pandemic, at least in comparison with the previous decade.

3

The perimeter of the Life Sciences value chain

3.1 THE SECTORS OF THE LIFE SCIENCES VALUE CHAIN

The Life Sciences value chain is a dense, diversified and interconnected ecosystem of public and private players, operating in the industry (pharmaceutical intermediates and active ingredients, drugs, medical devices and biotech research services, industrial gases for medical use), trade (wholesale and retail trade in pharmaceuticals, medical devices and health care articles) and health and social care services sectors. The value chain also transversally interacts with information technology and artificial intelligence operators. In Lombardy, players are integrated into a high-profile research and education system, consisting of 11 universities with Life Sciences disciplines and important research centres, business incubators and non-profit organisations.

Table 1 provides a detailed reconstruction of the Life Sciences value chain analysed here, identifying the sectors it includes and their respective Ateco codes. Please note that in this analysis, the economic contribution of companies operating in the digital sector is assessed to a limited extent only, because of the difficulty of finding statistics about the

value generated for the value chain by companies operating across multiple economic sectors.

For more details about the analysis, please refer to the Methodological Appendix.

→ **Table 1 - The structure of the Life Sciences value chain by sectors**

	ATECO Code 2007
INDUSTRY	
MANUFACTURING OF INDUSTRIAL GASES	**20.11**
MANUFACTURING OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS	**21**
in detail: Manufacturing of basic pharmaceutical products	21.1
in detail: Manufacturing of drugs and pharmaceutical preparations	21.2
MANUFACTURE OF IRRADIATION, ELECTROMEDICAL AND ELECTROTHERAPY EQUIPMENT	**26.6**
in detail: Manufacturing of electromedical equipment (including separate parts and accessories)	26.60.02
in detail: Manufacturing of other irradiation and electrotherapy equipment	26.60.09
MANUFACTURING OF MEDICAL AND DENTISTRY EQUIPMENT AND SUPPLIES	**32.5**
in detail: Manufacturing of medical furniture, medical, surgical and veterinary materials, dentistry equipment	32.50.1
in detail: Manufacturing of dental prostheses (including repairs)	32.50.2
including: Manufacturing of orthopaedic prostheses, other prostheses and aids (including repairs)	32.50.3
in detail: Manufacturing of ophthalmic lenses	32.50.4
in detail: Manufacture of frames for glasses of all kinds; mass production of ordinary glasses	32.50.5
REPAIR AND MAINTENANCE OF ELECTRONIC AND OPTICAL EQUIPMENT	**33.13**
in detail: Repair of electromedical equipment, medical, surgical and veterinary materials, dentistry equipment and tools	33.13.03
RESEARCH AND DEVELOPMENT IN THE FIELD OF BIOTECHNOLOGIES	**72.11**
WHOLESALE AND RETAIL TRADE	
AGEMTS SPECIALISED IN THE SALE OF OTHER PARTCICULAR PRODUCTS	**46.18**
in detail: Brokers in the trade of pharmaceuticals products and cosmetics	46.18.3
WHOLESALE TRADE OF PHARMACEUTICAL PRODUCTS	**46.46**
RETAIL TRADE OF DRUGS IN SPECIALIST SHOPS	**47.73**
RETAIL TRADE OF MEDICAL AND ORTHOPAEDIC ITEMS IN SPECIALIST SHOPS	**47.74**
HEALTH CARE SERVICES	
HEALTH CARE ASSISTANCE	**86**
in detail: Hospital services	86.1
in detail: Services of medical and dentistry practices	86.2
in detail: Other health care assistance services	86.9
RESIDENTIAL SOCIAL CARE SERVICES	**87**
in detail: Residential nursing care facilities	87.1
in detail: Residential care facilities for mentally impaired, mentally troubled or substance abusing individuals	87.2
in detail: Residential care facilities for the elderly and disabled individuals	87.3
in detail: Other residential social care facilities	87.9
SERVICES OF PHYSICAL WELL-BEING CENTRES	**96.04**
in detail: Thermal spas	96.04.2

4

The value of the Life Sciences value chain: a national benchmark

4.1 THE LIFE SCIENCES VALUE CHAIN

In Italy, the turnover of the whole Life Sciences value chain is estimated to amount to over 250 billion Euros in 2021 according to our initial calculations, growing by +6.9% vs. 2020 and by +10.1% vs. 2019. The value added, which also grew to more than 105 billion Euros in 2021 (+3.4% compared to 2020, +4.8% compared to 2019), shows a slight decrease in terms of its impact on the turnover (41.7% vs. 43.1% in 2020 and 44% in 2019). The latest update of the employment figure is still the one for 2019, when it amounted to 1.8 million, an increase of just a little more than 32,000 compared to 2017 (+1.8%)[1].

[1] Please refer to Assolombarda, The Relevance of the Life Sciences Supply Chain in Lombardy: benchmarking among Italian and European regions, 2020 edition.

→ **Table 2- Life Sciences value chain: main economic variables for Italy and Lombardy**

	Turnover (thousands €, 2020)	Turnover (thousands €, 2021 estimate)	Value added (thousands €, 2020)	Value added (thousands €, 2021 estimate)	Employees 2019
Italy	236,188,853	252,471,815	101,863,153	105,296,461	1,778,659
Lombardy	**70,736,772**	**74,556,197**	**26,012,149**	**26,912,492**	**346,303**

Source: elaborations on Istat and AIDA data

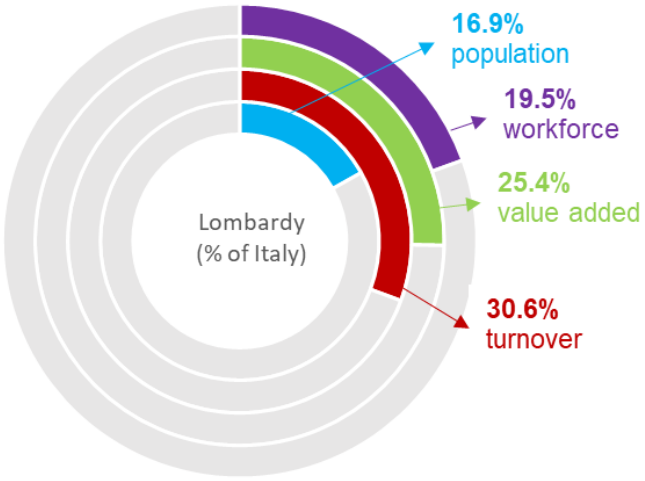
In economic terms, Lombardy continues to stand out on the national level as having the most developed and strongest Life Sciences value chain, with a turnover of more than 74.5 billion Euros in 2021 (+5.4% vs. 2020, +5.5% vs. 2019) and almost 27 billion of value added in the 2021 estimates (+3.5% vs. 2020, +5.8% vs. 2019). The number of employees in 2019 is over 346,000.

The contribution of the Lombard Life Sciences sector to the national value chain is therefore confirmed to be extremely significant, with a more than proportional representation in relation to its population: Lombardy, where more than one sixth of the national population (16.9%) resides, accounts for 19.5% of the workforce, 25.6% of the value added and 29.5% of the turnover of the Italian value chain in 2021.

The previous reports highlighted how the already significant contribution of Lombardy to the growth of Italian Life Sciences was further increasing until 2018 (+27.5% in Lombardy vs. +13.2% for Italy for the production value and +22.8% vs. +7.2% for added value between 2014 and 2018). Even in a context in which the contribution of the regional value chain remains extremely significant, between 2019 and 2021 the change in the regional turnover (+5.5%) was less significant than the national trend (+10.1%), while the change in value added was higher than the Italian figure (+5.8% vs. +4.8% respectively). The increase in the number of personnel was more noticeable (+3.6% in Lombardy between 2019 and 2017 vs. +1.8% in Italy).

All these observations confirm how the specialisation of Lombardy in the Life Sciences sector is strategic for the economic growth of the region and of Italy as a whole. Furthermore, despite the pandemic recession and the growing difficulties in the global supply and production chains, the figures for 2020 and 2021 confirm that the economic growth of the value chain has not stopped but, on the contrary, it has increased both at national level and in Lombardy.

→ **Figure 1- Life Sciences sector: impact of the main economic variables of Lombardy on the Italian total (2021)**



Source: elaborations on Istat and AIDA data

Analysing the individual sectors of the value chain, health care services at national level are confirmed as the component that mostly contributes to the overall generated value, in terms of both turnover (59.5% in 2021 estimates) and value added (76.0%). Next comes industry, which accounts for 25.6% of the turnover and 18.7% of the value added. Last but not least, there is trade, which accounts for 15.0% and 5.3% of the total respectively. The figures do not significantly differ from the ones reported in previous editions.

→ **Table 3 - Life Sciences Value chain by sectors Italy and Lombardy**

	Italy				Lombardy			
	Turnover		Value added		Turnover		Value added	
	thousands €	*% on value chain total*	thousands €	*% on value chain total*	thousands €	*% on value chain total*	thousands €	*% on value chain total*
2020								
Industry	60,370,992	25.6%	18,786,914	18.4%	31,167,045	44.1%	9,380,325	36.1%
Trade	35,269,162	14.9%	5,055,139	5.0%	15,503,527	21.9%	2,129,124	8.2%
Health care services	140,548,700	59.5%	78,021,100	76.6%	24,066,200	34.0%	14,502,700	55.8%
Value chain total	**236,188,853**	**100.0%**	**101,863,153**	**100.0%**	**70,736,772**	**100.0%**	**26,012,149**	**100.0%**
2021 estimates								
Industry	64,556,213	25.6%	19,672,550	18.7%	32,610,344	43.7%	9,655,563	35.9%
Trade	37,798,602	15.0%	5,567,210	5.3%	16,576,653	22.2%	2,375,930	8.8%
Health care services	150,117,000	59.5%	80,056,700	76.0%	25,369,200	34.0%	14,881,000	55.3%
Value chain total	**252,471,815**	**100.0%**	**105,296,461**	**100.0%**	**74,556,197**	**100.0%**	**26,912,492**	**100.0%**

Source: elaborations on Istat and AIDA data

In Lombardy, contributions are more evenly distributed between industry and health care services, reflecting the industrial specialisation within the regional Life Sciences value chain. In the 2021 estimates, industry accounts for 43.7% of the total value chain in terms of turnover, making it the most important segment, before services (34.0%). The latter, conversely, lead in terms of value added, with a share equal to 55.3% of the value chain, compared to an industry share of 35.9%. With regard to both of the considered parameters, trade ranks third, but still accounts for shares higher than the national figure (22.2% of turnover and 8.8% of value added).

4.2 INDUSTRY

Starting with the 2020 edition, the Report makes a distinction between industry, trade and services within the value chain. The selection of enterprises in the industry sector is carried out both by making reference to the Ateco activity codes and, for a sample of large enterprises/multinationals significant in economic terms, by assigning those enterprises having their own products on the market to this sector even if they belong to codes other than 'manufacturing'.

In Italy, the Life Sciences industry accounts, according to the 2021 estimates, for a turnover approximately equal to 64.6 billion Euros and for a value added close to 19.7 billion Euros. Both values show a significant increase compared to 2020 (+6.9% for the turnover and +4.7% for the value added) and 2019 (+11.5% for the turnover and +11.3% for the value added).

Approximately half of these economic figures are generated by industries based in Lombardy: 50.5% in terms of turnover and 49.1% in terms of value added. The data for Lombardy confirm, as a matter of fact, an extremely strong and consolidated sector, with a turnover equal to 32.6 billion Euros and an value added exceeding 9.6 billion in 2021, accounting for 30% of the turnover. Compared to 2020, the increase is equal to +4.6% in terms of turnover and +2.9% in terms of value added; compared to 2019, the same figures are +9.7% and +10.1%: in both cases, the performance is slightly lower than the Italian total.

→ **Table 4 - Industry focus: main economic variables for Italy and Lombardy**

	Turnover (thousands €, 2020)	Turnover (thousands €, 2021 estimate)	Value added (thousands €, 2020)	Value added (thousands €, 2021 estimate)	% share of Italian value added 2021
Italy	60,370,992	64,556,213	18,786,914	19,672,550	100.0%
Lombardy	**31,167,045**	**32,610,344**	**9,380,325**	**9,655,563**	**49.1%**

Source: elaborations on Istat and AIDA data

Finally, some additional considerations on the type of activity can be made, distinguishing between: production, corporate research centres, clinical trials or management offices.

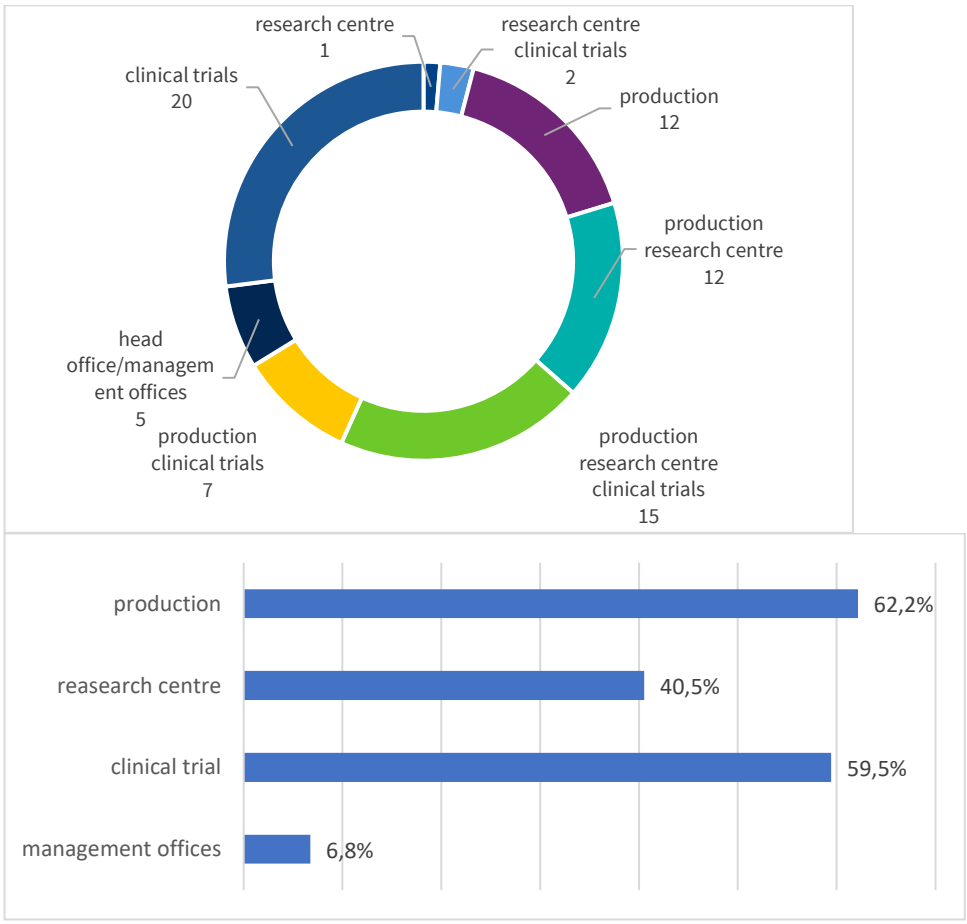
Analysing the 131 industrial companies mapped in the Italian value chain with a turnover higher than 100 million Euros (together they add up to more than 42 billion Euros), almost 80% have one or more production sites in the country, about 60% have a corporate research centre and another 60% carry out clinical trials. Interestingly, more than half of the large Italian companies active in clinical development are located in Lombardy.

As regards to the largest companies in Lombardy, of which there are 74 in total, half focus on a single activity in the region, while the remaining half combines several types.

Of these 74 companies, after excluding the 5 companies that only have management offices in Lombardy, the remainder are divided as follows:

- the vast majority (46) are manufacturers: approximately 60% of these also operate a research centre alongside production and almost half carry out clinical development;
- more than half (44) are involved in clinical trials, and almost half do so on an exclusive basis;
- a smaller number (30) has a corporate research centre, which in almost all cases supports production/clinical trials.

→ Figure 2 - The 74 largest industrial enterprises in Lombardy (turnover > 100 mln €) by activity



Source: Assolombarda and Life Sciences Associations

4.3 HEALTH CARE SERVICES

In 2021, health care services[2] generate a turnover of more than 150 billion Euros and an value added of 80 billion Euros in Italy. These two figures increased by +6.8% and +2.6% vs. 2020, and by +7.7% and +2.0% vs. 2019, respectively[3]. This growth, which is especially significant with regard to the first variable, is clearly at odds with the trend recorded by the economy as a whole and has been driven by an acceleration, unprecedented in the previous 15 years, in the funding of the public health system, which in the two-year period of the pandemic increased by 8.2% vs. 2019 (from +5.4% in 2020 to +2.6% in 2021)[4].

The total number of employees stands at 1.4 million[5], showing a slight decrease compared to 2020 (-0.8 %), but still increasing by 0.3 % compared to 2019. This difference is at least marginally attributable to the number of employees in the NHS. The latter have increased, especially in 2020, after years of steady decline. In 2020, the number of employees in the NHS was 665,000, a significant drop compared to the beginning of the decade (682,000 in 2011), but a marked increase compared to 2019 (650,000)[6]. It should be highlighted that the growth in the number of staff employed and contracted with the NHS is largely to be attributed to the draining of staff units from other, mostly private, health care sectors, both from the world of hospitalisation and especially from the sphere of residential and home services provided in the social and health sector. Many of the hirings announced and then implemented in 2020 by NHS companies involved figures such as physicians earning a specialisation, in retirement or in free-professional positions, which were rarely transformed into actual employment contracts.

The distribution of the value added of health care services in the Lombardy context is slightly higher than the population size: Lombardy, where 16.9% of the population resides, generates 18.6% of the value added. This distribution is driven by the significant health care activity carried out under the NHS, based on the distribution of the National Health Fund between regions on a per capita basis; this dynamic tends to automatically align the regional shares associated with population, turnover and value added. At the same time, misalignments such as the one occurring in Lombardy may result, on the one hand, from differences in the available services, such as the presence of highly specialised centres attracting non-resident patients, and, on the other hand, from a higher or lower per capita amount of private health care expenditure.

[2] The calculation of health care services also includes, in addition to public and private hospital services, specialist and outpatient services and socio-medical services with a predominantly socio-medical component, those enterprises providing services (mostly medical gas and medical device companies) to health care facilities. As a whole, these enterprises contribute with a production value equal to 2.3 billion Euros and an added value equal to 652 million Euros.

[3] To ensure comparability between the years, the percentage differences have been calculated without taking into account the values associated with the enterprises providing services to health care facilities.

[4] Armeni P., Borsoi L., Notarnicola E. and Rota S. (2022). NHS and SSR expenditure for health: break-down and evolution. In the OASI 2022 Report

[5] The employment figure for the service sector refers to 2021, in contrast to the one for the overall supply chain, which reports the information as of 2019, since no consolidated figure for 2021 and 2020 is available for the industry and trade sectors.

[6] Gugiatti A., Manfredi S., and Meda F. (2022). The structure and the activities of the NHS. In the OASI 2022 Report Elaboration from data of the Ministry of Economy and Finance - State General Accounting Office, 2022 Annual Accounts.

In 2021 Lombardy recorded an increase in the turnover equal to +7.9% compared to 2019, not very different from the national figure (+7.7%). In contrast, the value added increased by 1.2 % compared to the 2019, an amount lower than the national figure (+2.0 %). The different trend in value added between the national and regional level, as well as the dynamics diverging from that of the turnover, can be explained by a different dynamic of the costs for the purchase of intermediate goods and for personnel for health service providers, considering the peculiarity of Lombardy as the first region in Italy and among the western countries to face the Covid-19 emergency in spring 2020.

In terms of employees, the regional distribution is also largely aligned with the demographic distribution. In comparison with the 2019 data, there is significant growth at the regional level in Lombardy (+1,300 units), even though 2021 marked a setback on this front (-400 units between 2020 and 2021). Between 2019 and 2020, the growth in the number of NHS employees amounted to approximately 500 individuals.

→ **Table 5 - Health care services focus: main economic variables for Italy and Lombardy**

	Turnover (thousands €, 2020)	Turnover (thousands €, 2021 estimate)	Value added value (thousands €, 2020)	Value added value (thousands €, 2021 estimate)	% share of Italian value added value (2020)	Employees (2021)
Italy	140,548,700	150,117,000	78,021,100	80,056,700*	100.0%	1,426,000
Lombardy	**24,066,200**	**25,369,200**	**14,502,700**	**14,881,000**	**18,6%**	**259,700**

Source: elaborations on Istat data, * final data

4.4 SATELLITE INDUSTRIES OF THE LIFE SCIENCES VALUE CHAIN

This section is meant to show the valorisation of the satellite industries of the value chain, to provide an insight into the positive externalities and the indirect economic impact generated through the effects on other sectors of the economy. As in the remaining parts, the methodological choices and assumptions made are reported in the Appendix.
The results of this elaboration are provided in Table 6, which shows, in addition to the value added of the value chain shown in the previous table, the value added including the satellite industries and its incidence on the regional and national GDP for 2020 and the 2021 estimates of the same.

→ **Table 6 - Life Sciences Value chain: added value and added value including the ancillary industries for Italy and Lombardy**

	Value chain value added (thousands €)	Satellite industries value added (thousands €)	Value chain + satellite industries value added (thousands €)	GDP (million €, at current prices)	GDP % share of the value added (value chain + satellite industries)
2020					
Italy	101,863,153	83,091,049	184,954,202	1,660,621	11,1%
Lombardy	**26,012,149**	**24,885,140**	**50,897,289**	**367,167**	**13,9%**
2021 estimates					
Italy	105,296,461	83,841,083	189,137,543	1,782,050	10,6%
Lombardy	**26,912,492**	**24,758,694**	**51,671,186**	**397,330**	**13,0%**

Source: elaborations on Istat, AIDA and Prometeia data

In Italy, the value added of the satellite industries is approximately equal to 84 billion Euros in 2021, and when this figure is summed to the 105 billion Euros directly generated by the Life Sciences sectors, the overall value added of the value chain and satellite industries amounts to 189 billion Euros, i.e. 10.6% of the national GDP, a growing figure compared to the 10% recorded in 2018 by the previous Report.

In Lombardy, the contribution of the Life Science value chain and its satellite industries to the regional economy is confirmed to be higher than the national total and is equal to 13.0% in 2021 (12.8% in 2018), with an overall value added exceeding 51.5 billion Euros, further confirming the extent to which the Life Sciences represent a specialisation component for the Lombardy economy and important activators for other sectors of the territorial system. In other words, the overall direct and satellite value added of the Lombardy Life Sciences value chain is equal to 2.9% of the national GDP.

5

The pharmaceutical industry and health care services: European benchmark

5.1 THE BENCHMARK REGIONS

The analysis of the Life Sciences value chain is also carried out at international level, comparing Lombardy with Baden-Württemberg, Cataluña and Île-de-France, which are the most advanced European regions in the Life Sciences. For the selection of the benchmark regions, since the presence of employees engaged in health and social services shows a linear relationship with the regional population, we focused on the pharmaceutical industry, identifying the territorial unit with the highest share of employees compared to the European overall figure in each of the most developed national contexts in this sector (France, Germany and Spain).

As of 2020, the population of the benchmark regions varies between 7.6 million in Cataluña and 12.3 million in Île-de-France. The percentage of the population aged over 65 varies between 15.4% in the Île-de-France and 22.9% in Lombardy, in line with the Italian primacy as the oldest country in Europe, characterised by an unquestionably massive and growing demand for health care and especially social and health care. The population density is especially high compared to the European average (118 inhabitants/sq km): it varies from 239 inhabitants/sq km in Cataluña to 1,032 inhabitants/sq km in Île-de-France, with Lombardy in the middle (434 inhabitants/sq km).

In general, all the observed regions are highly urbanised areas, where the availability of health services is usually widespread, but where demand management is especially complex because of many factors: multiple stakeholders to be involved in health promotion and care pathway design, strong social inequalities, presence of specific health risk factors.

All four analysed regions are very important for the economy of their nation, with shares of the national generated value added generally ranging from 15% in Baden Wurttemberg to approximately 31% in Île-de-France, which includes the capital city of Paris that concentrates a significant share of economic activity because of the presence of several institutional sites. Lombardy, again, is in an intermediate position (22.1%).

→ **Table 7 - The European Benchmark Regions: Overview (2020)**

	Baden-Württemberg	Cataluña	Île de France	Lombardy
Population	11,103,043	7,671,252	12,348,605	9,981,554
% of population aged over 65	20.6%	19.3%	15.4%	22.9%
Population density (inhabitants/sq.km.)	314	239	1,032	434
Value added (million €)	458,825	194,365	632,657	330,046
% share of the value added on the national overall figure	15.0%	19,0%	30,8%	22,1%

Source: Eurostat

The analysis of the European comparison focuses on the two segments, the health care services and the pharmaceutical industry (excluding trade, unlike the section on the national comparison), which mostly contribute in terms of employment and value added to the overall Life Sciences value chain and for which comprehensive data are available.

5.2 THE PHARMACEUTICAL INDUSTRY

In the European comparison, the data confirm that even in 2020 the pharmaceutical industry in Lombardy generates a higher value added per capita than all other benchmark regions: 618 Euros per inhabitant. Cataluña and Île de France follow with 559 and 461 Euros respectively. In contrast, Baden-Württemberg generates an value added per

inhabitant equal to 424 Euros. Even though the orders of magnitude remain unchanged over time, intertemporal comparisons are not easy due to the presence of companies belonging to multinational groups, whose revenue allocation with respect to geographical area of activity may change over time.

The pharmaceutical industry in Lombardy also emerges as an important sector of the local economy when assessing the importance of the value added and turnover generated by the sector in the regional total (defined as the total referred to the regional enterprises registered in the ORBIS database). In Lombardy, in fact, the percentage share of value added from the pharmaceutical industry is 2% of the overall figure and that of turnover is 1.5%, aligned with the average of the benchmark regions. The only region with higher values is Cataluña (where is the value added share is 4% and the turnover share is 2.5 %). In comparison with the other benchmark regions, the Île de France has the lowest percentage indicators among the areas considered (0.8% and 0.7% of the total value of regional companies by value added and turnover respectively), reflecting the fact that the pharmaceutical industry, while extremely strong (the number of employees is the highest in absolute terms, almost 6,000 per million inhabitants), coexists in the Paris region with other equally developed segments of economic activity that reduce its relevance in relative terms. Similarly, Baden-Württemberg is home to other equally developed industrial (automotive, electronics, chemicals) and the tertiary (banking and insurance) sectors, and so the weight of the pharmaceuticals industry in the overall economy is low, equal to 1.3% in terms of value added and 1.6% in terms of turnover.

→ **Table 8 - Pharmaceutical industry indicators for Lombardy and European benchmark regions (2020)**

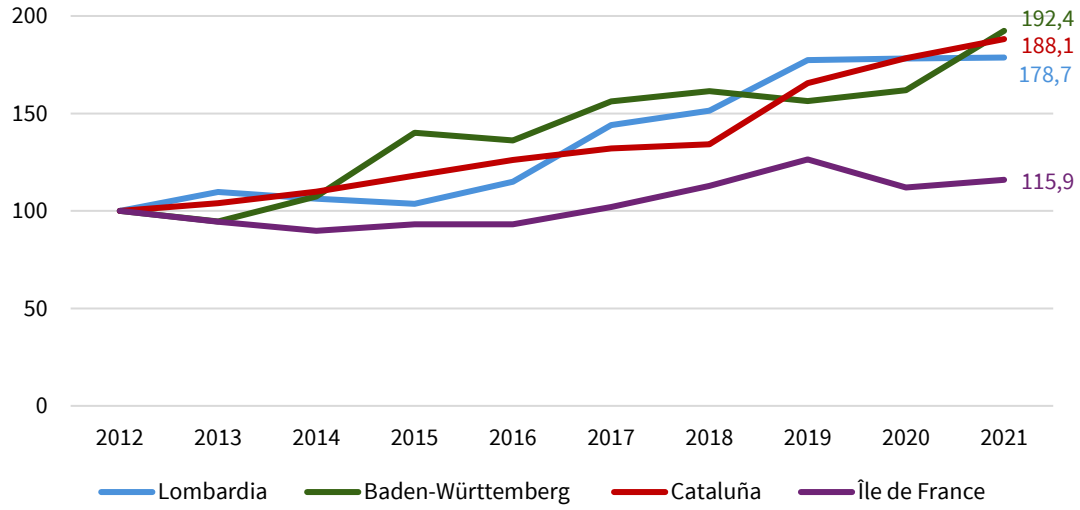
	Baden-Württemberg	Cataluña	Île de France	Lombardy
pharmaceutical industry value added Euros per inhabitant	424	559	461	**618**
% of pharmaceutical industry value added in the overall regional economy	1.3%	4,0%	0,8%	**2,0%**
% of pharmaceutical industry turnover in the overall regional economy	1,6%	2,5%	0,7%	**1,5%**
export billion Euros (2021)	29.6	7.2	7.6	**7.7**
pharmaceutical industry employees per million inhabitants (2019)	3,426	2,352	5,997	**2,265**

Source: elaborations on data from ORBIS, Eurostat, Istat, Destatis, Idescat, Direction générale des douanes et droits indirects

The aggregate of these indicators confirms that Lombardy is an area of excellence in the European pharmaceutical industry which, in recent years, has strengthened its competitive capacity and international outreach. In 2021, the exports of pharmaceutical companies in Lombardy amount to 7.7 billion Euros, almost equal to Île de France (7.6 billion) and slightly higher than the foreign sales of Cataluña (7.2 billion); in contrast, the

exports of Baden-Württemberg are four times higher (29.3 billion). The very strong growth dynamic over the last decade is interesting: almost +80% in Lombardy, +88% in Cataluña and +92% in Baden-Württemberg between 2012 and 2021 and just +16% in Île de France. However, it should also be noted that in 2020 and 2021, the growth of the pharmaceuticals exports from Lombardy was decidedly weak when compared to the German and Spanish regions: in 2021, the increase in the foreign turnover of Lombardy is just +0.7% compared to 2019, in stark contrast to the +23.1% of Baden-Württemberg and the +13.6% of Cataluña (Île de France, on the other hand, experiences a drop by -8.3%).

→ **Figure 3 - Pharmaceutical industry exports (2012=100)**



Source: Assolombarda based on data from Istat, Destatis, Idescat, Direction générale des douanes et droits indirects

Finally, the last indicator for the comparison between European regions is the number of employees in the pharmaceutical industry as a proportion of the resident population. Here, Lombardy (2,265 employees per million inhabitants) falls behind the benchmarks, among which Île de France stands out with a peak of 5,997 employees per million residents, followed by Baden-Württemberg and Cataluña (with 3,426 and 2,352 employees respectively). However, this position determines an excellent performance for the Lombardy industry, if the added value produced per employee (over 260,000 Euros) is considered.

5.3 HEALTH CARE SERVICES

This section provides data about the value added generated by the health care services segment (this includes hospital services, specialist and outpatient services, and socio-medical services with a predominantly socio-medical component) in the four analysed regions as well as its weight in the regional total. The overall value added generated in the four regions, taking into account both public and private service providers, amounts to more than 84 billion Euros, with the highest value in the Île de France region (34.4 billion Euros) and the lowest in Cataluña (10.6 billion). Lombardy is positioned in the middle, with

a figure equal to 14.6 billion. The same trend is confirmed in per capita terms, with Île de France having the highest value (2,786 euro per capita) and Cataluña the lowest (1,382 euro per capita). While significant differences emerge in absolute and per capita terms, the percentage share of the total regional economy shows much less heterogeneous values among the benchmark regions, with figures ranging from 4.4% in Lombardy to 5.7% in Île de France. Compared to the same data reported in the 2020 Report and referring to the year 2017, there is a marked divergence between Lombardy and the other observed regions, so much so that the range (i.e. the differential between the highest and lowest value), which increased from 0.4 to 1.3 percentage points, is mostly due to the modest growth of the figure for Lombardy.

→ **Table 9 - Health care services: territorial overview (2020)**

	Baden-Württemberg	Cataluña	Île de France	Lombardy
Health care services value added, Euros per inhabitant.	2,252	1,382	2,786	**1,463**
% share of the health care services value added in the overall regional economy	5.4%	5,2%	5,7%	**4,4%**

Source: elaborations on Eurostat data

It is worth mentioning, however, that for health services, it is not possible to define exchange value objectively and with certainty: the meaning of the value added is therefore weakened and subject to questionable interpretations. This is still the case even when health care charges are used because, even though they make it possible to determine a turnover, they are not expressive of the economic value of the service and are, by their very nature, differentiated from the pricing policies that can be adopted in other, more market-based sectors. For this reason, the assessment of the value generated by the process of production and distribution of goods and services does not represent a dimension sufficient to compare the care performance of the regions under examination. The performance comparison must take into account qualitative and quantitative components, which also express the contribution the system makes to the improvement of the health level of the population. This peculiarity of the sectors characterised by a strong presence of the public sector as a funder and producer became especially clear during the period of the Covid-19 emergency, for which it is even more difficult to determine a clear correlation between the actual production and its economic assessment.

The selected indices are thus aimed at assessing and comparing within an aggregated logic the performance of the health care services in the various regions, referring to structural, process and outcome dimensions, with the objective of clearly intercepting the ultimate institutional purpose of these activities, which lies in the satisfaction of the citizen need for care. In terms of outcome, some evidence on the impact of the pandemic on different contexts is also shown; even though it is not easy to determine a causal relationship between initial allocations and intermediate and final outcomes, it is useful

to show how, starting from different starting situations (even in terms of prevalence and incidence of the disease), the impact of Covid-19 was heterogeneous in different contexts.

Accordingly, the following input, output and outcome indices have been considered:

- medical staff per 1,000 inhabitants in 2019;
- hospital beds per 1,000 inhabitants in 2019;
- life expectancy at age 65 in 2019 and 2020;
- excess mortality in 2020.

→ **Table 10 - Health care services indicators for Lombardy and European benchmark regions (2019)**

	Baden-Württemberg	Cataluña	Île de France	Lombardy
Medical staff per 1,000 inhabitants	4.2	4.9	3.9	**3.7**
Hospital beds per 1,000 inhabitants	7.3	3.8	5.3	**3.5**
Life expectancy at age 65 (2019)	20.4	22.2	23.0	**21.8**
Life expectancy at age 65 (2020)	20.3	20.3	21.2	**19.1**
Excess mortality (2020)	5%	18%	16%	**30%**

Source: elaborations on Eurostat data and data from institutional sites

As highlighted in previous editions of the Report, the number of employees engaged in the provision of health care services is extremely heterogeneous. The German region of Baden-Württemberg had more than 17 medical personnel[7] per 1,000 inhabitants in 2017, Île de France had an intermediate figure of 13.3, while Lombardy and Cataluña had less than 10 professionals per 1,000 inhabitants. The differences can be attributed to a lower incidence of nursing jobs. On the medical side, for which an update for 2019 is available, there is less diversity, even though it confirms the ranking of the regions, which reflect the specificities of the national health systems they belong to. Lombardy ranks last with 3.7 medical staff per 1,000 inhabitants, compared to 4.9 in Cataluña, 4.2 in Baden-Württemberg and 3.9 in Île de France.

The second indicator measures the level of structural capacity in terms of beds and thus offers a proxy for the capacity of the different regional systems to provide hospital care. The German region of Baden-Württemberg has the highest number of beds per 1,000 inhabitants equal to 7.3, which is significantly higher than the other surveyed regions. Lombardy is the region with the lowest figure, with 3.5 hospital beds per 1,000 inhabitants (the figure for Île de France is 5.3 and for Cataluña is 3.8). As in the case of personnel, this result is definitely influenced by the specific health policies that have been implemented in individual countries (e.g. DM/70 in Italy), but also by the introduction of medical technologies that have made it possible to treat certain pathologies in an outpatient setting and under Day Hospital and Day Surgery procedures, reducing the required number of hospital beds for ordinary hospitalisation[8]. These dynamics, when considered together, have resulted in a generalised reduction in hospital capacity over time.

[7] Medical staff include both physicians and nurses.
[8] OASI 2019 Report.

The third and fourth indicators measure life expectancy at age 65 in the four regional contexts, for 2019 and 2020 respectively. Again, not insignificant differences are evident: even in 2019, and despite similar socio-demographic contexts, there is a difference of about 2.6 years between the region with the highest life expectancy at age 65 (23 years in Île de France) and the region with the lowest figure (20.4 years in Baden-Württemberg). The figure for Lombardy is in the middle, at 21.8 years, with a modest increase over 2017 (+0.4 years). The year 2020 marks a further point of divergence in the data: even though all regions record a negative variation, the range between the lowest (-0.1 years in Baden-Württemberg) and highest (-2.7 years in Lombardy) change is particularly significant, demonstrating the different impact of the Covid-19 pandemic in different geographical contexts. This figure is the result of the fifth indicator presented here, i.e. excess mortality, calculated as the percentage difference between mortality in 2020 and the average mortality recorded in the previous five-year period (2015-2019). Here, the difference between the figures for Lombardy (+30%), Baden-Württemberg (+5%) and the intermediate figures for Île de France and Cataluña (+16% and +18%) is clear and dramatic.

6

The Mega Trends of the Life Sciences Value chain

This section provides an overview of the main phenomena currently affecting the Life Sciences value chain. We are talking about more or less obvious phenomena characterising the development of the national Life Sciences ecosystem, which in the last three years had to deal with a complex health scenario in which areas of excellence, as well as areas for improvement, have emerged; areas on which, also thanks to the contribution of Next Generation EU, the whole public and private sector is working intensively, with challenging objectives that can further improve the quality, efficiency and effectiveness of the National Health Service and of the research and industry ecosystem, for the benefit of citizens.

Thanks to the contribution of the most important national representative organisations in the Life Sciences sector[9], we have identified three thematic clusters on which the ecosystem is strongly committed, from research to production to the delivery of treatments.

The first is linked to a topic for which the PNRR allocates considerable resources through both Mission 1 and Mission 6, for an amount exceeding 62.3 billion Euros: digitalisation.

[9] Anitec-Assinform, AIOP, Confindustria Dispositivi Medici, Farmindustria, Federchimica.

This is a topic that, when applied to this sector, is not only purely ICT-related but also healthcare-related. In fact, an interesting evolution of the digital health ecosystem is also taking place in Italy, thanks to the innovative capacity of the Italian business community. The "Cassa Depositi e Prestiti" has also decided to invest in this issue, financing the activation of a new accelerator that will stimulate the development of new companies and thus increase the competitiveness profile of Italy in this sector. In addition to this trend, there is also a growing interest in the development of decentralised trials, as shown on the following pages.

The second mega trend is associated with research and innovation. This is an area on which several billion Euros have been allocated at national and regional level, starting with the consolidation of technology transfer, with the ultimate goal of increasing the ability to translate research results into patents, and patents into enterprises. The overall investment of Life Sciences companies in research, development and innovation is growing in Italy and in Lombardy. More than 30% of the national investment - amounting to 2.7 billion Euros for the pharmaceuticals and medical devices sector alone - is concentrated in the region of Lombardy, which is also the main attractor of drug clinical trials in Italy.

The third identified trend regards the need to strengthen the supply and production chains at European and national level. The European Commission is investing in this phenomenon, also thanks to the Pharmaceutical Strategy for Europe, in order to reduce its dependence on countries such as China and India for the supply of active ingredients and intermediates. The high volatility of demand, the exponential increase in energy and raw material costs, and the rise in the cost of transport are phenomena with a high impact on the value chain, requiring the utmost attention of both the private and public system.

6.1 DIGITAL REVOLUTION: FROM THE DIGITALISATION OF VALUE CHAINS TO DIGITAL HEALTH

The state of the art of digital transformation in the Life Sciences value chain

The experience of the critical, sometimes dramatic, issues exposed by the pandemic crisis and the resulting funding opportunities offered by the PNRR represent new potential drivers for the development of digitalisation in the health care and life sciences world, from hospitals to territorial care. Digitalisation in health care represents an opportunity to make efficient use of the vast amount of information generated by the patient and system management processes, favouring the optimisation of procedures, the rationalisation of expenditure and the development of evidence-based health policies.

In Italy, the health care sector in the digital market grew by 9% in 2021 over the previous year[10]. The health care sector ranks first in the list of sectors where spending on digital technologies has grown the most, overtaking PACs (Central Public Administrations), local

[10] Anitec-Assinform, Il Digitale in Italia 2022. The estimate takes into account: Local Health Authorities (ASL) and Local Health Boards (AUSL), Hospital Companies and Hospitals, Pharmacies, Analysis Laboratories (ATECO codes 84.12.1, 86, 87, 88).

authorities and the banking sector. The estimates up to 2025 show even higher growth rates: the 2021-25 TACM (Average Annual Growth Rate) is estimated at 11.4%, with a market that could grow from a volume of 1.8 billion Euros in 2021 to an estimate exceeding 2.8 billion in 2025[11].

An important tool supporting this growth is the PNRR (*Piano Nazionale di Ripresa e Resilienza* - National Recovery and Resilience Plan). An important share of the overall funding for Mission 6 (Health) of the PNRR is aimed not only at the modernisation of the technological assets and at the structural strengthening of NHS hospitals, but also at enhancing the level of digitalisation of 280 of the 340 healthcare facilities with Level I and II Emergency and Admission Departments (DEAs) by 2025, ensuring the required support of an adequate data processing centre (DPC). The overall sum of 2.8 billion Euro, in addition to the digitalisation of hospitals, should allow the care of more than 200,000 patients and the implementation of the Electronic Health Record by 85% of general practitioners.

Currently, the main areas of investment in digital health can therefore be considered as *PNRR-driven.* This is the case with Electronic Health Records - there is no doubt that the increase in the resources invested in this area is linked to the FSE reform projects funded by the PNRR - and the development of Telemedicine, with the regions of Lombardy and Apulia playing a central role.

The digitisation process of the health ecosystem at national and regional level still has great potential for development. A look at the world of hospitalisation and the ASLs (Local Health Authorities) shows in fact a dynamic more oriented towards the allocation of investments aimed at upgrading the existing rather than at creating new services[12]. However, at regional level, the efforts made to develop monitoring dashboards for business intelligence activities and the development of data lakes and digital medicine (from telemedicine to telemonitoring with remote or home-based sensors and devices, remote health care, remote consultation and remote rehabilitation activities) are distinctive. At the same time, this major digital transition in health care also requires immediate action to upgrade the professional skills of all health care personnel, the digital skills of patients and caregivers, and a strengthening of IT support, as well as an appropriate upgrade of maintenance services for increasingly sophisticated equipment and devices.

Turning to the Life Sciences industry chain, from pharmaceuticals to medical devices, infrastructural renewal and cybersecurity are at the top of the agenda[13], but there is also a strong emphasis on the use of cloud technologies to support marketing and commercial operations[14].

To trace the frontier of digital health, it is useful to explore the applications of some emerging technologies in the digital world for the Life Science world. The Digital Enabler and Digital Transformer markets (e.g. Cybersecurity, IoT, Wearable, AI, Big Data, etc.). are

[11] Anitec-Assinform, Il Digitale in Italia 2022. Estimates published in July 2022.
[12] Ibidem.
[13] Ibidem.
[14] Assolombarda, 2022.

undoubtedly the most dynamic in the digital world, with growth rates well above double digits (e.g. TCAM 2021/25 IA: 20,9%; TCAM 2021/25 Blockchain: 26,5%[15]). These are technologies with a marked transversality, between different sectors and, as in the case of AI, even within the same sector (AI is used to make processes more efficient but also in products and services). In the Life Sciences, AI is now used transversally from patient care in facilities, to radio diagnostics to drug discovery activities in the pharmaceutical sector (it is no coincidence that, according to IDC data, the sector in which the private AI market is growing the most is the health sector[16]). Meanwhile, Big Data Analysis and Cybersecurity are increasingly central to the development of clinical trials. IoT and Wearables represent at the same time, now absolutely concrete, solutions essential for the development of new digital medicine solutions and innovative medical devices (including software-based ones, from drug support programmes to digital therapies).

The complex ecosystem of digital health in Italy is now finding fertile ground for development and growth at cross-sector level, across all stages of the Value chain, with an significant impact even on research, development and innovation processes. Thanks to digital cybersecurity solutions, capable of favouring data respect and protection, we can and must support the possibility of a secondary use of health data (including genomic, real-world and life ones[17]) by enhancing the national capacity to develop innovation for the patient.

The role of the pharmaceutical industry for the digital transformation in health care

As previously mentioned, the global pandemic has been an accelerator for the digital transformation process in the health system. Pharmaceutical companies have been at the forefront of this important evolutionary process.

Digitisation has affected both the drug production, management and information parts as well as the part that precedes development, research. In the first case, it is important to mention the production of drugs and medical gases through the implementation of validated software and 'data integrity' procedures used at the primary production and packaging stages. Companies also supported the development of increasingly digitised information to support increased citizen awareness towards OTC, as well as communication with health care professionals. Since the first months of the pandemic, the deployment and use of telemedicine platforms has seen a very strong increase (284 new services registered in 2 years, many implemented through public-private partnerships)[18] as it has guaranteed the continuity of care and assistance to patients who could not access hospital facilities. Despite the end of the state of emergency, interest in telemedicine services remained high even in 2022 on the part of all stakeholders: more than half of physicians and nurses and approximately 80% of chronic patients would like to continue using them in the future[19]. The Ministry of Health has moved along this path

[15] Ibidem.
[16] IDC, https://www.idc.com/getdoc.jsp?containerId=prEUR148297521
[17] Anitec-Assinform, Una Data Strategy per la Sanità italiana.
[18] Cicchetti A., Di Brino E. (edited by) (2022). Analisi dei modelli di risposta al Covid-19 in Italia: Instant Report ALTEMS #2020-2022. Una fotografia a due anni dal primo caso in Italia, Università Cattolica del Sacro Cuore.
[19] Osservatorio sanità digitale Politecnico di Milano, maggio 2022.

with the Guidelines for the realisation of a 'Digital Model for the Implementation of Home Care'.[20].

Digitalisation has also affected an area that is essential for drug development: clinical trials. In fact, according to a survey conducted in 2021 by Farmindustria among its members, 60% of the clinical trials submitted in Italy in 2019/2020 already contained one or more digital components[21]. Decentralised Clinical Trials are an internationally known phenomenon, which takes the form of 'fully decentralised CT' or, as is more often the case, 'hybrid' decentralised CT, depending on whether all or only some of the components are conducted remotely by means of digital technologies. According to the data of Clinical Trials Arena[22] in 2019 there were approximately 600 fully or partly decentralised studies, while estimates for 2022 mention approximately 1,300 clinical trials carried out using digital technologies worldwide. This hypothesis is supported by the observation of a high number of active clinical studies referring to a decentralised/remote component and that are currently present in the clinicaltrials.gov database, amounting to approximately 2,700 studies (survey carried out in March 2022)[23].

Statistics confirm that there is an increase in the use of digital technologies to access health care and that more and more people are equipping themselves with devices to monitor and track their health. It is clear that, even in the last two years, fertile ground has developed, ready to welcome new ways of conducting clinical drug trials.

What is still missing to promote the development of this new decentralised approach? In the first instance, it is necessary to develop a vision leading to the definition of a new clinical trial model. Transforming paper into digital format is not enough: clinical trials must be re-engineered and must necessarily be:

- patient-centered;
- mostly (or entirely) carried out at home, but under telemonitoring and telecontrol by clinical and health personnel;
- fully integrated into health care processes.

This would make it possible to obtain real-time data, cover larger geographical areas, and optimise the time of physicians, data managers, patients and clinical monitors[24], who can also perform part of the Source Data Review/Source Data Verification (SDR/SDV) remotely. This would also help reducing the difficulties at the experimental centres, which often lack monitoring space and may, for this very reason, limit the number of visits.

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[20] Decree of the Ministry of Health 29 April 2022 - O.G. General Series, nr. 120 dated 24 May 2022.

[21] See chapter 9.1 of the ISTISAN Report 22/4 "Decentralised Clinical Trials and Telemedicine: A New Approach to Clinical Trials to Facilitate Patient Care and Speed Up Research" published at https://www.iss.it/web/guest/-/rapporti_istisan_22_4_it

[22] See the article published at: https://www.clinicaltrialsarena.com/analysis/2022-forecast-decentralised-trials-to-reach-new-heights-with-28-jump/

[23] See the contribution "*Decentralized Clinical Trials: esperienze ed esempi*" by Eugenio Santoro, Roberto Ascione, Mariacristina Festa, Ilaria Maruti, Elisabetta Ravot, published in AAVV "*Implementazione degli Studi Clinici Decentralizzati in Italia: perché e come?*", Tendenze nuove, numero speciale 1/2022 published by Smith Kline Foundation and Fadoim, edited by Gualberto Gussoni *http://www.passonieditore.it/doi/tendenze/2022/01NS/TendenzeNuoveNS202201.pdf*

[24] Professionals operating in the field associated with the monitoring of drug clinical trials.

One of the most important novelties introduced thanks to DCTs is the possibility for the patient to automatically or periodically transmit data to the experimenter, thanks to the support of innovative digital and technological solutions; data that could also be collected by health professionals active on the territory (e.g. general practitioners), increasingly integrating clinical trials with medical practice. The real-time collection and analysis of information also enables the professional to set up predictive and timely intervention modes, aimed at anticipating diagnoses and planning possible treatment processes.

In order to enable the development of decentralised clinical trials in Italy, which would also make it possible to enhance the patient needs and to design more efficient, agile and accessible studies, it is necessary to work on a global strategy that would make it possible to produce operational guidelines, standardise data and digital infrastructures, invest in training for research staff and for all the players involved in clinical research (including the patient), promote the recruitment of patients remotely, enhance the digitalisation of trial centres, and encourage the introduction of figures such as the 'study coordinator'.

Medical devices at the heart of the digital transition of the healthcare world

The adoption of innovative and technologically advanced medical devices has allowed, in recent years, the genesis of a vast reservoir of information and data with a variety of potentials that are still largely unexploited. At a time when medicine is becoming increasingly individualised, digital health will increasingly play such a key role that major players in the field are preparing to adopt the proper strategies to achieve its value.

In this process, the health technology industry stands as a pioneer of the innovation and optimisation of the health service. Among the advantages of data generated by digital health in the medtech sector, one of the most important is the possibility of reducing the physical barriers between the practitioner and the patient through telemedicine programmes that move the place of care from the hospital to the home, while also giving the patient and their caregivers more responsibility.

This process will allow, on the one hand, a better management of resources allocated to medical care and, on the other hand, an improvement in the quality of the treatment process. The latter can also be enhanced by the contribution that digital health can make to the world of research and home care, which, during the pandemic, favoured the development of software and apps that still allow direct contact with the patient (from oxygen therapy to the verification of adherence, to the identification of any technical and pharmaceutical issues).

6.2 THE CONTRIBUTION OF THE COMPANIES TO THE RESEARCH AND DEVELOPMENT IN ITALY

The PNRR, through Mission 4 Education and Research, is also supporting an important process in the area of research and innovation to improve the competitiveness of the system.

The prerequisites of this mission aim at strengthening the conditions for the development of a knowledge-, competitiveness- and resilience-intensive economy, starting with the critical issues that overwhelmingly affect the scientific research sector.

The M4C2 component, called 'From Research to Enterprise', benefits from funding amounting to 11.4 billion Euros: this provision of resources is aimed at supporting investment in research and development, at the promotion of innovation and at technology dissemination, and at strengthening skills.

Eleven types of aggregate investments are envisaged, according to three lines of action, the implementation of which should ensure the operation of the whole research and innovation process chain: from basic research to technology transfer, with measures characterised both by the degree of heterogeneity of the networks between universities, research centres/bodies and companies, and by the degree of technological maturity.

The first operational step of these projects was presented by the Ministry of Universities and Research in June 2022; a plan that envisages the involvement of 144 universities, research institutes and companies throughout Italy and the creation of five National Research Centres within the value chain. All of this is supported by funding amounting to 1.6 billion Euros, which must promote the projects of a research network concerning five areas identified as strategic for national development: High-performance simulation, computing and data analysis; Agritech; Development of gene therapy and drugs with RNA technology; Sustainable mobility; Biodiversity.

The network is entrusted to aggregations of universities, public and private research organisations and bodies, as well as companies located in all Italian regions, with a Hub & Spoke governance structure, in which the Hub will be in charge of management and coordination activities and the connected Spokes will be in charge of research.
A total of 55 universities and colleges have been involved to date: many of them operate in several centres with professors, researchers and doctoral students from different departments. This involvement extends to the 24 public research bodies and to other public or private research organisations, which network the different institutes all over Italy, and to a number of companies (so far a total of 65 are participating in the 5 Centres).

The infrastructures that have been created will enable the scientific community to make use of the facilities, resources and services that have been put in place in the future. Sustainability is one of the key issues in the industry, and medical gases, for example, play an important role in emission abatement, energy consumption reduction and energy storage. In particular, research is oriented towards sustainable mobility, with R&D activities focusing on the use of hydrogen as an energy carrier, the reduction of environmental impact through the development of wastewater treatment technologies, the production of green CO2 and hydrogen, the optimisation of combustion and the sustainability of value chains, also with reference to CO2 for beverages and the recycling of materials.

The contribution of the pharmaceutical industry to the development of research and innovation

In 2021, the pharmaceutical industry in Italy invested 1.7 billion Euros in R&D, accounting for 6.3% of the overall R&D investment at national level and ranking among the most R&D-intensive sectors in the country[25]. This result confirms a growing dynamic that began about a decade ago and has intensified in recent years. Pharmaceutical research in Italy has many specialisations, ranging from biotech drugs, to vaccines, to blood products, with peaks of excellence in orphan drugs and advanced treatments. Research is increasingly being developed through an Open Innovation model based on the cooperation between companies and other players, especially public ones, in the national R&D ecosystem, within a network that brings together knowledge and skills.

The pharmaceutical industry is characterised by an R&D investment/added value ratio equal to 17%, well above the average of the medium-high-tech industries (11.3%) and of the manufacturing industry (5.5%)[26]. Compared to other industries, the pharmaceutical industry also stands out for the highest share of innovative companies, approximately 90%, and the highest expenditure on innovation per employee, approximately 3 times higher than the average for the manufacturing industry, and for the highest share of companies involved in innovation partnerships with Universities and Public Research Centres[27].

The role in clinical research is especially important: in fact, the pharmaceutical industry in Italy invests more than 700 million Euros per year[28] in this area, the highest contribution to the national research system with great added value. Investing in clinical trials, in fact, means: making innovative therapies available to patients; offering opportunities for professional growth to physicians and researchers, increasing scientific competitiveness. It also means providing the National Health Service with significant resources and lower costs since companies bear all the costs associated with the studies, such as hospitalisation, drugs and diagnostic tests. Clinical trials, therefore, not only benefit patients, but also provide an economic advantage for the NHS: according to a survey carried out by ALTEMS-Università Cattolica about the value of clinical trials in our country, the 'leverage effect' for every Euro invested by the pharmaceutical industry generates an overall benefit for the NHS equal to 3 Euros, in terms of both direct expenses related to the study and indirect expenses for the supply of drugs and patient management - expenses that translate into prevented costs for the public subject.

In the scenario just outlined, the region of Lombardy stands out for its prominence. The first region in Italy for pharmaceutical presence and, as this report shows, among the most important pharmaceutical regions in Europe, Lombardy is in fact the first region where the R&D investments of drug companies in Italy are concentrated, accounting for approximately one third of the overall figure (30%)[29]. In terms of R&D personnel, Lombardy also accounts for around half (46%) of total employment in pharmaceutical research. Moreover, according to the AIFA data for the last few years, more than 50% of national clinical trials are concentrated in Lombardy, also thanks to the presence of the main

[25] Farmindustria (2022), Indicatori Farmaceutici.
[26] Ibidem.
[27] Ibidem.
[28] Ibidem.
[29] Farmindustria (2022), Indicatori Farmaceutici.

public and private Scientific Hospitalization and Treatment Institutes operating nationwide.

A focus on medical gases

The medicinal gas sector has developed research activities aimed at new products and services in both the pharmaceutical and medical device sectors. In the pharmaceuticals area, R&D activity is mostly focused on the development of new gas mixtures, among which nitrogen monoxide mixtures, used for the intensive treatment of Covid-positive patients, and 50/50 nitrous oxide-oxygen mixtures, used as analgesic and pain-relieving agents, are particularly important.

In the field of medical devices, research is especially focused on the study of new products for the dosage and administration of medical gases to be used in hospital and home environments in order to ensure the administration of gas, in particular oxygen, under conditions of absolute safety for the patient and operators. Particular attention is also paid to the exposure of health care workers to nitrous oxide and, consequently, to systems that allow the gas to be removed from the exhaled breath of the patient, thus reducing the environmental impact and ensuring the sustainability of the product.

Globally, in recent years, thanks also to scientific and technological advances, pharmaceutical R&D has shown great vitality, with the number of products in development reaching a new record in 2021 (more than 18,000[30]), and a radical paradigm shift, from one-fits-all treatments to precision medicine.

Today, the pharmaceutical industry is the first sector in the world in terms of R&D investment, both in absolute value and as a percentage of turnover, and companies will invest 1,400 billion Euros between 2021 and 2026[31]: a great opportunity for Italy, which can translate into a further increase in employment and investment, but also a great challenge with other countries and macro-areas in terms of policies and incentives to attract investment shares.

This is why a more attractive environment is urgently needed to make the innovation ecosystem stronger and more competitive as a driver for R&D investments. In addition to a country-level strategy aimed at strengthening the coordination between stakeholders in order to improve skills and the ability to work as a system, it is important to act along a few main axes: incentive tools, including those linked to the PNRR and MISE, the regulatory framework (starting with the full implementation of EU Regulation No. 536/2014 on clinical trials and the application of tax credit), support for tech transfer processes, and support for measures aimed at attracting investments for the development of new start-ups and technological innovation.

[30] Citeline (2022).
[31] Farmindustria (2022), Indicatori Farmaceutici.

The role of red biotech in the growth of the Life Sciences ecosystem

Investment in biotechnological R&D by companies active in the sector (primarily those involved in Life Sciences) grew at a rate (+7.3%) higher than the one reported in the previous two years.

With regard to total R&D investments, 88% are made by the life sciences sector (health and GPTA); this percentage rises to 90% in the case of investments made by both the total biotech R&D companies and by the nationally controlled companies.
The concentration of R&D investments in the top 3 regions (Lombardy, Lazio, Tuscany) is close to 79% of the total in 2020, with Lombardy ranking first (36%) followed by Lazio (24%) and Tuscany (approximately 19%).

The contribution of biotechnology in the collective mobilisation phase for the fight against the SARS CoV-2 coronavirus has been decisive, in particular for the gene sequencing of the virus, for the identification of the receptor responsible for the disease and for diagnostics, and also in the search for an effective treatment through antiviral drugs and the testing of new monoclonal antibodies for prophylactic and therapeutic purposes. Italian biotech companies have thus been in the forefront of the battle against the pandemic, having continued their commitment and investment in the area of infectious diseases through 2021.

In addition to Covid-19, which was found to be the second leading cause of death after cancer, the interest of national biotech research is therefore confirmed and oriented towards the development of therapeutic solutions for oncology, there was also a great deal of focus on the development of investigational products in the area of infectious diseases. This is an area that has been subject to growing interest in recent years and has seen an increase in investment by companies. The above-mentioned areas of treatment interest also include the efforts of companies engaged in the treatment of rare diseases and in the development of advanced therapies better suited to the needs and characteristics of patients.

When compared with some of the European countries most active in clinical research, Italy ranks first in 2021 (46%) for the percentage of projects dedicated to rare diseases as a percentage of total active projects, followed by Germany (39%), France (38%) and Belgium (36%).

Most start-ups are characterised essentially as specialised providers of specific skills to 'traditional' companies that instead possess the complementary assets needed to reach the market and extract value from innovations (think of clinical trials to develop drugs rather than the regulatory processes to be followed to bring a new product to market, produce it and promote it). This leads to the creation of a network of strategic alliances and collaborations resulting in a division of labour in the production chain.

Moreover, empirical evidence points to a contribution of these enterprises to the creation of new employment that is significantly greater than their weight in the total employment figures (OECD, DSTI/CIIE(2018)3/REV1, The evaluation of the Italian 'Start-up Act'). In 2020,

65% of new jobs in biotechnology are attributable to innovative start-ups, even though they account for only 6% of total biotech employment in the same year.

Medtech companies for research and innovation in health care

The creation process of a medical device, from basic research to the finished product, is highly innovative and requires significant R&D investments. Moreover, once the finished product is manufactured, companies in the sector make significant investments in pre-market and post-market clinical investigations.
In order to gather the necessary information to investigate the activities of companies in terms of technological innovation in the medical technology sector, as such data are not available in other databases at national level, since 2011 Confindustria Dispositivi Medici has been carrying out the 'Survey on Investment in Production, Research and Innovation (PRI)' of the companies in the sector in Italy.

According to the estimate of Confindustria Dispositivi medici, since 2011 investments in research and innovation, which are developed along a path from basic research to the realisation of clinical investigations, have been approximately equal to 1 billion Euros and show a slight downward trend since 2015. It is also estimated that the percentage of employees in the sector involved in research and innovation activities fluctuates around 7% since 2015. The year 2020 is an exception, being the year of the start of the Covid-19 pandemic, as it was characterised by a very peculiar dynamic, with a sharp drop in the amount invested in pre-market and post-market clinical investigations. In the areas most affected by the epidemic, in fact, there have been numerous discontinuations of normal clinical trials, greater difficulty in starting new projects, and the enrolment of new patients in the ongoing studies has stalled. This situation has led to a contraction of the investments in research and innovation during 2020. The latest survey by Confindustria Dispositivi Medici concerning the investments in research and innovation in 2021, however, estimated a clear recovery, potentially due to companies in the sector carrying out in 2021 the investments they postponed in 2020.

In this context, the region of Lombardy emerges as one of the pillars of research and innovation in the Italian health technology sector. Since 2015, investment in research and innovation by the companies based in Lombardy has accounted for more than 30% of the overall investment in research and innovation by companies based in Italy. These investments are well distributed among the sectors of the medical device industry. In addition, the region of Lombardy is home to a number of technology parks and districts that aim at promoting interaction between the research system, the industrial fabric and public institutions in the health sector, in order to boost research and innovation in Italy. These include the Lombardy Life Sciences Cluster, the National Life Sciences Technological Cluster - ALISEI and the Milan Innovation District - MIND.

6.3 NATIONAL AND GLOBAL CHALLENGES FOR THE INDUSTRY: A FOCUS ON VALUE CHAINS

Foreword: global challenges for companies in the industry

The Covid emergency and recent current events, such as the Russia-Ukraine conflict, have highlighted the vulnerability of the European pharmaceutical value chain - more than 74% dependent on supplies of starting materials and intermediates from Asia - as well as the medical value chain, as evidenced by shortages of devices, which have been felt throughout Europe.

Our country, however, is able to produce more than 70% of all currently existing active substances, guaranteeing the supply of most medicinal products. As proof of the production capacity of the national value chain, Italy is home to more than 100 production plants in the chemical-pharmaceutical industry, more than half of which are located in Lombardy. However, raw material and energy costs represent a major challenge for the industry, and today the country is called upon to work on a system-wide level on such issues.

Digital innovation, which is affecting healthcare, pharmaceuticals and medical devices, represents an additional challenge for national production chains. In these sectors, and particularly in the drug industry, the value chain is strongly affected by external and international factors: transport chain, material planning, production and stock management. Here, digitalisation offers great opportunities for process optimisation, supporting a production chain that increasingly requires efficiency through the automation of the internal and external information flows (including digital logistics, which is essential to have structured and consistent data management across the whole logistics chain).

A further challenge on which the sector is working intensively is that of environmental sustainability, an issue on which the PNRR also allocates a large part of its resources, through Mission 2 'Green Revolution and Ecological Transition'. Looking at the manufacturing sector, with particular reference to manufacturers of active pharmaceutical ingredients (APIs), there has been a strong push towards green chemistry since the 1990s, which has subsequently become increasingly important. The increased use of synthetic processes based on flow chemistry, biocatalysis and mechano-chemistry is an important step towards greater sustainability, allowing companies to consume as little water and energy as possible throughout the whole production process and to minimise emissions of carbon dioxide and volatile organic compounds into the atmosphere.

Global value chains in pharmaceutical production and current challenges

With more than 34 billion Euros in production value, 85% of which is exported, today Italy is one of the leading pharmaceutical poles in the world and among the top players in the EU, with various production specialisations - biotech, vaccines, plasma-derived products,

advanced treatments and orphan drugs, CDMOs to name just a few of them[32]. This is the result of the huge investments of the last decade, which is also evident in the increase in the innovative content of exported products: from 2016 to 2021, the average value of exported drugs grew by 52%, more than the EU overall figure (+35%)[33].

With a significant presence of foreign-capitalised companies (58% of the total) and Italian-capitalised, strongly internationalised, companies (42%), the pharmaceutical industry in Italy is an industry that operates on a global scale, with articulated procurement chains. The industry, which is mostly concentrated in Lombardy with more than 30% of the Italian local units[34], was already affected before the pandemic by profound transformation and reorganisation processes linked to a new innovation stage, which after Covid-19 experienced a further acceleration, setting in motion attraction policies and localisation choices of investments worldwide, with a view to countering future exogenous shocks.

The European Commission, driven by the evidence that emerged during the pandemic, recognised the strategic value of the sector for health, safety and economic growth and proposed a new Pharmaceutical Strategy for Europe in 2020, with the aim of increasing the autonomy and competitiveness of the pharmaceutical sector on the continent. In particular, one axis of the strategy is aimed at strengthening the value chains, specifically as regards active ingredients and intermediates, for which the EU is highly dependent on countries such as China and India (more than 70% of the total amount of active ingredients and intermediates with the highest consumption comes, directly or indirectly, from these countries[35]).

The outbreak of the Russian-Ukrainian conflict has also contributed to the worsening of the post-pandemic scenario in terms of rising costs of raw materials and intermediate goods, of bottlenecks and supply difficulties, exacerbating tensions in the value chain.

Gas and energy costs for pharmaceutical companies in Italy have risen by up to +500% in fifteen months, accompanied by increases in all production inputs approximately equal to 50%[36]. These are very significant cost increases that the companies cannot pass on to the prices of reimbursable drugs, which are negotiated and regulated (and, in the last year, have even dropped by 1%). The result is heavy pressure on company margins, with a negative effect on the competitiveness of the industry, aggravated by the fact that - as shown by Confindustria data - the impact in other competitor countries is lower (especially in France, but also in Germany) due to lower energy costs.
The anticipatory indicators of companies point to continued tensions in the supply of production inputs in the coming months. In comparison to early 2022, there are more cases of shortages already detected and of companies indicating a short-term risk.

At the international level, the strategic nature of the pharmaceutical value chain and its strengthening were also reaffirmed at a recent meeting of the Trade and Technology

[32] Farmindustria (2022), Indicatori Farmaceutici.
[33] Ibidem.
[34] According to Assosalute, almost 50% of the companies producing or marketing over-the-counter drugs in Italy are located in Lombardy alone.
[35] Source: Efpia, IQVIA.
[36] Farmindustria (2022), Indicatori Farmaceutici.

Council[37], the top-level transatlantic consultation forum. Together with the other Life Sciences sectors, the pharmaceutical industry can contribute to the recovery and autonomy of the EU: health, in fact, is a European specialisation - compared to the world, Europe is worth 7% of the population, 25% of GDP and 50% of welfare.

In recent years, as well as in 2022, the pharmaceutical industry has contributed significantly to the growth of Italy, in terms of exports, added value and employment. And do not forget the positive externalities in terms of ancillary industries. Competition at the global level, however, is increasingly fierce and the game is also played with attractiveness policies both among macro-areas (Europe, USA, Asia) and among the European countries. France and Germany, for instance, are quickly implementing strong public policies and Spain, the UK and other European countries are doing the same.

That is why it is necessary to relaunch growth by making the country more attractive to investments, with new industrial policies, adequate resources, simple rules, and faster processes for the evaluation of new products and authorising production.

For example, the European State Aid system is essential in order to have suitable incentive instruments suitable for all territories and for all companies. It is not possible to 'play by ear' with temporary and limited derogations: here, structural action is required. When the tools are appropriate, the industry is there with projects that can be quickly implemented and with investment capacity.

It is a situation that must also be countered through sustainable expenditure management for companies and rapid authorisation processes to avoid drug shortages. And it is essential that the decision-making processes at EU level, and in particular the various initiatives envisaged by the Pharmaceutical Strategy - which will have very significant effects on Intellectual Property, access and the regulatory environment - are compatible with the need to attract investment, i.e. to retain and increase the competitiveness of the National System.

Even with regard to the combination of health and hi-tech, Europe must not become weaker than the USA and Asia. It can, and indeed must, play a strategic role in analysing the data of 500 million citizens who make use of the highest quality health care services in structured public health care systems every day.

The main trends in the value chains of the medical device industry

Medical technologies are characterised by certain peculiarities that make their value chain specific. Firstly, this is a strictly regulated sector: each device must comply with many complex safety standards, specifically designed to guarantee the health of patients. Secondly, in most cases medical devices are purchased by subjects (public or private) that can be traced back to the health service and, therefore, purchasing is done through public tender systems. These procedures aim at ensuring the continuous supply of necessary of the medical devices required by patients.

[37] Source: European Commission (2022); available at the following link: https://ec.europa.eu/commission/presscorner/detail/en/ip_22_3034

From this perspective, it is possible to conclude that, in the health technology value chain, the greatest value lies in two stages: on the one hand, R&D and regulatory compliance activities and, on the other hand, the sale and implementation of services associated with the product. With this in mind, most of the decisions concerning the design and sales process are made at company headquarters and are then forwarded to the production plants, which nowadays are spread all over the world.

With the advent of globalisation, the decision-making centres of companies are mainly located in the most economically advanced countries while, in recent years, the process of offshoring of production activity has intensified, especially towards countries with lower production costs.

7

Methodological Appendix

The valorisation of the Life Sciences value chain has 2020 as its time horizon, the last year for which the data required for analysis are available with a sufficient degree of systematicity. On the other hand, the value chain provides up-to-date figures for 2019 as regards the number of people employed in industry and trade. Where possible, first elaborations on 2021 data are included.

The analysis is based on a combination of information sources. As regards the national comparison, the analysis is carried out on the data of the Conti Nazionali-ISTAT (for the valorisation of the health care services sector - production value, added value, employees - and for the macroeconomic reference data), of the Archivio Statistico delle Imprese Attive (ASIA)-ISTAT (for the computation of industry and trade employees), of the AIDA-Bureau van Dijk database (for the analysis of the economic variables of industry and trade enterprises). The list of enterprises in each sector was selected on the basis of the ATECO codes of activity and in some cases was provided by the Trade Associations. Specifically, for a sample of large enterprises/multinationals, it was agreed to consider as industries those enterprises that have their own products on the market, and as traders those enterprises that do not have their own products but sell them. As regards the European comparison, the analysis is carried out on the data of the National and Regional Accounts

- Eurostat (for the valorisation of the economic variables of the health services and the number of employees employed in both the health care and the pharmaceutical industry) and the ORBIS-Bureau van Dijk database (for the analysis of the economic indicators of the pharmaceutical industry).

Detailed methodological information is provided below.

Methodological information for the calculation of the Life Sciences value chain at national level

Conti nazionali - ISTAT

The territorial economic accounts and aggregates of the Conti Nazionali ISTAT provide, for each regional context, only the added value per macro-branch of activity, without providing the production value figure. Moreover, the figure for health care services is not separated from that for social assistance. The following hypotheses and estimates were therefore required to reconstruct the added value and the production value of the health care services at local level:
In order to calculate the value added of health care services alone, starting from the available added value data for health and social care services, the value added rate of health care services as a percentage of the total found at national level for health and social care, i.e. 84.4% in 2020, was applied to all regional contexts. It was therefore necessary to assume that in all analysed regional contexts, the contribution to the generation of added value was equally divided between health and social care. Once the added value for health care services was calculated at the regional level, the production value was derived by assuming that the share of added value in the production at the local level was constant in all regions and equal to the national share in 2019 (56.7%).
A similar assumption was made for the calculation of health service employment: the Conti Nazionali ISTAT provide, at territorial level, total employment data for the health care and social services sector. For the calculation of employees at the territorial level in the area of health care alone, the incidence rate of employees in health care as a percentage of the total (health care plus social work) recorded at the national level in the year 2020, i.e. 72.2%, was applied to all the regional reference contexts.
For the purpose of calculating just the production value for health care in the year 2020, a further assumption was made based on the relationship between production value and the sum of public and private current health care expenditure from the Conti Nazionali ISTAT, applying the ratio between the two quantities, which was stable and equal to 1.1 in the ten years prior to 2019.

ASIA - ISTAT

The ASIA statistics of ISTAT concerning the employees of local units do not allow in some cases to accurately identify the branches of the Life Sciences chain as identified in this project because no six-digit disaggregation is available. As a consequence, in these cases, it was necessary to resort to the representation of a reality broader than the identified value chain life.
Specifically, these are the cases where a broader reality was used:
The Ateco segment 20.11 also includes the production of industrial gases not intended for medical use;

The Ateco segment 26.6 includes the sub-segments 26.60.02 *(manufacturing of electromedical apparatus (including detached parts and accessories))* and 26.60.09 *(manufacturing of other irradiation and electrotherapeutic equipment)* belonging to the life science value chain, but also includes the sub-segment 26.60.01 *(manufacturing of irradiation equipment for food and milk)* which cannot be attributed to this value chain.

The Ateco 72.11 segment also includes research in the field of green and white, as well as red, biotechnologies, which are not part of the life science value chain.

The Ateco segment 33.13 includes the sub-segment 33.13.03 *(repair and maintenance of electromedical, medical, surgical and veterinary equipment, dental appliances and instruments)* belonging to the life science value chain, but also includes the sub-segments 33.13.01 *(repair and maintenance of optical, photographic and cinematographic equipment (excluding video cameras))*, 33. 13.04 *(repair and maintenance of distillation apparatus for laboratories, centrifuges for laboratories and ultrasonic cleaning apparatus for laboratories)* and 33.13.09 *(repair and maintenance of other electronic equipment (excluding telecommunications and computers))* which cannot be attributed to this value chain.

AIDA - Bureau van Dijk

The query was set up on AIDA by providing the following criteria:

- inclusion of active companies only;
- exclusion of companies with consolidated balance sheets;
- exclusion of companies with negative added value;
- Attribution of the company to a region based on the address of its head office.

Methodological information for the calculation of the satellite industries of the Life Sciences value chain

As regards the requirement coefficients for internally sourced inputs, estimates prepared by the Comitato Tecnico Sanità Confindustria (2011) were used:

- pharmaceutical industry 1.654
- medical device industry 2.020
- wholesale trade 1.899
- retail trade 1.802
- health care services 1.709

The weighted average coefficient for the production values of the individual sectors was thus equal to 1.734.

To calculate the value added of the sattelite industries, the ratio between added value and production recorded on average in the Italian economy in 2019 (47.4%) and 2020 (48.7%) was used. This is a conservative assumption that assumes a constant generation of added value in all the sectors of the economy.

Methodological information for the calculation of the main economic aggregates of the health care services and of the pharmaceutical industry at European level

European System of National and Regional Accounts (Eurostat)

The territorial economic accounts and aggregates of the National and Regional Accounts of Eurostat provide, for each regional context, only the added value per macro-branch of activity. The figure for health services is therefore included in the macro-branch for public administration, which includes defence, compulsory social insurance, education, health and social welfare. The following hypotheses and estimates were therefore required to reconstruct the added value of the health care services at local level:

For Baden-Wurttemberg, Cataluña and Île-de-France, the added value of regional health care was calculated on the basis of how much health care impacts the added value of the public sector at national level;

For Lombardy, however, the aggregate figure for health and social care is available, and the national coefficient for the added value of health care services in relation to the national total for health and social care, i.e. 84.4% for 2020, has been applied to it.

ORBIS - Bureau van Dijk

The query for the calculation of the economic aggregates of the pharmaceutical industry was set up in ORBIS with the following criteria:

- Inclusion of active companies only;
- Exclusion of companies with consolidated balance sheets;
- Exclusion of companies with negative value added;
- Attribution of the company to a region based on the address of its head office.

For the valuation of the value added, if the 2020 figure is missing and only the 2019 figure is available, the 2019 figure is retained, but it is adjusted for the observed % change for companies reporting both years as available.

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