ASSOLOMBARDA
Confindustria Milano, Monza e Brianza, Lodi

The importance of the Life Sciences value chain in Lombardia: a comparison between Italian and European Regions

2018 Edition

REPORT NO. 07/2018

Prepared by
Area Centro Studi, Settore Organizzazione Sviluppo e Rapporti Associativi

In cooperation with

The Federchimica Associations involved were

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Contents

1. Introduction

Preamble

The works that let the creation of the life sciences value chain in Lombardia Report began in 2017, leading to a document that has become a support instrument for Assolombarda, in particular, for the definition of the strategic guidelines for projects and activities referring to the life sciences area. Its importance also stems from the innovative methodological approach with the involvement of the life sciences Trade Associations in the analysis and drafting of the final document, which considered an overview of the life sciences system by moving beyond the fragmentation of data and information for the individual sectors that make up the system.
Moreover, the importance of the life sciences sector in the Lombardia region also made it necessary to analyse and constantly monitor the value generated by the value chain, through the use of an analysis and monitoring system that could provide a snapshot of this "ecosystem" on a year by year basis. In Within this perspective, the Report comes in 2018 to its second edition, strategically integrating itself within the perimeter of the “Life Sciences Hub” project, that was created due to the definition of a Deputy Chairmanship on Research, Open Innovation, Life Sciences, EMA and Technopole of Ms Elena Zambon, Chair of the Zambon Group.
Indeed, the strategic project wants to develop ventures and advocacy activities in synergy with national trade associations, making Assolombarda the regional linchpin for national policies within the life sciences segments. The project aims to develop through six strategic guidelines:

- promote the visibility of the value chain at a national and international level
- add value to the scientific and industrial excellences in the life sciences sector, while highlighting the distinctive characteristics of the Lombardia Region
- develop suitable international managerial skills and profiles for facilitating the recruitment of talent
- develop a community in the life sciences sector, while also facilitating the sharing of knowledge and experience between companies and research centres
- promote, in cooperation with the Lombardia Life Sciences Cluster, a dialogue between companies and research centres, while promoting the research and innovation capacity of the entire public and private ecosystem
- promote the visibility of the sector at a national and international level, including through high profile international events

Therefore, a document shared by all the operators of the system, which successfully captures the value of the life sciences value chain in Lombardia, becomes an instrument of major strategic importance to support the concrete actions of Assolombarda in the life sciences sector.

Objectives

The objective of This report is to promote and analyse the entire life sciences value chain in economic terms on an annual basis, moving down from the production of pharmaceutical intermediates and active ingredients, drugs, medical devices, gases for medical use and from biotech research services upstream, including the various intermediation phases, to healthcare services downstream.
The analysis defines the value chain both at the national and regional levels with a focus on Lombardia and other Italian benchmark regions - i.e. Emilia-Romagna, Lazio, Piemonte, Toscana and Veneto - identified as such because comparable to Lombardia in social and economic terms.
The document also aims at comparing Lombardia with selected benchmark regions in Europe - i.e. Baden-Württemberg, Cataluña and Île de France - which show similar economic structures, play a highly significant role in their national economies and, above all, they are the most developed areas in Europe in life sciences along with Lombardia. The European comparison is conducted with regard to two major segments of the life sciences value chain, the pharmaceutical industry and the healthcare services, with an additional focus on scientific research.
The project is the result of a working group involving Assolombarda, AIOP, Assobiomedica, Lombardy Life Sciences Cluster, Farmindustria and the Federchimica Associations (Aispec, Aschimfarma, Assobiotec, Assogastecnici and Assosalute), with the scientific support of CERGAS-SDA Bocconi.

Credits

The report was written by: Stefania Saini and Felice Lopane (Assolombarda). We would also thank Alberto Ricci and Francesco Petracca (CERGAS Bocconi) for their scientific support.
Furthermore, special thanks to the following contributors: Angelo Cassoni from AIOP, Paolo Gazzaniga and Sara Carbone from Assobiomedica, Carlo Riccini and Riccardo Pareschi from Farmindustria, Juliette Vitaloni from Federchimica, Leonardo Vingiani and Rita Fucci from Assobiotec, Vera Codazzi from Lombardy Life Sciences Cluster, Cristian Ferraris and Valeria Negri from Assolombarda.

2. Main results: life sciences by figures

- In Italy the life sciences value chain reported a value of production of more than 207 billion Euro in 2016, a value added of 95.5 billion and a workforce of more than 1.7 million people.
- Lombardia is the Italian most developed region with a value of production of 63.4 billion Euro, a value added of more than 23.5 billion and a workforce of 347 thousand. Lombardia region respectively represents a share of 31%, 25% and 20% of the previous national figures, while it represents 16% of the total Italian population.
- Considering both the direct contribution and the satellite activities, in Italy the value added of the life sciences value chain makes up 10.0% of Italian GDP, while in Lombardia it accounts for 12.4% of the regional GDP, with an overall value of 45.8 billion Euro (2.7% of national GDP). This demonstrates that the health-related sectors represent a key specialisation component for Lombardia's economy.
- In Europe, Lombardia is amongst the leading pharmaceutical regions alongside Cataluña, Baden-Württemberg and Île de France: in particular, it generates a per capita value added which exceeds its benchmarks (537 Euro per inhabitant) and the incidence of the sector value added on the total regional one is the highest (2.2%) after Cataluña (2.5%). With regard to the healthcare services segment, Lombardia is affected by lower healthcare intensity than in the other regions being considered; nevertheless, the incidence of the healthcare sector value added on the regional total (4.3%) is in line with the benchmarks and, above all, Lombardia is characterised by an extremely virtuous performance considering hospitals, with lower inappropriate hospitalisation rates (for chronic illnesses such as asthma, hypertension and diabetes) than in the benchmark regions (137 units every 100 thousand inhabitants).
- In the European comparison, the scientific density in Lombardia, measured in terms of life sciences scientific articles per million inhabitants, is in line with the levels in Cataluña (627 and 606 articles respectively) but is lower than in Baden-Württemberg (731 articles) and significantly lower than Île de France (which has almost 1,400 articles). Regional figures are more homogeneous in terms of research "quality": 2.2% is the share of highly cited articles in the total scientific production in Lombardia (compared to 3.1% for the top performer Baden-Württemberg).

3. Scope of analysis

Box 1 illustrates in detail the life sciences value chain, and identifies the segments that make it up:

- the industrial value chain (pharmaceutical intermediates and active ingredients, drugs, medical devices and biotech research services, and starting from this edition, also the manufacturing of industrial gases for medical use segment);
- commercial activities (wholesale and retail sale of pharmaceutical products and medical devices and healthcare items);
- healthcare services and social care services with a prevalence of the healthcare component.

The business areas of each segment are detailed with indication of the respective NACE codes.

The European comparison focuses on the segments "Manufacturing of basic pharmaceutical products and pharmaceutical preparations" and "Healthcare services".

Box 1 - Sectoral composition of the life sciences value chain

Sector	NACE 2007 Code
INDUSTRY	
MANUFACTURE OF INDUSTRIAL GASES	**20.11**
MANUFACTURE OF BASIC PHARMACEUTICAL PRODUCTS AND PHARMACEUTICAL PREPARATIONS	**21**
of which: Manufacture of basic pharmaceutical products	21.1
of which: Manufacture of pharmaceutical preparations	21.2
MANUFACTURE OF IRRADIATION, ELECTROMEDICAL AND ELECTROTHERAPEUTIC EQUIPMENT	**26.6**
of which: Manufacture of electromedical equipment (including detached parts and accessories)	26.60.02
of which: Manufacture of other irradiation and electrotherapeutic equipment	26.60.09
MANUFACTURE OF MEDICAL AND DENTAL INSTRUMENTS AND SUPPLIES	**32.5**
of which: Manufacture of furniture for medical use, medical equipment, medical and surgical and veterinary material, equipment and instruments for dentistry	32.50.1
of which: Manufacture of dental prostheses (including repairs)	32.50.2
of which: Manufacture of orthopaedic prostheses, other prostheses and supports (including repairs)	32.50.3
of which: Manufacture of ophthalmic lenses	32.50.4
of which: Manufacture of frames for spectacles of all types; serial manufacturing of spectacles	32.50.5
REPAIR OF ELECTRONIC AND OPTICAL EQUIPMENT	**33.13**

of which: Repair and maintenance of electromedical equipment, medical and surgical and veterinary material, equipment and instruments for dentistry	33.13.03
RESEARCH AND EXPERIMENTAL DEVELOPMENT ON BIOTECHNOLOGY	**72.11**
SALES	
AGENTS SPECIALISED IN THE SALE OF OTHER PARTICULAR PRODUCTS	**46.18**
of which: Agents specialized in the sale of pharmaceutical products and cosmetics	46.18.3
WHOLESALE OF PHARMACEUTICAL GOODS	**46.46**
DISPENSING CHEMIST IN SPECIALISED STORES	**47.73**
RETAIL SALE OF MEDICAL AND ORTHOPAEDIC GOODS IN SPECIALISED STORES	**47.74**
HEALTHCARE SERVICES AND THERMAL FACILITIES	
HUMAN HEALTH ACTIVITIES	**86**
of which: Hospital activities	86.1
of which: Medical and dental practice activities	86.2
of which: Other human health activities	86.9
RESIDENTIAL CARE ACTIVITIES	**87**
of which: Residential nursing care activities	87.1
of which: Residential care activities for mental retardation, mental health and substance abuse	87.2
of which: Residential care activities for the elderly and disabled	87.3
of which: Other residential care activities	87.9
PHYSICAL WELL-BEING ACTIVITIES	**96.04**
of which: Spas	96.04.2

4. Methodology

The assessment of the life sciences value chain:

- is drawn on 2016 data, as these are the latest available and enough systematic data useful for the analysis. Data about the workforce and the healthcare services segment are updated to 2015.

- considers the following economic aggregates: employment[1], value of production[2] (the sum between the value of the goods produced and the services supplied to citizens by all segments of the value chain), value added[3] (measures the increase in value deriving from production factors compared to the goods and resources that were initially available).

- is based on a mix of information sources. With regard to the national comparison, the analysis is conducted on data from the National accounts/ISTAT (for the calculation of the healthcare services segment - value of production, value-added, workforce - and for the key macroeconomic data), the statistical archive of active enterprises (ASIA)-ISTAT (for the calculation of people employed in the industry and the sales workforce), the AIDA-Bureau van Dijk database of the financial statements of more than 500,000 Italian companies (for the analysis of the economic dimensions of companies in the industry and the sales segment). The list of companies for each segment was selected based on the NACE business codes and in certain cases was provided by the trade associations. The analysis through the AIDA database has certain limitations as it was not possible to classify certain companies in an unambiguous manner within the segments of the value chain since they carry out a range of activities. With regard to the European comparison, the analysis was carried out using data from the national and regional accounts - Eurostat (for the quantification of healthcare services in economic terms and of the number of workers employed in the healthcare sector and in the pharmaceutical industry) and the ORBIS-Bureau van Dijk database (for an analysis of the indicators of the pharmaceutical industry).

For more information on the methodology used please refer to Box 2 and Box 3 in Appendix I and Box 4 in Appendix II.

[1] Employed individuals are defined as employees and self-employed workers providing full or part time work to the company. The data analysed calculate the individual headcount, net of any duplications due to the simultaneous use of a single worker in more than one segment.
[2] Value of production and value added are calculated at current prices.

5. The value of the life sciences value chain: national benchmarks

The life sciences value chain

Table 1 shows the measures of the main aggregates of the life sciences value chain at a national level and in the main Italian regions.

Table 1 - Life sciences value chain: main economic aggregates for Italy, Lombardia and national benchmark regions (2016)

	Resident population	Value of production (thousand €)	Value added (thousand €)	Workforce (2015)
Italy	60,665,551	207,532,396	95,597,792	1,745,172
Lombardia	**10,008,349**	**63,411,692**	**23,510,181**	**347,380**
Emilia-Romagna	4,448,146	15,340,308	7,678,598	146,699
Lazio	5,888,472	26,837,462	11,201,568	190,399
Piemonte	4,404,246	12,160,138	6,543,688	127,619
Toscana	3,744,398	14,513,041	6,603,383	114,340
Veneto	4,915,123	14,013,771	7,193,184	151,089

Source: based on ISTAT, AIDA data

In Italy the value of production of the entire life sciences value chain amounted to more than 207 billion euro in 2016, +4.7% compared to 2014[3], with a value added which also increased up to 95.5 billion euro (+2.7%), whose incidence on the national figure stayed stable at 46.1%. There were more than 1.7 million people employed in 2015, with an increase of 16 thousand units compared to 2014.

In the comparison with national benchmarks, Lombardia again proves to be the region with the most developed life sciences value chain in economic terms, with a total value of production of 63.4 billion euro and a value added of more than 23.5 billion: data highlight a very significant growth in the last two-year period, at a much faster rate than what observed at a national level (+13.7% vs +4.7% referring to the value of production; +13.4% vs +2.7% referring to the value added)[4].

[3] Assolombarda Confindustria Milan Monza and Brianza, *La rilevanza della filiera Life science in Lombardia: benchmarking tra regioni italiane ed europee*, 2017 edition.

[4] This positive difference compared to the national figure is only partially attributable to the addition of the industrial gases manufacturing segment, which is worth 2.1 billion in terms of value of production and 700 million in terms of value added, which for more than 90% is concentrated in Lombardy.
Indeed, industrial gases only account for approximately 25% of the increase in the value of production and value added registered in Lombardy for the period 2014-2016.

In Lombardia, where approximately one sixth of the national population resides (16.5%), we find 19.9% of the workforce, 24.6% of the value added and 30.6% of the Italian value chain. These findings confirm Lombardia's specialisation on life sciences. The other benchmark regions have an incidence on national totals which essentially reflect the distribution of the population (Table 2).

Table 2 - Life sciences value chain: incidence on Italian total of the main economic indicators for Lombardia and the national benchmark regions (2016)

	Resident population	Value of production	Value added	Workforce
Lombardia	**16.5%**	**30.6%**	**24.6%**	**19.9%**
Emilia-Romagna	7.3%	7.4%	8.0%	8.4%
Lazio	9.7%	12.9%	11.7%	10.9%
Piemonte	7.3%	5.9%	6.8%	7.3%
Toscana	6.2%	7.0%	6.9%	6.6%
Veneto	8.1%	6.8%	7.5%	8.7%

Source: based on ISTAT, AIDA data

Looking at the individual segments of the value chain, at the national level healthcare services show the most significant contribution to the value of production (61.4%), value added (80.1%) and workforce (79.3%).

The calculation of the economic dimensions covered by the analysis for the healthcare sector is shown in Table 3.

Table 3- Healthcare services focus: main economic dimensions for Italy, Lombardia and national benchmark regions (2015)

	Value of production (thousand €)	Value added (thousand €)	Share on Italian value added in %	Workforce
Italy	127,364,700	76,586,200	100.0%	1,383,400
Lombardia	**23,306,291**	**14,014,403**	**18.3%**	**250,166**
Emilia-Romagna	10,709,543	6,439,800	8.4%	116,111
Lazio	13,382,136	8,046,868	10.5%	144,583
Piemonte	9,878,424	5,940,036	7.8%	107,510
Toscana	8,162,641	4,908,312	6.4%	88,974
Veneto	9,956,536	5,987,006	7.8%	108,252

Source: based on ISTAT data

Healthcare services (including public and private hospital activities, specialist and outpatient services, social healthcare services with the prevalence of the socio-medical component) generated in 2015 a value of production of more than 127 billion euro (+4,4% compared to 2014) and a value added of 76.6 billion euro (+2.1%). The total workforce is almost 1.4 million, which is essentially the same as in 2014, despite the reduction in 2014-2016 in the number of national healthcare service workers by approximately 15 thousand units (from 663 to 648 thousand)[5]. To the total number of public employees, one must add approximately 55

[5] Ministry of Economics and Finance -General State Accounting Office, 2015 Annual accounts.

thousand units of accredited staff (freely chosen GPs and paediatricians)[6] who are also directly connected to the National Healthcare service. Private hospitals employ approximately 120 thousand professionals and the remaining 600 thousand people employed in healthcare services work in daycare, medical laboratories and dentistry practices, or they operate in residential and domiciliary social healthcare services.

The distribution of the value added in healthcare services amongst the various regions closely reflects the demographic distribution: Lombardia, where 16.5% of the national population resides, generates 17.8% of the overall value added of healthcare services. The significant public involvement and the necessary granularity of healthcare and social care services ensure indeed a fair distribution of production and the resulting value added.

Alongside healthcare services, which generate 14 billion of value added, in Lombardia commercial activities and industry together generate another 9 billion Euro, with the industrial value chain - comprising a varied series of sectors, from pharmaceutical intermediates and active ingredients, to drugs, to medical devices, to biotech, to industrial gases for medical use - accounting for the largest share. In particular, at the industrial level pharmaceuticals represent the most significant segment in terms of value of production, value added and workforce (Table 4).

Table 4 - Pharmaceutical industry in focus: main economic aggregates for Italy, Lombardia and national benchmark regions (2016)

	Value of production (thousand €)	Value added (thousand €)	share of Italian value added in %	Workforce
Italy	30,698,517	9,352,277	100.0%	57,573[7]
Lombardia	**14,881,415**	**4,348,902**	**46.5%**	**25,812**
Emilia-Romagna	1,465,137	557,095	6.0%	3,795
Lazio	8,370,861	2,225,423	23.8%	12,439
Piemonte	701,147	270,027	2.9%	1,759
Toscana	3,322,391	1,191,438	12.7%	6,882
Veneto	1,137,463	469,978	5.0%	3,586

Source: based on ISTAT, AIDA data

In Italy in 2016, the pharmaceutical industry reported a value added of 9.4 billion euro, with a significant increase compared to the level of 8.3 billion achieved in 2014 (+12.8%) while the value of production increased from 28.1 to 30.7 billion (+9.1%).

The data for Lombardia highlight how consolidated the sector is, with a value of production of 14.9 billion euro (from 13.6 in 2014, +9.6%), a value added of 4.3 billion (from 3.8 in 2014, +13.0%), and a 29% share of the value of production.

Almost half the economic values for Italy (48% of value production and 47% of value added) and the workforce (45%) is in Lombardia, a demonstration of the significance of the pharmaceutical industry in the region.

[6] 2015 Statistical Yearbook for the National Healthcare System.
[7] The difference with the figure by Farmindustria, which amounts to 64 thousand workers, derives from an ad hoc calculation made using ISTAT data.

The ancillaries of the life sciences value chain

The next step of the analysis is the appraisal of the value chain's ancillary activities, to quantify the positive externalities and indirect economic impact generated through the spillovers on other sectors of the economy. The methodological choices and assumptions made are shown in Box 3 in Appendix I.

The results of this calculation are presented in Table 5 which, in addition to the value added of the value chain reported above as well, shows the value added including the ancillaries and their incidence on the regional and national GDP.

Table 5 - Life sciences value chain: value added and value added including the ancillaries for Italy, Lombardia and national benchmark regions (2016)

	Value added value chain (thousand €)	Value added ancillaries (thousand €)	Value added value chain + ancillaries (thousand €)	GDP (thousand €)	value added (value chain + ancillaries) as a % of the GDP
Italy	95,597,792	73,157,429	168,755,221	1,680,948,100	10.0% *(of national GDP)*
Lombardia	**23,510,181**	**22,353,312**	**45,863,493**	**368,582,400**	**12.4%**
Emilia-Romagna	7,678,598	5,407,626	13,086,224	153,927,100	8.5%
Lazio	11,201,568	9,460,498	20,662,066	186,483,200	11.1%
Piemonte	6,543,688	4,286,581	10,830,269	129,698,500	8.4%
Toscana	6,603,383	5,116,005	11,719,388	112,454,800	10.4%
Veneto	7,193,184	4,940,007	12,133,191	155,837,400	7.8%

Source: based on ISTAT, AIDA data

In Italy the value added of the ancillaries was 73.1 billion euro in 2016, equal to 76.5% of the direct value added. The total value added, 168.8 billion euro, corresponds to 10%[8] of the national GDP. This value is stable if compared to 2014 one, which highlights a similar growth trend for the value added (including ancillaries) and the national GDP over the period.

However, in Lombardia in 2016 the life sciences direct and indirect contribution to the regional economy increased by more than 1p.p. compared to 2014, to 12.4% of regional GDP (and 2.7% of national GDP) with an overall value added of more than 45.8 billion euro. Life sciences contribution to the economy in Lombardia is higher than both the national average and the benchmark regions figure, where the incidence varies from 7.8% in Veneto to 11.1% in Lazio. This is a further proof of the importance of the health-related sectors in terms of Lombardia's economic specialisation.

[8] Confindustria calculates a value of 10.7% in 2015 (see the 2018 report on the health supply chain, "Filiera della salute - Rapporto annuale 2018"). Please note that this study is based on a methodology and on data sources that are sometimes different from those used by Confindustria to enable a significant analysis at the regional level, nevertheless the conclusions are similar.

6. The pharmaceutical industry, healthcare services and research in life sciences: European benchmark

The analysis of the life sciences value chain was also conducted at an international level, by comparing Lombardia with Baden-Württemberg, Cataluña and Île-de-France which are the most advanced European regions in the life sciences field. Regions were selected based on the following considerations: since the number of workers involved in healthcare and social services is directly correlated with the regional service catchment area, the analysis focus was on the pharmaceutical industry, identifying in each of the most developed countries in this sector (France, Germany and Spain) the territory with the highest share of persons employed with respect to the European total. The benchmark regions[9] have a population which ranges from 7.4 million inhabitants in Cataluña to 12.1 in Île de France (10.0 Lombardia, 12.1 Baden-Württemberg) and are of great importance to the economy of their countries (with shares of generated national value added ranging between 15% and 22%, up to 30% in Île de France which also includes the capital Paris and which therefore has a significant concentration of economic activities given the proximity with institutional headquarters).

Table 6 - European comparison: territorial focus

	Lombardia	Baden-Württemberg	Cataluña	Île de France
Population (million, 2016)	10.0	10.9	7.4	12.1
Value added (million €, 2015)	323,012	414,241	186,480	597,386
Share of regional value added as a % of national total	21.8%	15.2%	19.0%	30.4%

Source: Eurostat

The international comparison focuses on two segments, healthcare services and pharmaceutical industry - which have a more significant contribution to the overall

[9] Based on the Eurostat NUTS classification, code ITC4 identifies Lombardia, code DE1 Baden-Württemberg, code DE2 Bayern, code ES51 Cataluña, code FR10 Île de France.

value of the life sciences value chain in terms of employment and value-added - and offers a focus on scientific research in all areas of life sciences.

Healthcare services

Table 7 shows the data relating to the value added generated by the healthcare services segment in the four regions examined and its weight relative to the regional value added. The value added generated in the four regions amounts overall - considering both public and private providers - to 63.8 billion euro, with a maximum value in the region of Île de France (24.9 billion euro) and the minimum value in Cataluña (6.5 billion euro). Lombardia stands in the middle, with a figure of 14.0 billion in terms of value added. While there are significant differences in absolute terms, the percentage incidence on the total value added of the regional economy is much more similar across the benchmark regions, standing within a range of 3.5% in Cataluña and 4.4% in Baden-Württemberg (4.3% in Lombardia).

Table 7 - Healthcare services: territorial focus (2015)

	Value added healthcare services (million €)	Regional value added (million €)	healthcare services share of the value added as a %
Lombardia	**14,014**	**323,011**	**4.3%**
Baden-Württemberg	18,333	414,240	4.4%
Cataluña	6,464	186,480	3.5%
Île de France	24,939	597,385	4.2%

Source: based on Eurostat data

However, the value generated in the production and distribution of healthcare goods and services is not an ideal measure for comparing the performances of the regions in terms of welfare. Indeed, in the case of healthcare services it is not possible to define in an objective and indisputable way the exchange value, therefore the meaning of value added is weakened and subject to interpretations that are not robust. This also applies in the event of healthcare fees which, despite enabling us to determine a value of production, do not express the economic value of the service. Moreover, they are by their very nature differentiated from pricing policies adopted in other sectors based on market factors. The comparison of healthcare performance based on economic aggregates is further complicated by presence of different healthcare service models, with different weights attributed to the public and to the private sectors, and the respective operational criteria. As a result, the indicators selected to evaluate and compare on an aggregate basis the performance of healthcare services refer to process and outcomes, with the aim of clearly identifying the ultimate institutional purpose of this activity, which is the satisfaction of the need for citizens to receive assistance. For more details and the methodological specifications please see Box 4.

The indicators considered are (Table 8):

- qualified healthcare workers per 1,000 inhabitants;
- life expectancy at 65 years of age;
- composite index of inappropriate hospitalisation.

Table 8 - Indicators of healthcare services for Lombardia and European benchmark regions (2015)

	Qualified healthcare workers per 1,000 inhabitants	Life expectancy at 65 years of age	Indicator of inappropriate hospitalisation
Lombardia	**11.7**	**21.0**	**136.6**
Baden-Württemberg	20.7	20.1	532.8
Cataluña	12.9	21.4	179.4
Île de France	15.8*	22.7	300.9

(*) 2014 figure
Source: based on Eurostat data, institutional websites

As highlighted in the previous edition of the Report, the pool of workers providing healthcare services is extremely heterogeneous. Indeed, the German region of Baden-Württemberg has a level of healthcare workers[10] exceeding 20 units per 1,000 inhabitants in 2015, which is decidedly higher than the other regions considered. The number of workers involved in healthcare in the German regions translates into a much higher care coverage than the other regions. Île de France has an intermediate level, equal to 15.8 units (figure last updated in 2014), while Lombardia and Cataluña have less than 13 professionals per 1,000 inhabitants, which is especially due to a lower incidence of nursing professionals. Even after the reviews of 2014 data, Lombardia's update figure is still the lowest among the one observed.
About the second indicator, which measures life expectancy at 65 years of age in the four regions, the differences are not insignificant: despite similar social demographic situations there is a difference of almost 3 years between the region with the highest life expectancy at 65 years of age (22.7 years in Île de France) and the one with the lowest level (20.1 years in Baden-Württemberg). The figure for Lombardia is in an intermediate position, with a value of 21 years.
Finally, the third indicator measures the appropriateness of the hospital activity, by integrating in a single composite indicator the hospitalisation rates for three of the main chronic illnesses (asthma, hypertension and diabetes) for which an effective treatment should mainly take place at a territorial level. Although the data is influenced by different healthcare models and by the different supply of the hospital network, Lombardia and Cataluña have an extremely virtuous performance, with hospitalisation rates of less than 200 per 100,000 inhabitants. The difference to the benchmark regions is due in particular to diabetes (with hospitalisation rates of less than 100 units per 100,000 inhabitants in Lombardia, compared to values in the order of 250 for Baden-Württemberg) and hypertension (where Lombardia has the minimum value of 34). Île de France positions itself on an intermediate level, due to a hospitalisation rate that, among benchmark regions, is very limited for hypertension, intermediate for diabetes and the highest for asthma (95.9 every 100,000 inhabitants).

The pharmaceutical industry

Economic aggregates were computed for the pharmaceutical industry as well, to calculate useful indicators to compare the industry performance among the benchmark regions.

[10] Healthcare staff includes: doctors, dentists, nurses, physiotherapists, midwives.

The indicators considered and reported in Table 9 are:

- pharmaceutical value added per inhabitant (Euro);
- % of pharmaceutical value added on total value added for regional companies;
- % pharmaceutical turnover on total turnover for regional companies;
- number of workers in pharmaceutical industry per million inhabitants.

For the purposes of calculating these indicators, regional companies are understood to be those registered in the ORBIS database that was used to appraise economic aggregates.

Table 9 - Indicators of healthcare services for Lombardia and European benchmark regions (2015)

	Value added per inhabitant	Share of the of value added as a % of the total regional companies one	Share of the sector turnover as a % of the total regional companies one	Workers per million inhabitants
Lombardia	**537**	**2.2%**	**1.6%**	**2,183**
Baden-Württemberg	323	1.9%	1.7%	2,948
Cataluña	356	2.5%	2.1%	2,796
Île de France	517	1.2%	1.2%	3,659

Source: based on ORBIS, Eurostat data

Data show that the pharmaceutical industry in Lombardia generates a per capita value added that is higher than all the benchmarks: 537 euro per inhabitant, which is just above Île de France's (517 euro), and much higher than in Baden-Württemberg (323 euro) and Cataluña (356 euro).

The pharmaceutical industry in Lombardia emerges as the linchpin of the local economy even when considering the weight of the value added and turnover generated by the pharmaceutical industry compared to the total for the regional companies registered in the ORBIS database. Indeed, in Lombardia the percentage share of the value added of the pharmaceutical industry on the total one is 2.2%, (which is higher than the average of the benchmarks, 1.9%) while the incidence on the turnover is 1.6% (in line with the average). The values are only slightly lower than in Cataluña (2.5% is the incidence on value added and 2.1% the incidence on turnover). In the comparison with the other benchmarks, Île de France and Baden-Württemberg have a lower incidence in terms of both value added (1.2% and 1.9% respectively) and turnover (1.2% and 1.7% respectively).

On the whole, these indicators demonstrate that Lombardia is a leading light in the European pharmaceutical industry, which has in recent years increased its competitive capacity and international scope. Indeed, between 2010 and 2017, the pharmaceutical industry in Lombardia increased its exports by 59%, more than the European average (+42%) and more than the large European countries (+50% Germany, +20% Spain, +14% UK, +9% France).

This is a very significant result in terms of spillovers: in recent years both regional and national trends show that the increase in pharmaceutical production in Italy was 100% correlated to exports upsurge, by so being able to keep up employment rates in the sector and to generate value added all throughout the value chain.

riuscendo così a sostenere i livelli occupazionali nel settore e continuando a generare valore in tutta la filiera.

Finally, the last indicator for the European comparison is the number of workers in the pharmaceutical industry over the resident population. In terms of this indicator Lombardia is behind the benchmarks (2,183 workers per million inhabitants), which are topped by Île de France with 3,659 workers per million residents, followed by Baden-Württemberg and Cataluña (respectively with 2,948 and 2,796 workers per million residents).

Research in life sciences

A further area of focus is linked to research and scientific production in all areas of life sciences (Table 10).

Table 10 - Research in life sciences: Lombardia and European benchmark regions (2016)

	Life sciences articles per million inhabitants	% highly cited life sciences articles
Lombardia	**627**	**2.2%**
Baden-Württemberg	731	3.1%
Cataluña	606	2.7%
Île de France	1,396	2.3%

Source: Assolombarda on Incites-Thomson Reuters data

In 2016, the scientific production was similar in Lombardia and Cataluña, with 627 and 606 articles per million inhabitants respectively. This performance is lower than both Baden-Württemberg (731 articles) and especially Île de France one, which significantly outperforms all benchmarks with almost 1,400 articles.

On the other hand, all regions are more homogeneous in terms of research "quality": indeed, the share of highly cited articles on the total scientific production varies within a range of 0.9 percentage points, from 3.1% in Baden-Württemberg to 2.2% in Lombardia.

7. Discussion

This document quantifies the value of the life sciences value chain, which includes research and development activities, industrial production, the commercialisation of goods and the supply of final services in the form of medical care. Moreover, this report offers an estimate of the ancillaries activated by this value chain. The analysis is focused on Lombardia's data, with a comparison to national data, with the one of the most significant Italian regions from a socio-economic perspective (Emilia-Romagna, Lazio, Piemonte, Toscana, Veneto), as well as data of European regions that, along with Lombardia, are the most advanced in life sciences (Baden-Württemberg, Cataluña and Île de France).

In 2016, life sciences generated in Lombardia 23.5 billion euro of value added and ancillaries amounting to a further 22.3 billion. The two largest segments of the value chain are healthcare services (14.0 billion of value added, i.e. 59.6% of the total value added of the value chain) and pharmaceutical industry (4.3 billion, 18.5%). Considering also the ancillaries, the life sciences value chain in Lombardia represents 12.4% of the regional GDP, while at a national level the life sciences incidence is 10%. Therefore, this sector of specialisation is particularly significant for Lombardia's economy and even more for the national value chain, since Lombardia accounts for 24.6% of the value added of the national life sciences and 19.9% of the related workforce, while the regional population is 16.5% of the national one.

The significance of the life sciences value chain in Lombardia is due to the major presence of the industrial segment which, considering pharmaceuticals, generates 46.5% of the national value added. Looking at the supply of healthcare services, the incidence of the regional value added is 18.3%. In terms of healthcare services, some additional indicators are useful to provide a snapshot of the segment which, even in Lombardia, represents the driving force of the entire value chain and is largely funded by public health expenditure. In Lombardia it is registered the lowest country health expenditure share of the GDP (5.2% compared to a national average of 6.9%, in 2016)[11]; however, per capita public health expenditure is in line with national levels (1,931 euro compared to a national average of 1,899 euro, +1.7%)[12].

It should also be noted that in Lombardia the percentage of health expenditure destined to the supply of services by accredited private providers represents the 41.7% of the total, compared to a national average of 34.9%[13]. Even the private health expenditure levels are significantly higher compared to the national levels (752 euro per capita compared to 560 euro, +34%)[14]. This figure is a distinctive trait of the situation in Lombardia. This also applies for out-of-pocket expenditure for drugs and, specifically, drugs not requiring prescriptions or self-medication.

[11] Armeni P., Bertolani A., Costa F., *La spesa sanitaria: composizione ed evoluzione*, in Rapporto OASI 2017, a cura di CERGAS, Milano, Egea, 2017.
[12] Ibidem.
[13] Ibidem.
[14] Del Vecchio M., Fenech L., Rappini V., *I consumi privati in sanità*, in Rapporto OASI 2017, a cura di CERGAS, Milano, Egea, 2017.

Indeed, Lombardia's residents spend more than 44 euro compared to a national average of 40 euro[15].

In the European comparison, Lombardia has a lower healthcare coverage intensity than the benchmarks, which is mainly due to the lesser use of non-medical healthcare professions, especially if comparing Lombardia to very rich and most evolved healthcare systems in this regard, like the German one. Nevertheless, Lombardia (along with Cataluña) has a virtuous performance of hospital activities compared to the other benchmark regions, thanks also to lower inappropriate hospitalisation rates (137 units every 100 thousand inhabitants). Moreover, the incidence of the value added generated by healthcare services compared to the overall regional figure (4.3% in Lombardia) is aligned with the other benchmarks.

Lombardia stands out at the European level in the pharmaceutical field thanks to a per capita value added that is higher than the benchmarks (537 euro per inhabitant), a relative weight of 2.2% of the regional companies' total value added (behind only Cataluña with 2.5%), a strong international propensity (exports +59% between 2010 and 2017, an higher increase than the one of the major European countries).

Therefore, in Lombardia there is a health value chain that, given a level of public funding comparable to other areas in Italy, has seen a considerable development of the private sector in the segments of drug manufacturing (for prescription and over-the- counter products), medical devices and biotech research services, as well as the supply of services from accredited private providers and independent private patients. This dynamic production system is a key component of Lombardia's economy, which could develop itself thanks to the traditional strengths of the local socio-economic ecosystem: a favourable geographic position, a solid infrastructure network, availability of income and capital for companies and families, manufacturing tradition, an active and professional voluntary sector, state-of the-art research and innovation hubs like universities and IRCCS (Italian hospitals of relevant national interest for their research activity).

The qualitative and quantitative analysis of the value chain represents a preliminary step for reflecting on the future of the sector and on opportunities for its further development. To complete the analysis, it could be useful to present certain features that characterise the life sciences value chain: some are shared by the entire value chain and demonstrate the existing interconnections between the segments that make it up, while other features are specific to each segment. Together these features make life sciences a sector that should be protected and ideally further developed both at the Lombardia level and at the national level, by public and private players.

- The healthcare value chain is driven by the personal care services sector which, at national level and in Lombardia, is mainly funded by public resources. Furthermore, as explained above, in virtue of a progressive reduction of healthcare financing, it is undergoing to a process involving an increase of private expenditure (both intermediated and out-of-pocket). Unlike in many other crucial domains (education, universities, justice, central government authorities) only a small part of the public expenditure is allocated for the direct payment of salaries and wages, while the majority is used to purchase goods and services from the private sector (which in part flow into the value

[15] Federchimica-Assosalute, *Numeri e indici dell'automedicazione*, edizione 2017.

chain and in part in the ancillary industries). Purchases account for 64% of public health expenditure at the national level and 69.4% at the regional one[16]. Therefore, health is one of the few aggregates of public expenditure (along with defence and transport) that can be examined in terms of industrial policy and not just in terms of the impact on individual consumption. The significant presence of excellent institutions, which attract public and private interest from all throughout the country (with a 60% prevalence of the private component), makes the segment of services for people able to position itself as an attractor of patients and an exporter of a modern and efficient organisational model (just think of the outcome indicators in relation to the resources that are actually used) both at the European and at the global level. This, in a process that could represent a sort of "internationalisation" with a very positive spillover effect for all the value chain and on citizens' healthcare status, by prompting important investments in technologies and innovation.

- In physiological terms, the life sciences sector has a high research intensity which is increasingly leveraged on an open innovation model: R&D processes that are increasingly developed in partnership increase the capacity to generate positive spillover effects on the territorial network for research and innovation. This structural feature should be promoted in Lombardia, in order to intensify its role as an international innovation hub.

- The most significant contribution to research in quantitative terms comes from pharmaceutical companies which invested 1.5 billion in research and development in Italy in 2017[17] (7% of the total for research at the national level, up +20% in the last three years alone), and employed at 6,400 workers in this area. The pharmaceutical industry in Lombardia contributed to approximately one third of the national investment in research and development, with centres of excellence in both basic research and clinical research.
  At a national level - and in a prominent manner in Lombardia - there is a growing level of specialisation in areas with a high innovative potential, such as drugs for gene therapy and cell therapy, orphan drugs, biotechnological diagnostics, vaccines, nanobiotechnologies, blood derivatives, gender medicine as well as genomics and management of big data. Italy is also a European leader in advanced therapies: indeed, three of the six therapies authorised in Europe are the result of Italian research, and all of them are linked to Lombardia's research institutions.
  Aside from attracting capital from abroad, research from companies in Lombardia has proven its standards of excellence by providing innovative treatments for previously untreatable illnesses. In terms of attracting investments, a key role is played by clinical trials, which at the national level amounted to investments of 1 billion per year, of which 700 million is for drugs. In recent years Italy has increased its share of clinical trials conducted in Europe (20% of the total compared to 18% in 2012 [18]), with a growing component of trials on biotech drugs. In Italy 40% of drugs in clinical trials are

[16] The aggregate expenditure includes all items excluding those for staff and publicly funded primary healthcare. The estimate is based on 2016 data reported by Armeni P., Bertolani A., Costa F.,*La spesa sanitaria: composizione ed evoluzione*, in Rapporto OASI 2016, a cura di CERGAS, Milano, Egea, 2016.
[17] Farmindustria, *Indicatori farmaceutici*, luglio 2018.
[18] AIFA, *Clinical trials of Drugs in Italy*. 16th National report, 2017.

biotech drugs and in particular, recombinant proteins, vaccines, monoclonal antibodies, advanced treatments which include products for cell/gene therapy and regenerative medicine. These activities are of great value to the entire country and almost half of them are carried out in cooperation with leading institutions in Lombardia.
Investing in clinical trials means offering patients innovative treatments, while offering doctors and researchers the chance to grow professionally, as well as ensuring significant resources to the healthcare service at lower costs, since companies cover all the connected expenses, such as hospitalisation, drugs and diagnostic examinations. For example, it has been calculated that for every euro invested in clinical trials on cancer, which is an area of specialisation for research in Lombardia, the system saves 2.2 euro[19].

- Within the health value chain even more mature sectors can contribute to the financial sustainability of the national and regional healthcare service and to the promotion of human health. This is the case for the segment of over-the-counter drugs, and self-medication drugs, for which more than 46% of companies who manufacture and/or commercialise these drugs operates in Lombardia[20]. The segment of self-medication drugs can contribute to research and innovation in the pharmaceutical sector enabling the allocation of resources and investments from drugs that have reached maturity (and for which research costs have been amortized) to innovative drugs; moreover, enabling citizens to manage minor health issues in an informed and responsible manner it enables the impact on public health expenditure to be limited.

- In the production of pharmaceutical active ingredients, Italy is an established industrial powerhouse at the global level, with a market share of 9% and more than 85% of production destined for foreign markets[21]. More than half of the companies in the sector is in Lombardia with production destined to generic drugs, custom synthesis and custom manufacturing in partnership with client pharmaceutical companies. The sector invests 3% of turnover in applied research, guaranteeing the optimisation of processes and high-quality standards which have enabled Italian manufacturers to establish themselves even in markets with very strict controls (America, Europe and Japan).

- In research and innovation, biotech companies involved in the healthcare sector emerge as particularly dynamic players and as a driving force for the entire segment of biotechnologies. In the national landscape, the highest concentration can be found in Lombardia[22]: 132 biotech local units operate in the healthcare sector (of these, 52 are involved in biotech R&D) which represent 45% of the total companies and 35% of the national turnover, with significant investments in intra-mural R&D (more than 100 million euro per annum). In particular, the sub-group of companies dedicated to R&D represents the real driver of innovation in the biotech segment, thanks to the

[19] Farmindustria, *Indicatori farmaceutici*, luglio 2018.
[20] Federchimica.
[21] The data in this section comes from Federchimica.
[22] The data in this section comes from Assobiotec-ENEA, *Le imprese di biotecnologie in Italia 2018 - Facts & Figures*.

transfer of the results of public and academic research to applied research that is of industrial interest. This driver acts as a catalyst for a research model that is increasingly collaborative, representing the real foundation where the activities of the other players connect to within an open innovation framework.

- In the context of technologies for health, which is a fast-developing area at the global level in terms of scientific, technological and market innovation, even the sector of medical devices plays an important role. It is the point of arrival for technologies from the most diverse areas, in which the relations between the clinical sector, companies, start-ups and research centres are extremely close. Along with Emilia-Romagna, Lombardia is the region with the highest concentration of start-ups involved in businesses that are of interest for this sector [23]. Medical technologies contribute significantly to safeguarding the health of citizens, by providing cutting-edge instruments for prevention, treatment and rehabilitation. The sector of medical devices therefore represents a sector with a high concentration and intensity of innovation, which contributes significantly to the improvement of the healthcare service and has a low impact on overall health expenditure.

- A special area of the value chain is that of medical gases, which are recognised as drugs (Italian legislative decree 178/91) and governed by specific provisions in terms of their manufacturing and commercialisation, and homecare service providers for patients with chronic illnesses and which are able to ensure very precise qualitative standards for treatments, which are also certified by the patients' medical practitioners. Given the forecasted increase of persons over the age of 65 (which in Italy will increase from 22.3% to 26.9% of the population between 2017 and 2030[24]), homecare represents a strategic instrument to support the sustainability of the healthcare service and welfare system.

- The healthcare value chain represents a large reservoir of highly qualified job opportunities. In Italy the national healthcare service employs 256,067 graduates, which represents 39.4% of the total healthcare service's employees and 20.6% of total graduates working in the Italian public sector, only behind the education sector (577,779 graduates)[25]. Mangers, a category which makes up the clear majority of the medical staff, represents 20% of the national healthcare service workforce[26]. Managers or assistant managers represent 22.9% of the workforce in the pharmaceutical industry, compared to an overall 4.5% across all industries[27]. The same figure is 26.6% in Lombardia, where the overall percentage of managers and associate managers across all firms is 7.0% of the workforce[28].

- The value chain represents a traditional area of female employment in a country where a low level of participation by women is often considered as a factor that is limiting economic growth, social fairness and - in certain respects - the recovery of birth rates by distinguished institutions (including the Bank of

[23] Assobiomedica, *Rapporto PRI - Produzione Ricerca e Innovazione,* edizione 2017.
[24] ISTAT.
[25] Ministero dell'Economia e delle Finanze - Ragioneria Generale dello Stato, Conto annuale 2016.
[26] Ibidem.
[27] Calculations based on INPS data, statistical database on employees in 2016.
[28] Ibidem.

Italy)[29]. In the national healthcare system female employment is 65.4%, compared to a level of 56.7% for the public sector as a whole[30]. Moving to the private sector, at a national level in pharmaceutical companies' female employment is 41.3%, in medical devices it is 44%[31], which is in line with the total for all sectors, while in private companies providing healthcare services the percentage is 77%. In Lombardia these percentages are 46.9% for pharmaceutical companies and 79% for companies providing healthcare services, compared to the total for all companies which is 43%[32]. It should be noted that within life sciences there are also growing levels of female participation in more qualified and managerial roles: 40% of doctors in the national healthcare system, with values exceeding 60% for under 40-year-old, while amongst non-medical managers of the national healthcare system the figure is 66%. In terms of the managers of pharmaceutical companies at a national level, women make up 28% of the total compared to 15% of the total for all companies; in Lombardia the percentages are 31% and 17% respectively[33].

Given the high level of female participation, in the companies of the life sciences value chain there are many corporate welfare services for women to achieve a balance between their career, family and private life: training and education services for children, nurseries, canteens, wellness and prevention services. By way of an example, in the industrial sector in Italy 1 female worker in 4 has access to corporate welfare instruments[34], whereas in pharmaceutical companies in Lombardia and Italy 100% of women has access to supplementary welfare and healthcare services, 70% has access to assistance services (in 32% of cases for family members who are elderly or not self-sufficient). Finally, more than 90% of workers in pharmaceutical companies has services such as transport, canteens, or other fringe benefits. And there are also facilitations like part-time or smart working solutions.

[29] Lotti F., *Crescita economica, equità, uguaglianza: il ruolo delle donne*, Roma, 18 ottobre 2011.
[30] Ministero dell'Economia e delle Finanze - Ragioneria Generale dello Stato, Conto annuale 2016.
[31] Assobiomedica.
[32] Calculations based on INPS data, statistical database on employees in 2016.
[33] Ibidem.
[34] Farmindustria.

8. In depth analysis: clinical trials in Italy and in Lombardia

The value of clinical trials

As the data in this Report demonstrates, life sciences represent a vibrant sector which is fundamental for the growth of our country and for improving the quality of treatments and service offered to citizens. For this reason, one of Italy's primary objectives is that of guaranteeing the right level of investments for the sector. According to ISTAT data, in 2016 public entities, public and/or private universities and no profit entities invested approximately 1.9 billion euro in R&D activities linked to medical and scientific research (with a compound annual growth rate of 1.3% between 2012 and 2016)[35]. Another 1.5 billion euro must be added to the previously mentioned resources (up 22% between 2012 and 2017), since it was invested by companies from the bio-pharmaceutical sector alone: this contribution amounts to 7% of the total R&D investments in our country[36].

Clinical trials are a fundamental part of research, for which the pharmaceutical industry invests approximately 700 million euro per annum. On top of these resources, the medical devices industry invested 231 million euro in clinical trials in 2016. The objective of these investments is to identify treatments and solutions that can improve the management of patients and reduce the incidence and prevalence of communicable and non-communicable diseases, limiting the negative impact on citizens' health status and on the sustainability of the national healthcare system. Therefore, it represents a virtuous cycle that generates innovation and savings for the system, as it has been shown by numerous sectoral studies. Considering the current financial situation of the national healthcare system this is a highly relevant issue. Indeed, the current forecasts by the Italian Ministry of Economics and Finance show a significant reduction of the ratio between public health expenditure and GDP (from 6.7% to 6.3% between 2016 and 2020)[37], making it fundamental to put in place value-based healthcare strategies, along with policies to maximize investments in the healthcare sector.

Although there is no overall data on trials conducted in Italy, we can use data which are published by the Italian Drug Agency (AIFA). In 2016 AIFA approved 660 trials, up 13.2% from 2013. Companies play a key role in these studies as they are funding promoters in 74.2% of cases. In rare diseases (where 164 studies were approved in 2016), the contribution of resources from for profit promoters is even higher, accounting for 84.1% of cases.

[35] ISTAT, Research and Development Database, 2018
[36] Farmindustria, *Indicatori Farmaceutici*, luglio 2018.
[37] Ministero dell'Economia e della Finanza, DEF. Nota integrativa, 2017.

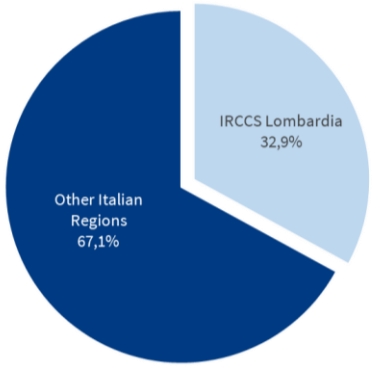
Italy also has a very important role in the European project Voluntary Harmonisation Procedure (VHP), which involves AIFA, and enables a simultaneous and coordinated assessment of clinical trials for all EU Member States involved in the study (the programme is open to multicentric clinical trials from phase I to phase IV). In 2016, in the context of VHP, Italy and the UK were the two leading EU nations in terms of the number of trials (as reference authorities), with 27 and 37 clinical trials respectively[38]. A picture demonstrating that Italy could become the leading EU nation in this area if able to take advantage of the simplification introduced by reg. 536, and at the same time to create a more competitive system for clinical research.

Looking at regional data, Lombardia is one of the leading regions in the sector of clinical trials thanks to different factors, such as the high number of Italian and multinational companies operating in life sciences in the region. It is important to highlight that, according to AIFA data, the region attracts on average 56.6% of clinical trials activated in Italy in the pharmacological area[39]. This has also been made possible due to the number of Contract Research Organizations (CRO) operating in Lombardia, 54 according to AIFA's records, which represent 56% of the total CROs that are headquartered and operate in Italy [40]. The robustness of the segment is also linked to the presence of numerous centres of excellence for medical and scientific research, including 19 IRCCS, 7 Health Protection Agencies (ATS), 9 Local Social Healthcare Agencies (ASST, which correspond to 10 different hospitals), 7 Universities (including 2 private ones) with medical faculties and 32 research centres. Aside from many institutions, the area also presents a sizeable research workforce. Within the universities clinics and research centres, there are a total of 6,000 researchers specialising in medicine and pharmacology[41]. Finally, in the territory operates an organization founded in 2011 by the Lombardia Region that is entirely dedicated to biomedical research - the Regional Foundation for Biomedical Research (FRRB) - which has the objective of redistributing local and European resources for innovative research projects with a high impact on the national healthcare system and on citizens' health status.

An even more segmented analysis, that involved all the IRCCS operating in Lombardia [42], confirms the scale and significance of the clinical research activities conducted in the area. By adapting information taken from the database ClinicalTrials.gov[43], during the course of 2016, the IRCCS in Lombardia conducted a total of 303 trials, 32.9% of the total reported for Italy (920 clinical trials) by all the research centres.

[38] AIFA, *Clinical Trials of Drugs in Italy*. 16th National report, 2017
[39] AIFA, *Clinical Trials of Drugs in Italy*. 12th National report, 2013
[40] AIFA, CRO autocertificate (DM 15/11/2011), 31 dicembre 2012.
[41] I rettori delle Università lombarde per EMA, 19 ottobre 2017.
[42] Centro Cardiologico Monzino, Eugenio Medea, Fatebenefratelli, Fondazione Don Gnocchi, Fondazione Mondino, Humanitas, I.N.R.C.A., Istituto Auxologico Italiano, Istituto Europeo di Oncologia, Istituto Nazionale Tumori, Istituto Neurologico Carlo Besta, Istituto Ortopedico Galeazzi, Istituto Ricerche Farmacologiche, Maugeri, MultiMedica, Ospedale Cà Granda, Ospedale San Raffaele, Policlinico San Donato, Policlinico San Matteo.
[43] The platform, which is managed by the National Library of Medicine (NLM) of the National Institute of Health (NIH) in America, enables the institutions involved in medical-scientific research to add, on a voluntary basis, the data for the trials commenced by the centre. Given the high number of studies recorded on the platform, the data represent a good proxy for the situation regarding trials in Italy.

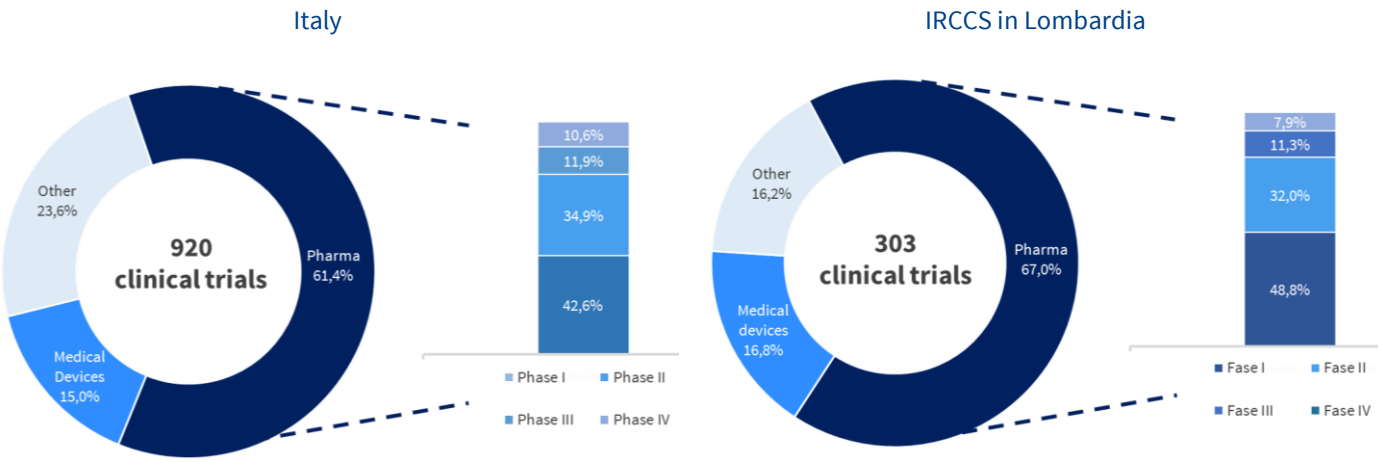
Figure 1 - Clinical trials in Italy: focus on IRCCS in Lombardia (2016)



Source: Assolombarda on ClinicalTrials.gov, 2018

67% of trials activated in Lombardia by the IRCCS regard drugs and the pharmaceutical sector (5.6% more than the national level), 16.2% is related to medical devices (1.8% more than the national level), while 16.8% is related to other areas[44] (7.4 percentage points under the national level).

Figure 2 - Distribution of clinical trials by study area (2016)



Source: Assolombarda on ClinicalTrials.gov, 2018

Looking at the types of studies followed and started by the IRCCS operating in Lombardia, those involving interventional research make up 81% of the total, while observational studies account for 19% of the total. Moreover, the patient registries, which fall within observational studies, represent 5% of the total. The breakdown is similar at a national level, indeed interventional studies make up 78% of the total, while observational studies make up 22% of the total, of which 5% are patient registries.

[44] Including medical procedures, radiation, diet.

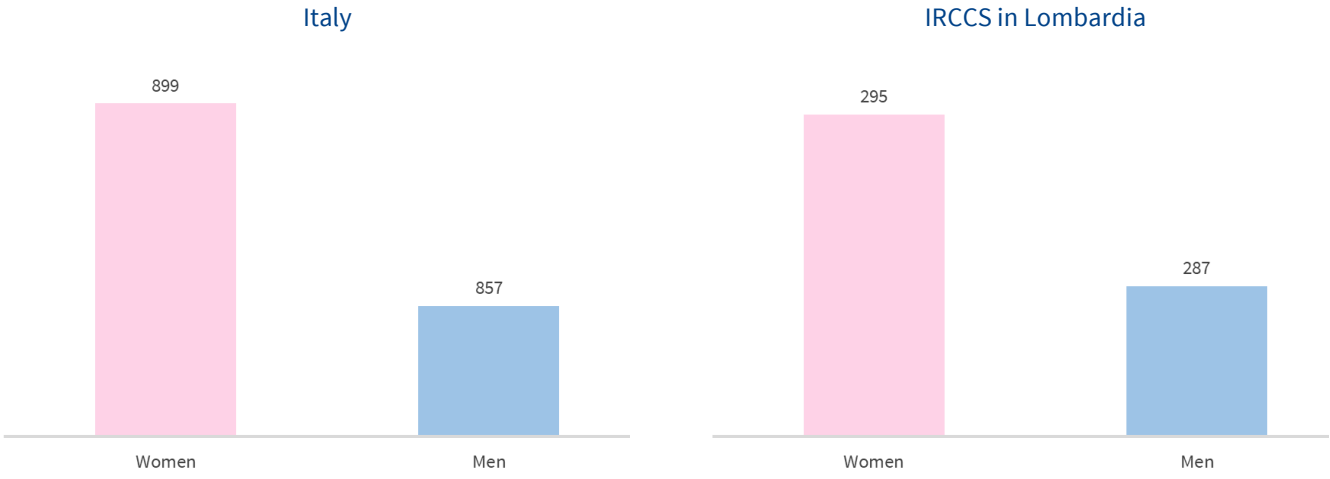
Table 11 - Distribution of clinical trials by study area (2016)

Type of trial	Italy	IRCCS in Lombardia
Interventional study	78%	81%
Observational study	22%	19%
Of which: Patient registries	5%	5%

Source: Assolombarda on ClinicalTrials.gov, 2018

There are more than 18,700 patients involved in Italian clinical trials, which is equal to 13% of the patients involved in clinical trials conducted by institutions operating in Italy. Looking at the gender of patients involved in clinical trials, at a regional and national level, we can see that there is a greater incidence of female participants. Indeed, regarding IRCCS in Lombardia, women and men are involved in 295 and 287 trials respectively (899 and 857 for the Italian sample).

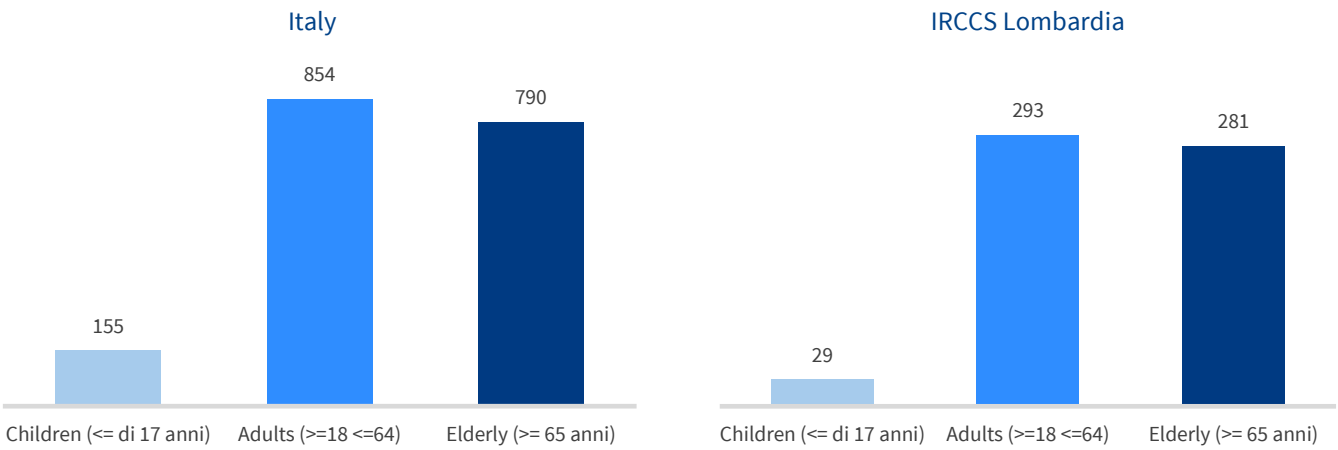
Figure 3 - Distribution of clinical trials by gender of patients enrolled (2016)



Source: Assolombarda on ClinicalTrials.gov, 2018

Breaking down the trials using the patients' age criteria, there is a clear prevalence of adult enrolees (people aged 18 to 64) and elderly one (people aged 64 and over). The adult population was involved in 293 trials, i.e. 96.7% of total trials started in the IRCCS operating in Lombardia (compared to a national figure of 92.8%). The elderly bracket is next, with participation in 281 trials, i.e. 92.7% of cases (compared to a national figure of 85.9%). A marginal number of studies involves younger patients, below 18 years of age, who are involved in 29 studies, 9.6% of cases (compared to a national figure of 16.8%).

Figure 4 - Distribution of clinical trials by age of patients (2016)

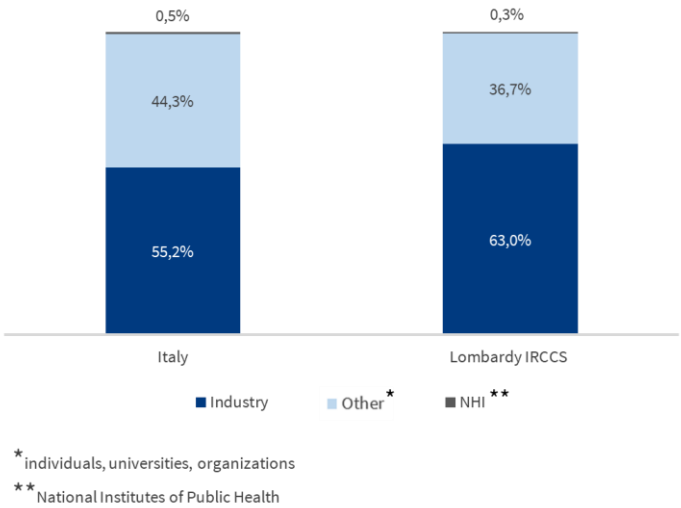


Source: Assolombarda on ClinicalTrials.gov, 2018

Data regarding the distribution of trials by age and gender highlight the absence of a strong focus on specific studies for the both the female and paediatric population, in line with the national data reported by AIFA regarding pharmacological studies. Indeed, at a national level, pharmacological studies dedicated to the female population represent only 5.5% of the total, while those focused on paediatric age patients amount to 8.6%. The number of clinical trials dedicated to the elderly population is even lower and amounts to 1% of the total[45].

Finally, even the analysis of this kind of data confirms the significance of investments in trials generated by companies. Regarding the IRCCS operating in Lombardia, 63% of trials are financed and promoted by the industry, 36.7% by other organisations and third parties (no profit entities, universities and individuals), while 0.3% is funded by central public health authorities. However, at the national level, companies finance 55.2% of trials, while 44.3% if financed by other organisations and third parties, and finally 0.5% is funded by central public health authorities.

Figure 5 - Distribution of clinical trials by type of sponsor (2016)



Source: Assolombarda on ClinicalTrials.gov, 2018

[45] AIFA, *Clinical trials of drugs in Italy*. 16th National report, 2017.

The figures that have been reported, representative of a statistically significant sample, show the strength of Lombardia in terms of trials at a national level. Not only in terms of trials activated at the regional level as a percentage of the national one, or in terms of patients involved in these trials compared to the national value, but also because of the significant number of life sciences companies, research centres and organisations operating in the sector, thus making Lombardia a vibrant and competitive region, able to generate innovation. Given the potential positive impact of clinical trials both on the health status of patients and on the sustainability of the national healthcare service, there is a clear need to trigger industrial and supply chain policies to support the players operating in the sector. Therefore, it is fundamental to start from preserving the current clinical trials organisational system and promoting synergies between different players within the supply chain, through both public and private ventures. This should be done with the objective of creating a virtuous system that is able to promote innovation and competitiveness while attracting investments from abroad, generating employment, health and well-being at a regional and national level.

9. Appendix I

Box 2 - Methodological information about the calculation of the life sciences value chain at the national level

National accounts - ISTAT

The accounts and territorial economic aggregates from ISTAT's National Accounts report for every region the value added by the macro area of activity only, without providing figures on the value of production. Moreover, the figure for healthcare services also includes social assistance. In order to calculate the value added and value of production of healthcare services at a local level the following hypotheses and estimates were required:

- To calculate the value added of healthcare services alone, starting from the available data on the value added of healthcare services and social services, we applied to all regions the national healthcare services' value-added rate of healthcare and social assistance total, which was 85.4% in 2015. It was therefore necessary to assume that in all the analysed regions the contribution to the value-added was distributed with equal weights between healthcare and social services. Once regional healthcare services' value added was calculated, the value of production was determined by assuming that incidence of the value added on the production at a local level was constant in all regions and equal to the share at national level (60.1% in 2015).

- A similar assumption was formulated for computing the number of the health care system workers: the ISTAT National Accounts provide overall employment data for the healthcare and social segments at a regional level. To quantify the workforce at a regional level for the healthcare sector only we applied to all the regions considered the healthcare sector workforce share of total (healthcare plus social workers) that was reported at a national level in the year 2015, i.e. 74.1%.

ASIA - ISTAT

ISTAT's ASIA statistics on the workforce of active companies sometimes do not allow to identify in a precise manner the segments of the life sciences value chain identified in this project because a five/six-digit breakdown is not available. As a result, in these cases it was necessary to use data referring to a broader context than the life sciences value chain in question.
Specifically, the following cases are when data relating to a broader context were used:

- The segment Ateco 20.11 also includes the production of industrial gases not for medical use;

- The segment Ateco 26.6 includes the sub-segments 26.60.02 (*manufacture of electromedical equipment (including detached parts and accessories)*) and 26.60.09 (*manufacture of other irradiation and other electrotherapeutic equipment)* which belong to the life sciences value chain, but also sub-segment 26.60.01 (*manufacture of irradiation equipment for foodstuff and milk*) that is not associated with this value chain.

- Segment Ateco 72.11, besides from red biotech, includes green and white biotech research, which is not part of life sciences value chain.

- Segment Ateco 33.13 includes sub-segment 33.13.03 (*repair of electromedical equipment, medical and surgical and veterinary material, equipment and instruments for dentistry)* which belongs to the life sciences value chain, but also sub-segments 33.13.01 (*repair of optical, photographic and cinematographic equipment (excluding video cameras*)), 33.13.04 (*repair of distillation equipment for laboratories, centrifuges for laboratories and the machinery for cleaning using ultrasounds for laboratories*) and 33.13.09 (*repair of other electronic equipment (excluding those for telecommunications and computers)*) which are not part of this value chain.

- Segment Ateco 46.18 includes sub-segment 46.18.3 (agents specialized in the sale of pharmaceutical products and cosmetics) which belong to the life sciences value chain, but also sub-segments 46.18.1 (agents specialized in the sale of paper products, stationery, books), 46.18.2 (agents specialized in the sale of audio and video consumer electronics, electrical material for domestic use, electrical appliances) and 46.18.9 (agents specialized in the sale of sporting equipment, bicycles and other products) that are not part of the value chain.

AIDA - Bureau van Dijk

The query was set up on AIDA using the following criteria:

- Inclusion of active companies only
- Exclusion of companies with consolidated financial statements
- Exclusion of companies with a negative value added
- Companies were assigned to a region based on the address of the registered office

Box 3 - Methodological note on the calculation of the ancillary activities of the life sciences value chain

- In terms of the coefficients for the inputs of internal origin we used the estimates prepared by the Confindustria Technical Committee on Health (2011):
  - Pharmaceutical industry 1.654
  - Medical devices industry 2.020
  - Wholesale trade 1.899
  - Retail trade 1.802
  - Healthcare services 1.709

  The weighted average coefficient for the value of production of each segment was 1.734.

- To compute ancillaries' value added we used the ratio between the value added and the average production reported in the Italian economy in 2016, which was equal to 48%. This is a conservative assumption that considers a constant value added in all sectors of the economy.

10.Appendix II

Box 4 - Methodological note on the calculation of the main economic aggregates for healthcare services and the pharmaceutical industry at international level

European System of National and Regional Accounts (Eurostat)

The accounts and territorial economic aggregates from Eurostat's National and Regional Accounts provide for every region the value added by macro area of activity only. Therefore, the figure for healthcare services falls within the macro area relating to the government, which includes defence, mandatory social insurance, education, health and social assistance. In order to calculate the value added of healthcare services at a local level the following hypotheses and estimates were required:

- For Baden-Wurttemberg, Cataluña and Île-de-France the value added of regional health was calculated based on the share of health over the value added of the public sector at the national level;
- For Lombardy, instead, the figure is an aggregate of healthcare and social assistance, to which we applied the national coefficient of value added of healthcare services over health and social assistance national total, which was 85.4%.

To quantify employment in healthcare services a first step was taking the total healthcare sector workforce from Eurostat which refers to practising professionals. Nurses and midwives for the German Lander were calculated on the basis of the ratio of doctors/nurses at a national level in Germany. For the calculation of the workforce of the pharmaceutical industry we instead used regional employment figures by Eurostat.

AIDA - Bureau van Dijk

The search for the calculation of the economic aggregates of the pharmaceutical industry was made through ORBIS with the following criteria:

- Inclusion of active companies only
- Exclusion of companies with consolidated financial statements
- Exclusion of companies with a negative value added
- Companies were assigned to a region based on the address of the registered office
- For the appraisal of the value added, where the 2015 figure was missing:
  - if only the 2014 figure was available, this was left unchanged
  - if only the 2016 figure was available, this was left unchanged
  - if both the 2014 and 2016 was available, an average of the two was calculated