LIFE SCIENCES & HEALTH SECTOR

AN IN-DEPTH OVERVIEW OF THE LIFE SCIENCES & HEALTH SECTOR IN BRABANT

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Index

Index

Colophon

Brabant, the Netherlands – Life Sciences & Health industry, an Overview/Publication of the Brabant Development Agency (BOM), Tilburg, the Netherlands

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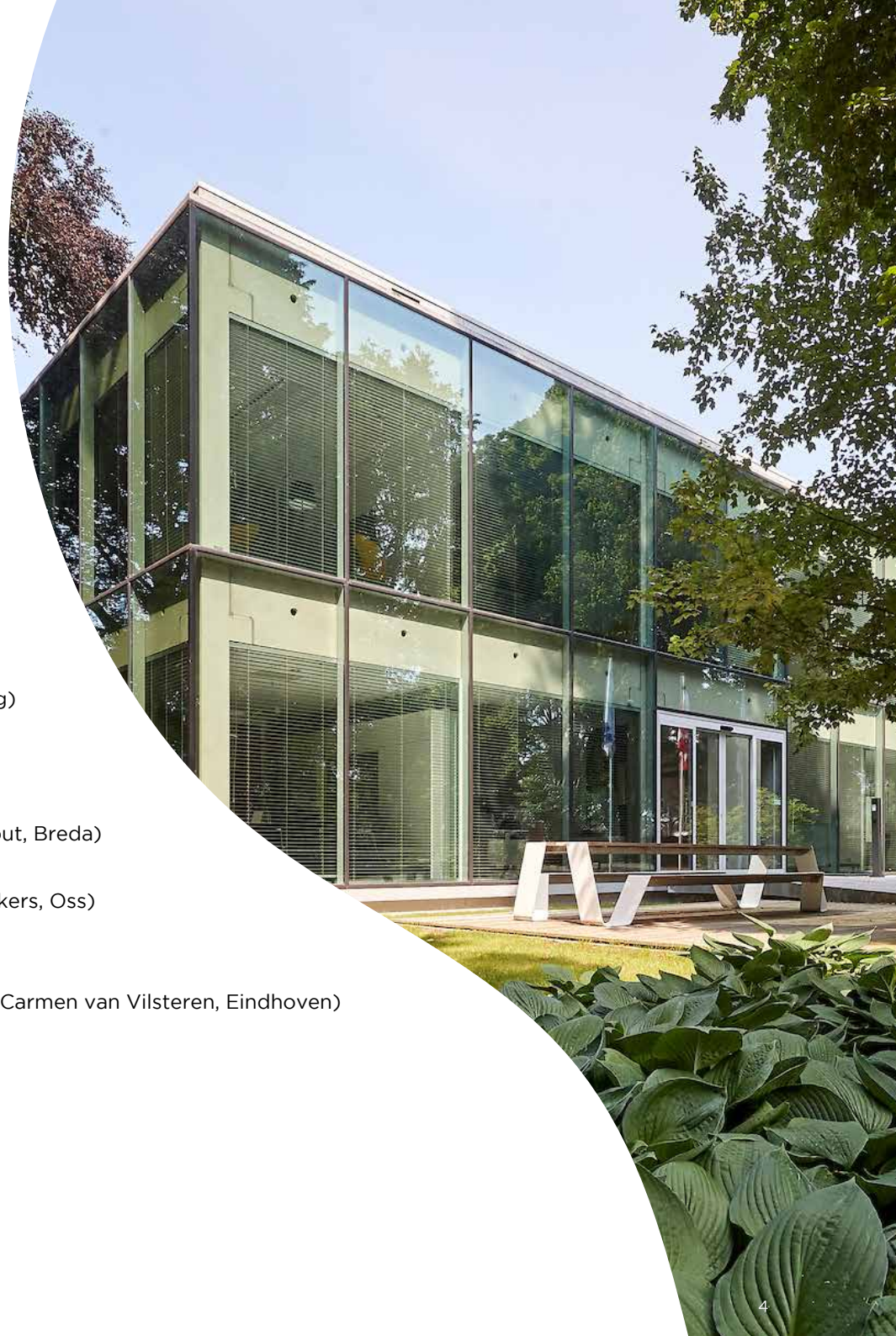
DESIGN

Maan identity. design. content. - Ulvenhout



1. INTRODUCTION TO THE STUDY

Life Sciences & Health Sector in Brabant

An in-depth overview

Dear Reader,

We are the Brabant Development Agency (BOM) and we are proud to present to you our new in-depth review of the Life Sciences & Health industry in Brabant. Brabant is a part of the Netherlands that is very well-connected with and a close part of the life sciences and health community in the country.

The goal of this review is to provide you with a detailed overview of the Life Sciences industry in Brabant, including the strengths and opportunities the region has to offer. The industry has undergone dramatic growth in Brabant in recent years. Between 2014 and 2018 the number of LS&H organisations in Brabant increased by 11.1%, while its employment figures grew even more at 15.4%. One of the strengths of Brabant is the distinctive and constructive model of cooperation. In short, building partnerships in the region is a quick and fluid process – faster than anywhere else. Individuals and companies wanting to join the club and make a contribution will quickly and easily reap the rewards.

So who are we? We are the Brabant Development Agency. Based in Tilburg, our BOM Foreign Investments & International Trade department assists new and existing foreign companies to make optimal use of the opportunities offered by Brabant as a business location. We also provide hands-on support to companies based in Brabant that are growing their business abroad.

We hope you will enjoy reading this in-depth review, and if you would like to know more about what Brabant has to offer, then please feel free to reach out to us!

With kind regards,
Thijs Taminiau

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This review is a sequel to the first Life Sciences & Health overview created for and by BOM Foreign Investment & Trade in 2015, which was authored by Ms Yvonne Kemps. The review aims to provide a comprehensive overview of the Life Sciences & Health (LS&H) industry in Brabant. Our target audience is primarily current and potential investors in and/or innovation partners for the industry in Brabant, but also includes policy-makers, industry organisations and media representatives with an interest in the industry who would like to learn more.

The review is based on desk research, extensive data-analysis, stakeholder interviews and interviews with industry specialists as well as intensive teamwork between the authors and representatives of BOM and its key partner organisations in Brabant.

The report contains Brabant-specific facts and figures but is written with the clear understanding that the Life Sciences & Health industry is a global one where regional and even national borders are of little importance. This is why the report focuses in its entirety on the province of Brabant embedded in a wider national perspective of the Netherlands operating on a world market.

Our overview is laced with profiles of inspiring regional and national actors in the Life Sciences & Health industry and it also contains information on international trends and developments.

The review aims to give the reader an accurate picture of what Brabant has to offer. While we have strived to make it as complete and accurate as possible, we would like to hear readers' comments and thoughts, which will prove valuable for future editions. We hope that this review will both provide valuable insights and prove to be an entertaining read.

We would like to acknowledge and thank all our contributors for the input they provided. We would not have been able to accomplish our task without them.

Ben Engel, Engel – Een Heldere Blik
Henry de Vaan, Fanion Onderzoek & Advies

2. INTRODUCTION TO BRABANT, THE NETHERLANDS

A. What has Brabant got to offer?

The Dutch province of Noord-Brabant is located in the southern part of the Netherlands, strategically situated between Amsterdam Schiphol Airport, Europe's leading seaport in Rotterdam, the Port of Antwerp, Brussels and the major German economic heartland of the Rhine-Ruhr region. Brabant covers an area of 5,082 km2, making it the second largest province in the Netherlands, and is home to some 2.5 million people spread across 62 municipalities.

- From a geographic perspective, Brabant offers easy access to 170 million Europeans within a 500 km (310 m) radius. Physical and telecommunication infrastructure are best-in-class when it comes to establishing head office, marketing and sales, R&D, manufacturing and/or logistics operations.

- In terms of costs, the Netherlands has a company-friendly tax structure when compared to most other European countries.

- Research, product and process development and manufacturing are part of Brabant's DNA. Ranging from primary production in agriculture and the food industry to the manufacture of semi-finished products all the way through to OEM manufacturing for the most complex electronic, biopharmaceutical, nutraceutical and IT products and equipment, all of these activities can be found in the region in abundance.

- The well-developed industrial and knowledge networks or 'ecosystems' in the High Tech Systems, Logistics, Life Sciences & Health, AgriFood, Chemicals and Aerospace industries offer opportunities for joint ventures at a very high level. Cross-industry partnerships in the region are a given.

Source: BOM, Info & Graphics

B. Brabant's main benefits

The province of Brabant offers both the business-friendly environment of the Netherlands and also has a number of favourable geographical benefits:

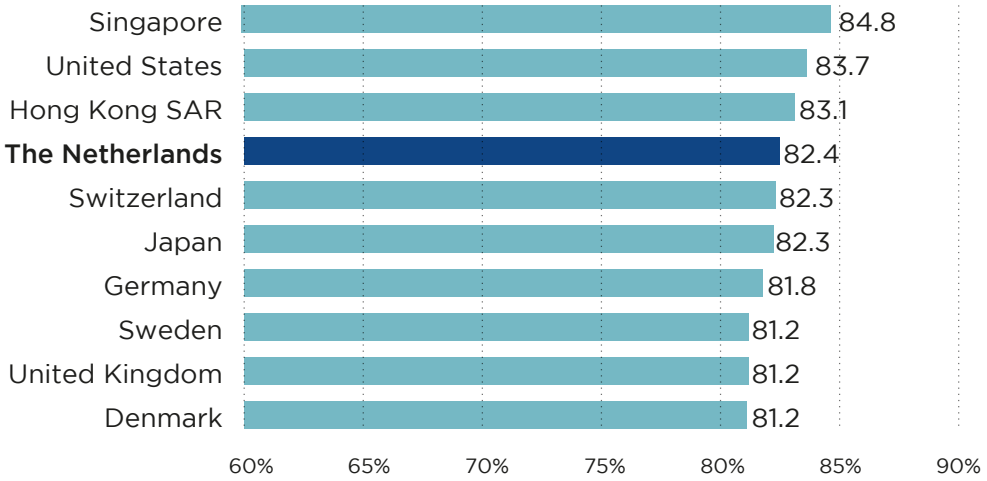
The Netherlands as a whole and Brabant offer:

- an attractive tax climate, including personal and corporate income tax and value-added tax (VAT)
- a stable economic, political and social climate
- competitive labor costs

Brabant is particularly strategically well-located in Europe because:

- it is centrally located in north-western Europe
- it is easily accessible
- it has excellent infrastructure

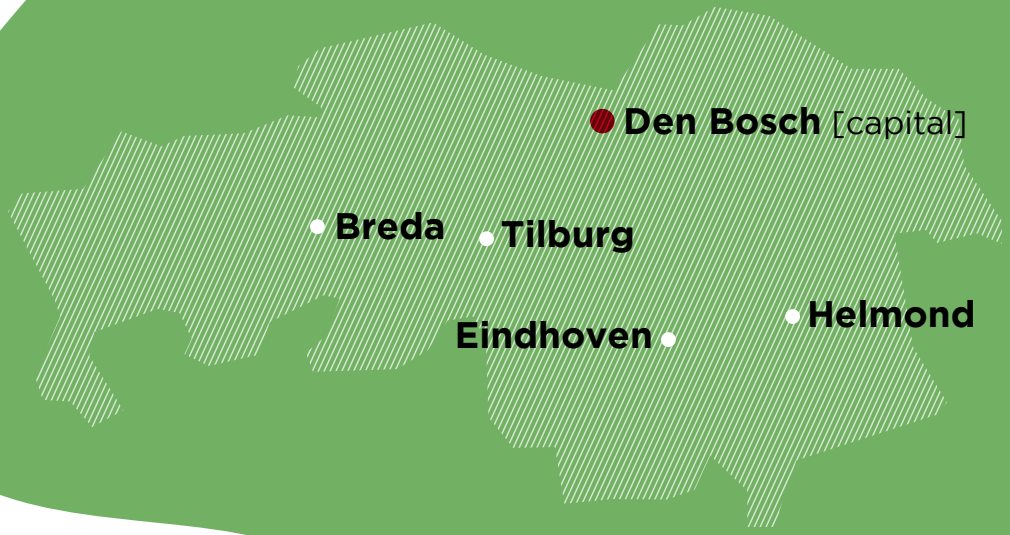
As a whole, time and time again, the Netherlands – with Brabant as its innovative heart – has proven to be a very competitive economy on a global scale!



THE NETHERLANDS, ONE OF THE WORLD'S MOST COMPETITIVE ECONOMIES (WORLD ECONOMIC FORUM (2019) – THE GLOBAL COMPETITIVENESS REPORT 2019

C. Brabant's main cities

Covering 5,000 square kilometres (2,000 square miles), almost 15% (2.5 million inhabitants) of the Dutch population lives in Brabant. The capital of Brabant is Den Bosch, while its largest city is Eindhoven followed by the cities of Tilburg, Breda, Den Bosch and Helmond.



D. Brabant: industry, science and innovation

Brabant is a productive, highly industrialised and knowledge-intensive province in the Netherlands and as such provides attractive opportunities to companies looking for (partnerships in) industrial innovation and/or state-of-the-art manufacturing.

In fact, Brabant is the most intensive region in the Netherlands when it comes to R&D and one of the most innovative regions in Europe, as aptly illustrated by the following three facts:

1. **30% of all industrial R&D in the Netherlands is undertaken in Brabant**
2. **50% of all European patent applications from the Netherlands are generated in Brabant**
3. **Brabant holds fifth place in Europe for regions with the highest number of patent applications**

Source: BOM, Info & Graphics

With over 34,000 people engaged in R&D activities, Brabant can provide the required brainpower thanks to its bright people and numerous research and educational institutes. Geographical clustering results in ready partnerships between businesses, universities and public research institutions. Cooperative R&D results in a mutual bolstering of strengths and inspiration and involves sharing technological know-how, expensive research facilities and being a part of national and European technology programmes. This distinctive collaborative research style is the secret to significantly advancing R&D and innovation activities.

THE NETHERLANDS AND BRABANT - UNIVERSITIES AND PATENT APPLICATIONS

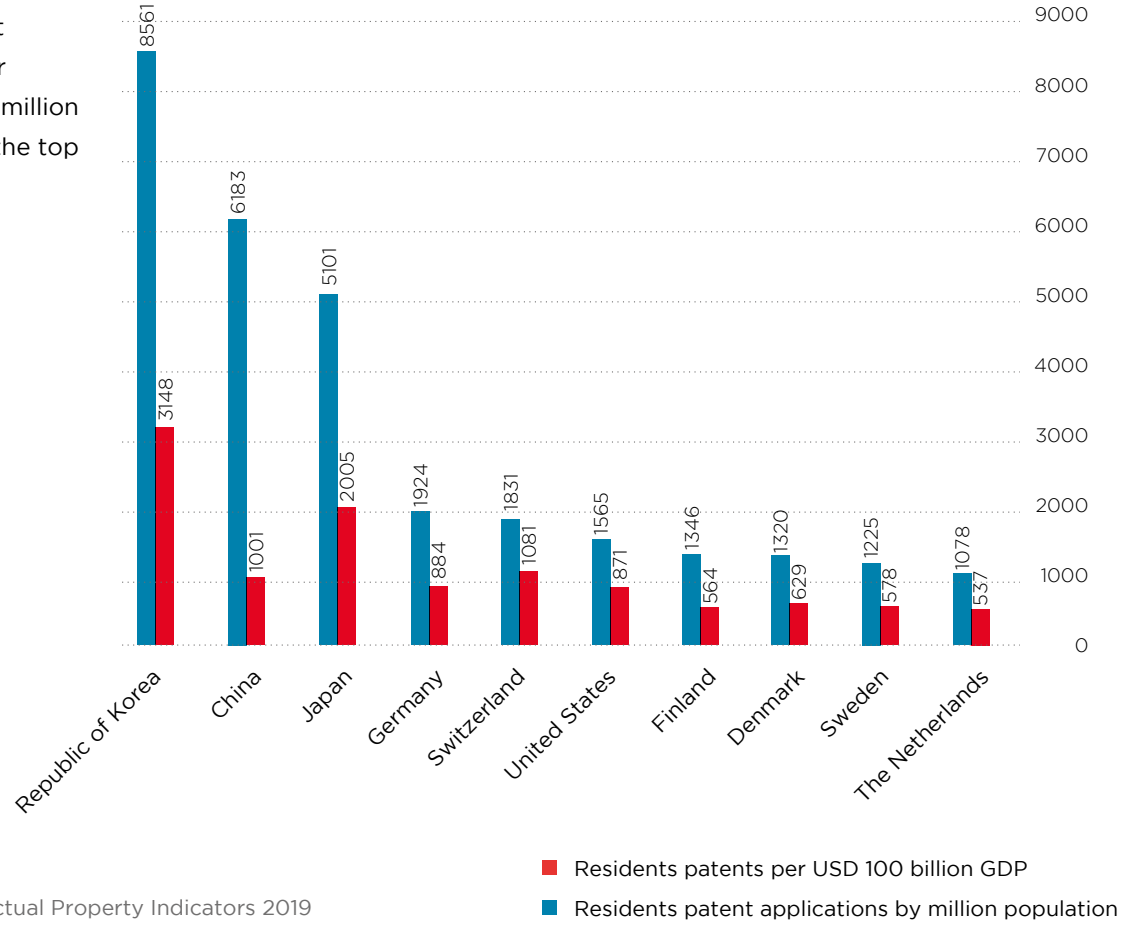
The Netherlands has a large number of high-quality universities and knowledge institutions, which is also why the country took fourth place in the Global Innovation Index 2019 of the World Intellectual Property Organization (WIPO) and is ranked tenth among countries with highest number of patent applications in proportion to GDP and population.

GLOBAL INNOVATION INDEX 2019

1.	Switzerland	67.24
2.	Sweden	63.55
3.	United States of America	61.73
4.	**The Netherlands**	**61.44**
5.	United Kingdom	61.30
6.	Finland	59.83
7.	Denmark	58.44
8.	Singapore	58.37
9.	Germany	58.19
10.	Israel	57.43

NETHERLANDS IN THE GLOBAL TOP 10 FOR PATENT APPLICATIONS

Resident patent applications per billion $ GDP & million population for the top 10 origins 2018

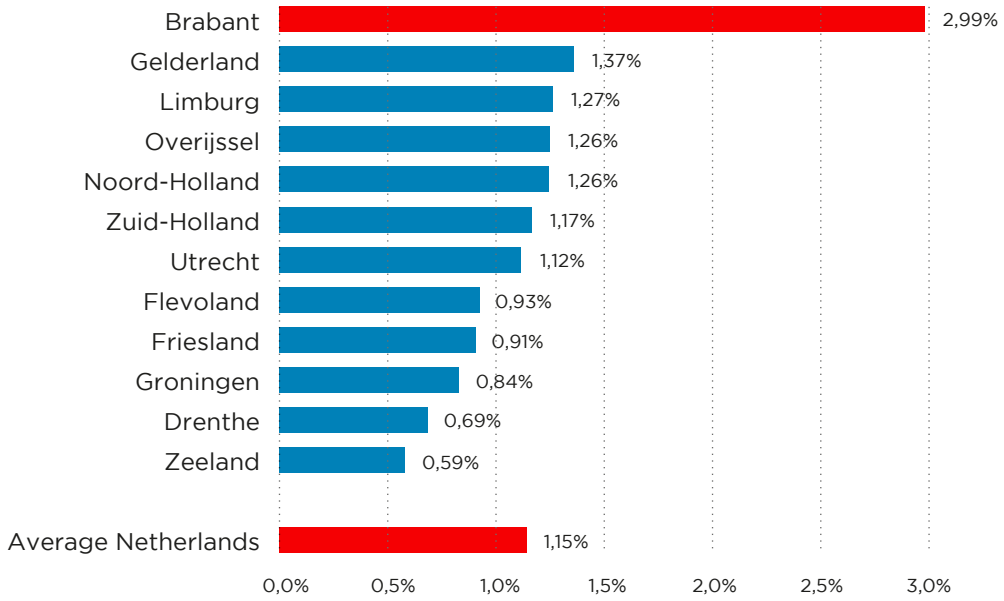


Sources: WIPO (World Intellectual Property Organization) 2019, World Intellectual Property Indicators 2019

HIGH R&D LEVELS IN BRABANT

Brabant has the most R&D activity of all provinces in the Netherlands. Total private sector R&D expenditure in proportion to regional gross domestic product is 2.99%, more than double the national average (1.15%).

PRIVATE R&D EXPENDITURE IN (PERCENTAGE OF GDP) IN 2017



Source: Statistics Netherlands (2019), adapted by Fanion Onderzoek & Advies

HIGH-SCORING R&D REGION IN EUROPE

Brabant is well-known for its activities and strong showing in industrial R&D. On the European stage, Brabant ranks fifth in the list of regions with the highest number of patent applications.

LEADING EUROPEAN REGIONS IN PATENT APPLICATIONS AT THE EUROPEAN PATENT OFFICE 2018

	Region	Country	2018	Growth
1	Bayern	Germany	8.238	8.8 %
2	Île-de-France	France	6.713	-4.4%
3	Nordrhein-Westfalen	Germany	5.125	3.9%
4	Baden Württemberg	Germany	5.082	2.2%
5	**North Brabant**	**The Netherlands**	**3.582**	**-0.8%**
6	Stockholm	Sweden	2.280	7.7%
7	Hessen	Germany	2.205	-0.5%
8	Greater London	Great Britain	1.943	11.9%
9	Niedersachsen	Germany	1.712	16.6%
10	Rhienland-Pfalz	Germany	1.598	0.9%
11	Vlaanderen	Belgium	1.482	7.2%
12	Hovedstaden	Denmark	1.465	9.8%
13	Lombardia	Italy	1.406	-1.5%
14	Auvergne-Rhône-Alpes	France	1.319	3.0%
15	Vaud	Switzerland	1.192	1.2%
16	Helsinki-Uusimaa	Finland	1.188	-11.4%
17	South Holland	The Netherlands	1.066	3.2%
18	Austria West	Austria	1.023	4.4%
19	Zürich	Switzerland	1.014	7.3%
20	Basel-Stadt	Switzerland	980	3.7%

Source: European Patent Office in Link Magazine (March 2019)

E. Facts and figures

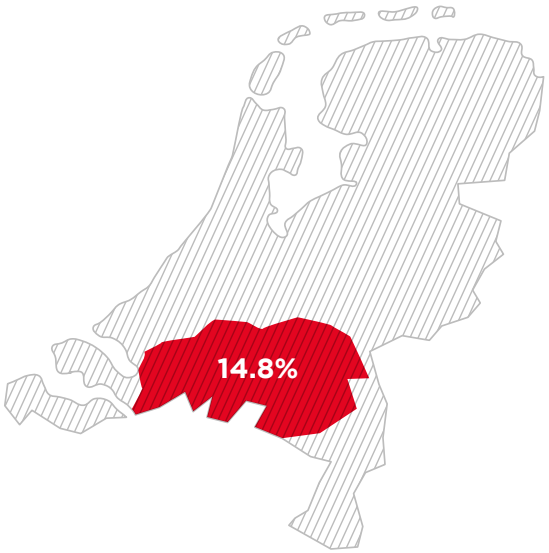
DEMOGRAPHICS

Population as of 01-01-2019
Brabant 2,544,806 14.8%
The Netherlands 17,282,163 100%

Population growth in 2018
Brabant 0.65%
The Netherlands 0.59%

Population density per km²
Brabant 416
The Netherlands 513

Non-Dutch nationals 2019
Brabant 151,254 5.9%
The Netherlands 1,110,859 6.4%



Age groups

	The Netherlands	Brabant
0 - 14	16.1%	15.5%
15 - 64	65.1%	64.9%
65+	18.9%	19.7%
Total	100%	100%

Source: Statistics Netherlands, Eurostat, LISA, BOM, Province of Brabant

THE ECONOMY

GDP for 2018 (in euros x1000, market prices)
Brabant 116,090,000 15%
The Netherlands 774,039,000 100%

Economic growth 2018
Brabant 3.0%
The Netherlands 2.6%

Total own R&D spend as a % of GDP 2017
Brabant 3.06%
The Netherlands 1.98%

Companies
Brabant 231,990 14.2%
The Netherlands 1,630,070 100%

Jobs
Brabant 1,297,560 15%
The Netherlands 8,651,830 100%

Foreign companies 2019
Number of companies in Brabant 1,660
Brabant workforce 119,870

Industrial property
Total available in January 2019 (ha) 1,790
Immediately available in January 2019 (ha) 790

3. INDUSTRY OVERVIEW

A. Database

The definition of the Life Sciences & Health industry is based on the Standard Business Classification (SBI), and the branches that fall under it can be found in the graphic below. There are four major different groups: Pharmaceuticals, Medical Technology, Research and Wholesale. The wholesale branch is an addition to the regular definition of Life Sciences & Health as determined by Statistics Netherlands for the Dutch government's Priority Industry policy.

LIFE SCIENCES & HEALTH

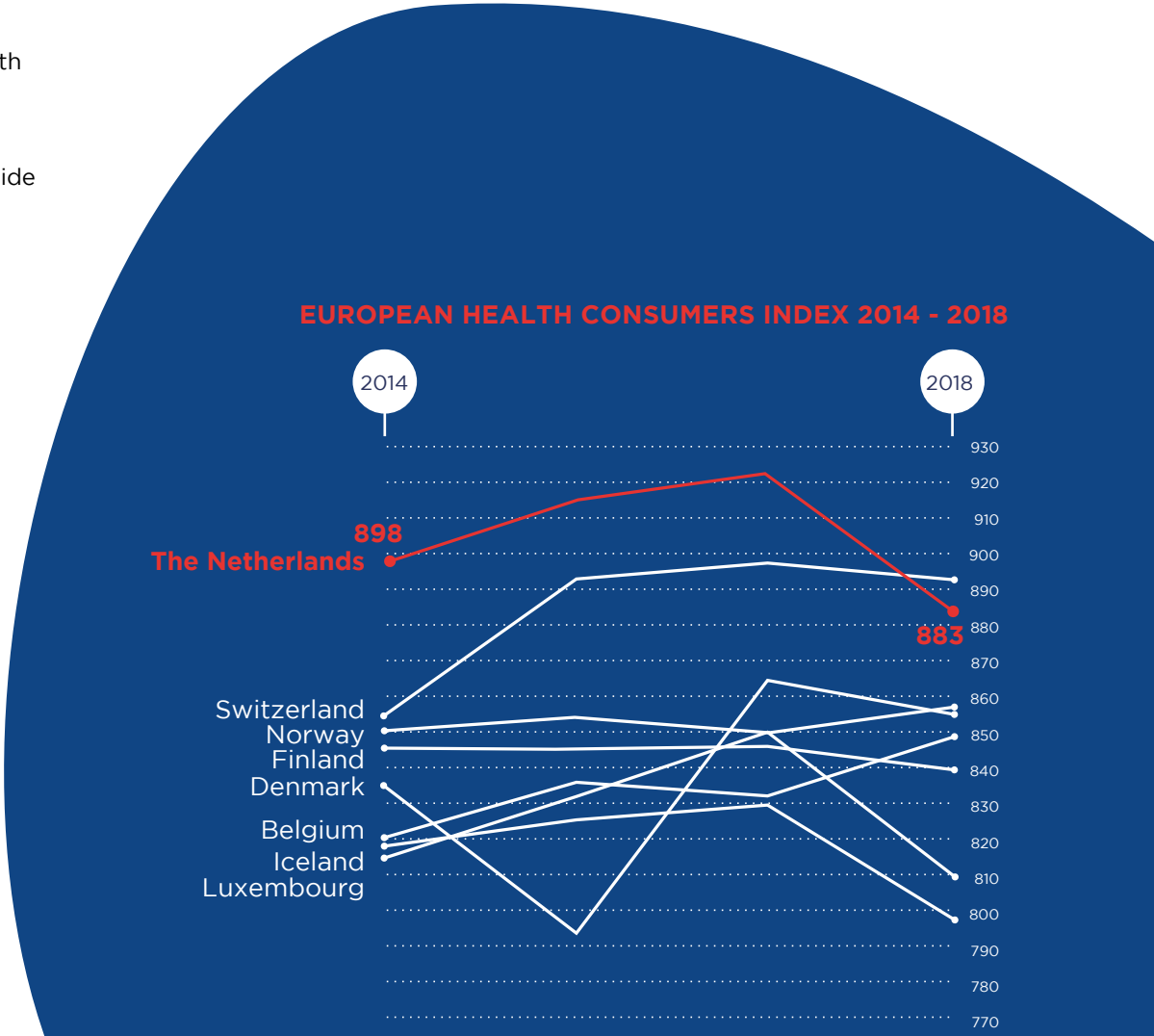
PHARMACY	**MEDICAL TECHNOLOGY (MEDTECH)**	**RESEARCH**	**WHOLESALE**
2110	2660	72112	46461
2120	32501	72193	46462
	32502		

- **2110 Manufacture of basic pharmaceutical products**
- **2120 Manufacture of pharmaceutical preparations**
- **2660 Manufacture of irradiation, electromedical and electrotherapeutic equipment**
- **32501 Dental laboratories**
- **32502 Manufacture of medical instruments and supplies (excluding dental laboratories)**
- **46461 Wholesale of pharmaceutical goods**
- **46462 Wholesale of medical and dental instruments, nursing and orthopaedic articles and laboratory equipment**
- **72112 Biotechnical research and development of medical products and pharmaceutical processes and of food**
- **72193 Research and development on health and food (excluding biotechnical)**

In addition to the companies selected on the basis of this specific data definition, there is a large group of other companies in Brabant also active in the Life Sciences & Health industry, such as related research companies, technical companies and logistics service providers. This group will also be discussed in this review.

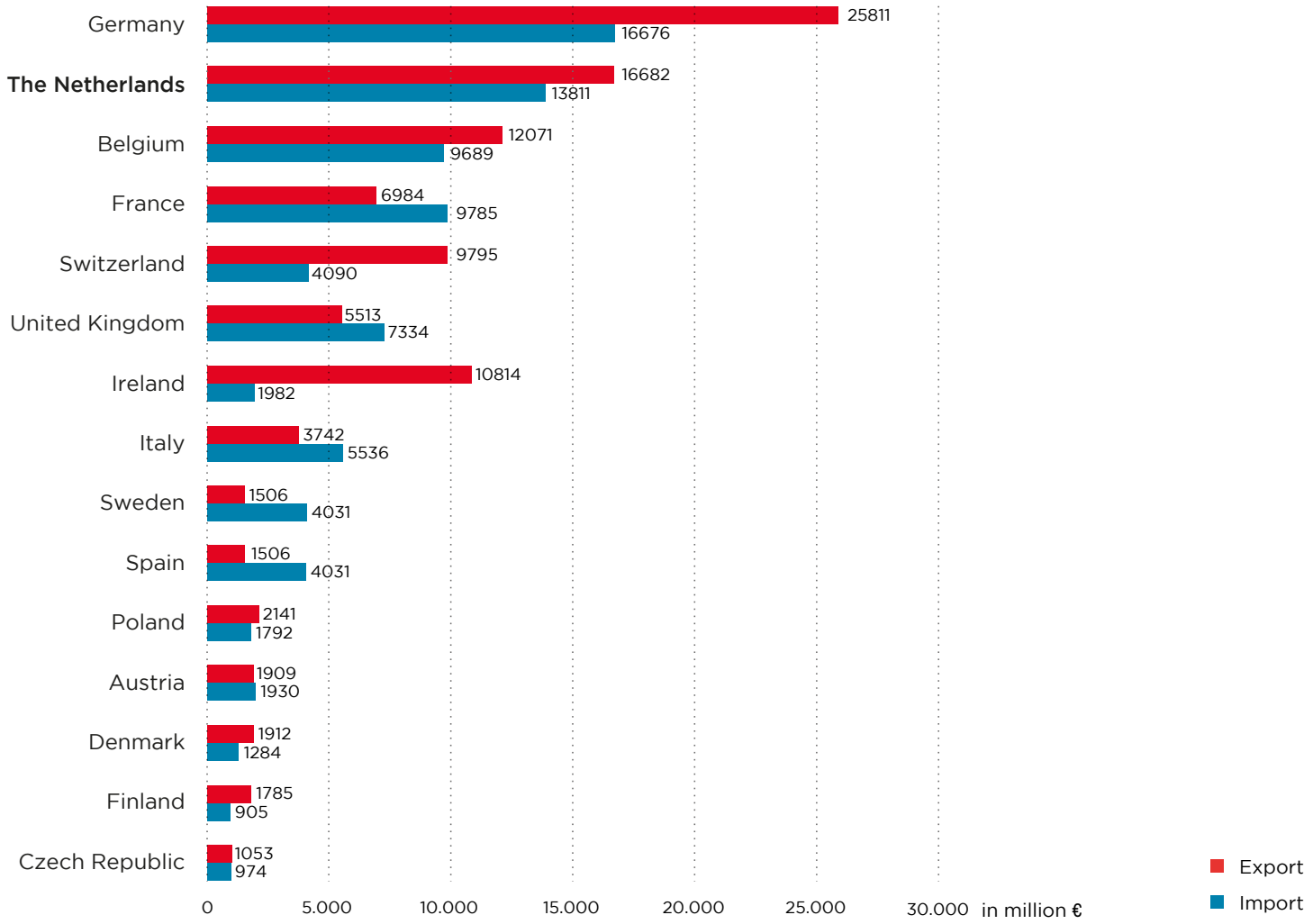
B. The Dutch healthcare sector - an international perspective

1. The Dutch Healthcare System: Dutch healthcare is ranked in the Top 10 globally, and in the European Health Consumer Index the Netherlands has held first place in four of the last five years.
2. The medtech market: when it comes to medtech, the Netherlands is the second largest trading market for medical devices in Europe. Exports, both within and outside the EU, totalled €16.6 billion in 2017.
3. The (bio)pharmaceutical market: for medicinal and biopharmaceutical products, the Netherlands is the fourth-largest exporter to countries outside the EU, with a total export value of over €14 billion.



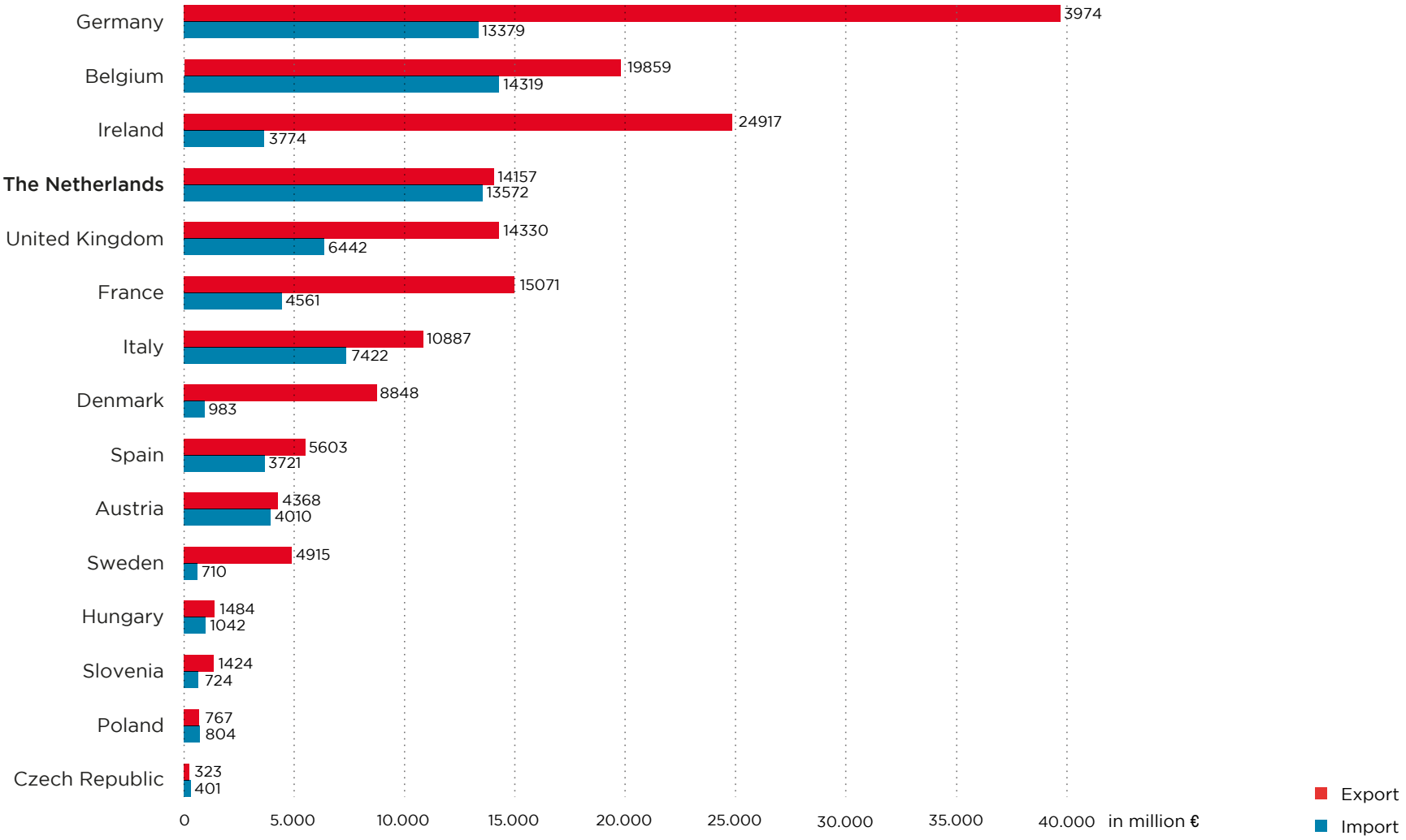
Source: Health Consumer Powerhouse, adapted by Fanion Onderzoek & Advies

EXPORTS AND IMPORTS OF MEDICAL DEVICES PER COUNTRY (INCLUDING INTRA-COMMUNITY TRADE), IN MILLIONS OF EUROS, 2017



Source: Medtech Europe, The European Medical Technology Industry – in figures 2019, adapted by Fanion Onderzoek & Advies

ADDITIONAL EU TRADE IN MEDICINAL AND PHARMACEUTICAL (OTHER THAN MEDTECH) PRODUCTS PER MEMBER STATE, 2018



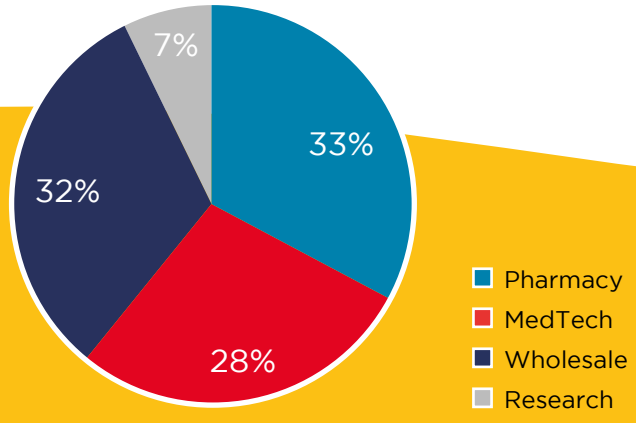
Source: Eurostat COMEXT database, adapted by Fanion Onderzoek & Advies

C. Brabant life sciences industry (under the priority industry definition in the Netherlands)

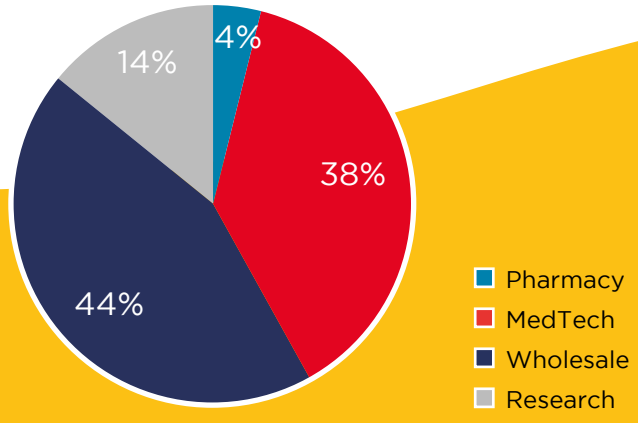
There are 910 Life Sciences & Health companies in Brabant, employing 18,160 people – 15.6% of all Dutch Life Sciences & Health companies and 23.5% of Dutch industry employees. This means that Brabant accounts for a large proportion of all Dutch life sciences jobs.

The majority of these companies are involved in wholesale, followed by medtech. Although pharmaceutical companies only represent 4% of companies in the industry, they account for 33% of jobs. The pharmaceutical industry is made up of relatively large companies in employment terms (on average 150 jobs per company), while the companies in the other branches are relatively small (10-14 jobs per company).

JOBS IN LS&H IN BRABANT



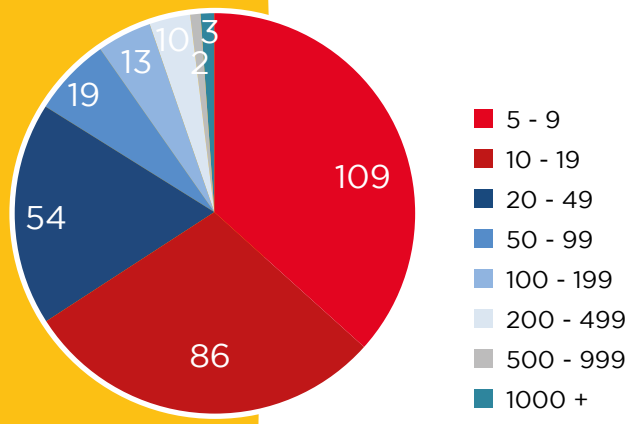
COMPANIES IN LS&H IN BRABANT



Source: Brabant Register of Companies and LISA 2018, adapted by Fanion Onderzoek & Advies

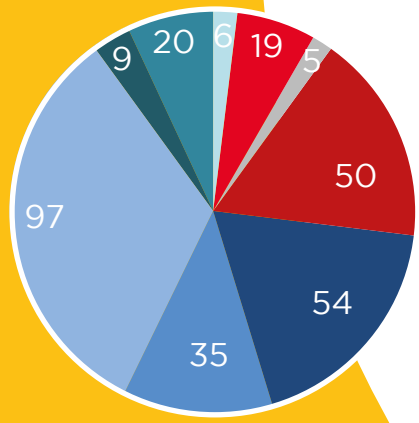
NUMBER OF COMPANIES CATEGORIZED BY SIZE

(number of jobs – minimum of 5 employees) – 295 companies in total



NUMBER OF COMPANIES PER BUSINESS ACTIVITY

(total no. of companies: 295 (5 employees or more))



2110	Manufacture of basic pharmaceutical products
2120	Manufacture of pharmaceutical preparations
2660	Manufacture of irradiation, electromedical and electrotherapeutic equipment
32501	Dental laboratories
32502	Manufacture of medical instruments and supplies (no dental laboratories)
46461	Wholesale of pharmaceutical goods
46462	Wholesale of medical and dental instruments, nursing and orthopaedic articles and laboratory equipment
72112	Biotechnical research and development on medical products and pharmaceutical processes and of food
72193	Research and development on health and food (not biotechnical)

Source: Brabant Register of Companies 2014-2018, LISA 2014 and 2018

NUMBER OF COMPANIES PER BUSINESS ACTIVITY (TOTAL NO. OF COMPANIES: 295 (5 EMPLOYEES OR MORE))

- The largest proportion of companies can be found in **wholesale of medical and dental equipment**, etc. Some of these companies are large, including Zimmer Biomet Global SCC, Medtronic Trading, B. Braun Medical and Medipoint, but in general they are small, regional companies that supply regional, local and national healthcare centres

- Another large subsegment is formed by the dental laboratories and **manufacturers of medical instruments and supplies**. This group generally consists of local firms that manufacture prostheses and function mainly for the regional market. There are large companies in this segment as well: prosthetics' company Össur has major facilities in Eindhoven

- **Manufacture of basic pharmaceutical products**, which covers companies like Patheon, by Thermo Fisher Scientific, MSD Pharmaceutical Operations, MSD Biologicals and MSD Animal Health, Ardena and Agglomix

- Aspen, Amgen, MSD, MSD Animal Health, Dechra Pharmaceuticals and Brocacef are examples of companies that are active in the **manufacture of pharmaceutical preparations**

- Philips Healthcare, VDL ETG (Enabling Technology Group), GE Healthcare Life Sciences Core Imaging and Medtronic represent the **manufacture of irradiation, electromedical an electrotherapeutic equipment** branch

- **Biotechnical research** is principally performed by innovative SME companies such as BioConnection, Hycult Biotech, PharmaCytics, ImmunoPrecise Antibodies Europe and SoliPharma

- **Research and development on health and food** is undertaken by Charles River Laboratories, Eurofins Central Laboratory, RPS Analyse, Illumina Netherlands, Venn Life Sciences and Nutrilab

THE LARGEST LS&H COMPANIES IN BRABANT (NUMBER OF JOBS)

Company	City	Product	Main activities	Country of Origin	# of Jobs
MSD	Oss	Pharmaceutical products (human health)	Production	USA	>1,000
Philips Health Care	Best	Medical systems and devices	Production and R&D	Netherlands	>1,000
Philips Research	Eindhoven	R&D for healthcare systems and cures	R&D	Netherlands	>1,000
MSD Animal Health	Boxmeer	Animal pharmaceuticals	Production and R&D	USA	> 1,000
Amgen Europe	Breda	Pharmaceutical products	Wholesale/Distribution	USA	800-1,000
Aspen	Oss/Boxtel	Pharmaceutical products	Production	South Africa	800-1,000
Charles River Laboratories	Den Bosch/Schaijk	R&D for health	Laboratory/Test Centre	USA	200-500
Patheon – by Thermo Fisher Scientific	Tilburg	Pharmaceutical products	Production and development	USA	200-500
Thermo Fisher Scientific	Breda	Biotechnical research and equipment	Supply Laboratory equipment	USA	100-200
Thermo Fisher Electron Microscopy Solutions (former FEI)	Eindhoven	Medical research equipment	Production and R&D	USA	500-800
Alliance Healthcare	Den Bosch/Veghel	Pharmaceutical products	Distribution	Switzerland	200-500
Zimmer Biomet	Breda	Orthopaedic products	Distribution	USA	200-500
Medtronic Trading	Eindhoven	Medical equipment	Marketing and Sales	USA	200-500
Janssen Cilag (Johnson & Johnson)	Breda	Pharmaceutical products	Marketing and Sales/R&D	USA	200-500
VDL ETG Enabling Technologies Group	Eindhoven	Medical equipment (semi-finished products)	Production/R&D	Netherlands	200-500
Eurofins Scientific	Breda, Oosterhout, Oss, Eindhoven	Laboratory services/R&D	R&D	Netherlands	200-500
Boeren Medical	Eindhoven	Medical equipment and products	Wholesale	Netherlands	100-200
Dechra Pharmaceuticals (formerly Eurovet Animal Health)	Bladel	Animal pharmaceuticals	Production	UK	100-200
Tjaopack	Etten-Leur	Pharmaceutical packaging	Production/Distribution	Netherlands	100-200
B. Braun Medical	Oss	Medical devices	Distribution	Germany	100-200
GE Healthcare Life Sciences Core Imaging	Eindhoven	In-vivo diagnostics and imaging technologies incl. ultrasound and radiology	Sales/Service Centre	USA	100-200
Covetrus Animal Health	Cuijk	Animal healthcare products and medicines	Wholesale	USA	100-200
Össur	Eindhoven	Prosthetics	Distribution	Iceland	100-200
Illumina	Eindhoven	Medical systems and devices	R&D/Sales	USA	100-200
Brocacef	Eindhoven	Pharmaceutical products	Wholesale/distribution	Germany	100-200

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

THE PROVINCE OF BRABANT AS PART OF THE NETHERLANDS

Brabant holds a strong position in the Netherlands when it comes to the Life Sciences & Health industry, especially in the irradiation, electromedical and electrotherapeutic equipment (i.e. imaging, sensors, monitoring, etc), the basic pharmaceutical products and the pharmaceutical preparations manufacturing branches as well as the wholesale of medical and dental instruments, nursing and orthopaedic articles and laboratory equipment branch.

Some 40% of all Dutch jobs in basic pharmaceutical products and pharmaceutical preparations manufacturing are found in Brabant. Brabant is even more dominant when it comes to the manufacture of irradiation, electromedical and electrotherapeutic equipment, such as imaging, health monitoring and sensor equipment, with a share of three-quarters of all jobs in the Netherlands. The province once again has an above-average share in the wholesale of pharmaceutical goods and medical and dental instruments, etc.

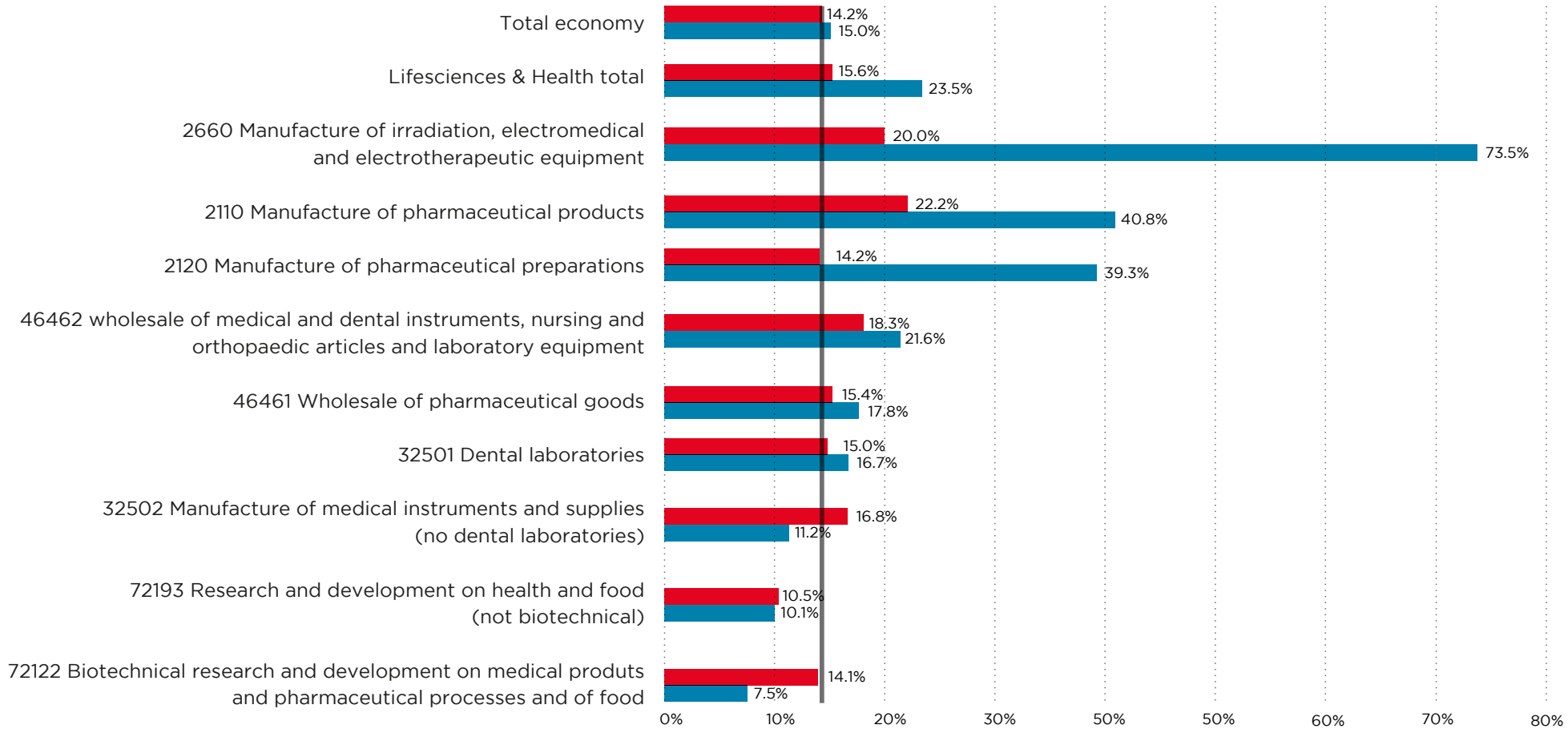
In biotechnical research and R&D for health and food, Brabant's share of the total number of jobs is below average – a fact that is evidently due to registration and administration issues. The databases that are used are dependent on whether companies update their details with the Chamber of Commerce and the provincial government, how they perform those updates and how accurate those updates are. Biotechnical research in Brabant is not a huge business, but it is growing relatively rapidly in locations such as Pivot Park in the field of biopharmaceuticals. R&D for health and food is a major activity in Brabant, as the province is also a major AgriFood region. Examples of these Brabant-based companies include Danone, Nutricia, Cosun, SuikerUnie, Unilever, MARS and FrieslandCampina.

OVERVIEW OF LS&H IN TERMS OF EMPLOYMENT FIGURES AND COMPANIES IN BRABANT AND IN THE NETHERLANDS IN 2018

Branch	Jobs			Companies		
	Brabant	NL	Share	Brabant	NL	Share
2110 Manufacture of basic pharmaceutical products	600	1,470	40.8%	10	45	22.2%
2120 Manufacture of pharmaceutical preparations	5,430	13,800	39.3%	30	204	14.2%
2660 Manufacture of irradiation, electromedical and electrotherapeutic equipment	3,050	4,140	73.5%	10	50	20.0%
32501 Dental laboratories	820	4,910	16.7%	190	1,257	15.0%
32502 Manufacture of medical instruments and supplies (excluding dental laboratories)	1,140	10,110	11.2%	150	883	16.8%
46461 Wholesale of pharmaceutical goods	2,430	13,660	17.8%	110	715	15.4%
46462 Wholesale of medical and dental instruments, nursing and orthopedic articles and laboratory equipment	3,390	15,690	21.6%	290	1,596	18.3%
72112 Biotechnical research and development on medical products and pharmaceutical processes and of food	180	2,350	7.5%	40	312	14.1%
72193 Research and development on health and food (excluding biotechnical)	1,130	11,250	10.1%	80	790	10.5%
Total for Lifesciences & Health	**18,160**	**77,380**	**23.5%**	**910**	**5,852**	**15.6%**

Source: Brabant Register of Companies and LISA 2018

BRABANT'S SHARE OF JOBS AND COMPANIES IN THE NETHERLANDS



Source: Brabant Register of Companies and LISA 2018, adapted by Fanion Onderzoek & Advies

GROWTH OF COMPANIES AND JOBS

The Life Sciences & Health industry has grown significantly in both the Netherlands and in Brabant. Between 2014 and 2018, the number of companies in Brabant increased by 11.1%, outperforming the Netherlands' growth rate of 8.4%. In respect of number of new jobs, the difference between Brabant (at 15.4%) and the Netherlands as a whole (10.2%) was even more pronounced over the same period.

Biotechnical research and development has grown at a particularly rapid rate, and Brabant is catching up with the rest of the Netherlands in this field. The number of biotechnical companies grew by 43% in Brabant and employment almost tripled (an increase of over 260%).

This spectacular growth is largely the result of the success of Brabant's biopharmaceutical research campus, Pivot Park, and the neighbouring MSD (Merck) Pharmaceutical Operations and Biologicals and Aspen. Over the space of seven years, Pivot Park, building on the foundations laid by Organon Research, has grown to become home to 60 biopharmaceutical research companies, contract research organisations (CMOs), contract manufacturing organisations (CROs) and research institutes employing close to 600 people. Examples of highly successful and fast-growing companies include BioConnection, Ardena, Glycostem, NTRC, Lead Pharma, Synaffix and Acerta Pharma. In 2018 AstraZeneca bought a majority (55%) equity stake in Acerta Pharma for approximately $4 billion, but Acerta Pharma's very successful drug discovery and development team remains at Pivot Park. In fact, AstraZeneca is moving an additional clinical trial expertise centre to Pivot Park.

Other branches in Brabant with rapid employment growth are the wholesale in pharmaceuticals (a growth of 24%) and medical, dental, laboratory and orthopaedic equipment and nursing goods (up 26%) and manufacture of basic pharmaceutical products (up 39%) branches.

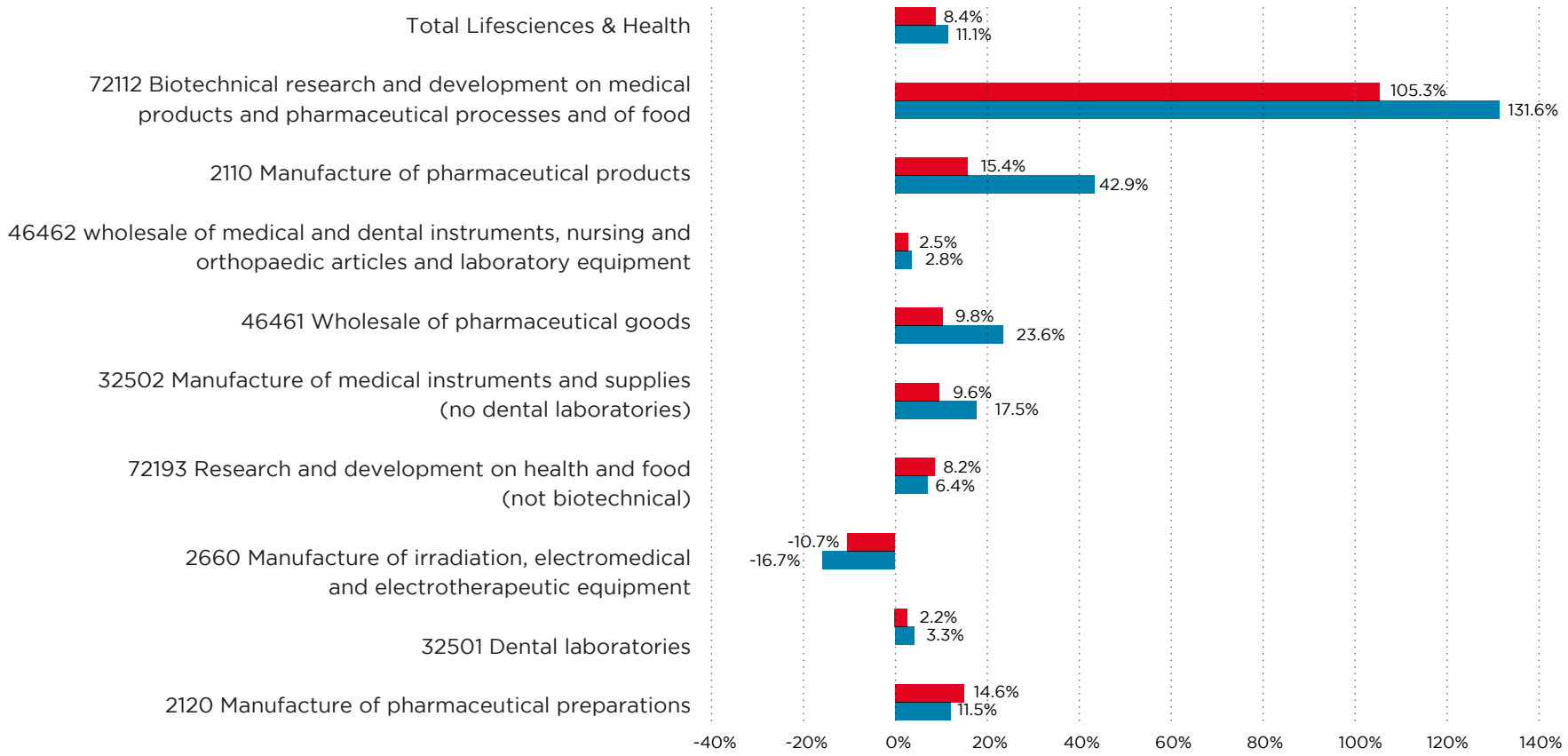
The manufacturing of irradiation, electromedical and electrotherapeutic equipment branch registered a slight decrease – a surprising development, given that Brabant generally excels in medtech, under which this branch falls. But it should be noted that there are very few companies in this category (12 companies in 2014 in Brabant), and the big ones are really big, such Philips Healthcare and Research. A closer examination of the data has revealed that, in the four years after 2014, five small companies either left Brabant, shut down a subsidiary or changed their activity code, while three companies joined this small group – a net loss of two companies. The number of jobs in this sector has increased over the same period in Brabant. And so, this apparently surprising statistic does not pose a threat to the branch's status in Brabant.

GROWTH OF LIFE SCIENCES & HEALTH COMPANIES AND JOBS, 2014-2018

		JOBS						COMPANIES					
		BRABANT			NETHERLANDS			BRABANT			NETHERLANDS		
		2014	2018	growth	2014	2018	growth	2014	2018	growth	2014	2018	growth
2110	Manufacture of basic pharmaceutical products	430	600	39.2%	1,170	1,470	26.1%	7	10	11.5%	39	45	15.4%
2120	Manufacture of pharmaceutical preparations	5,180	5,430	4.7%	13,180	13,800	4.8%	26	29	3.3%	178	204	14.6%
2660	Manufacture of irradiation, electromedical and electrotherapeutic equipment	2,710	3,050	12.3%	3,880	4,140	6.7%	12	10	-16.7%	56	50	-10.7%
32501	Dental laboratories	770	820	6.1%	4,850	4,910	1.2%	182	188	6.4%	1,230	1,257	2.2%
32502	Manufacture of medical instruments and supplies (excluding dental laboratories)	960	1,140	18.4%	9,230	10,110	9.6%	126	148	17.5%	806	883	9.6%
46461	Wholesale of pharmaceutical goods	1,960	2,430	23.8%	12,510	13,660	9.2%	89	110	23.6%	651	715	9.8%
46462	Wholesale of medical and dental instruments, nursing and orthopedic articles and laboratory equipment	2,700	3,390	25.8%	14,280	15,690	9.9%	284	292	2.8%	1,557	1,596	2.5%
72112	Biotechnical research and development on medical products and pharmaceutical processes and of food	50	180	259.2%	1,240	2,350	89.5%	19	44	42.9%	152	312	105.3%
72193	Research and development on health and food (excluding biotechnical)	970	1,130	16.6%	9,910	11,250	13.5%	78	83	131.6%	730	790	8.2%
Total for Life Sciences & Health		**15,740**	**18,160**	**15.4%**	**70,240**	**77,380**	**10.2%**	**823**	**914**	**11.1%**	**5,399**	**5,852**	**8.4%**

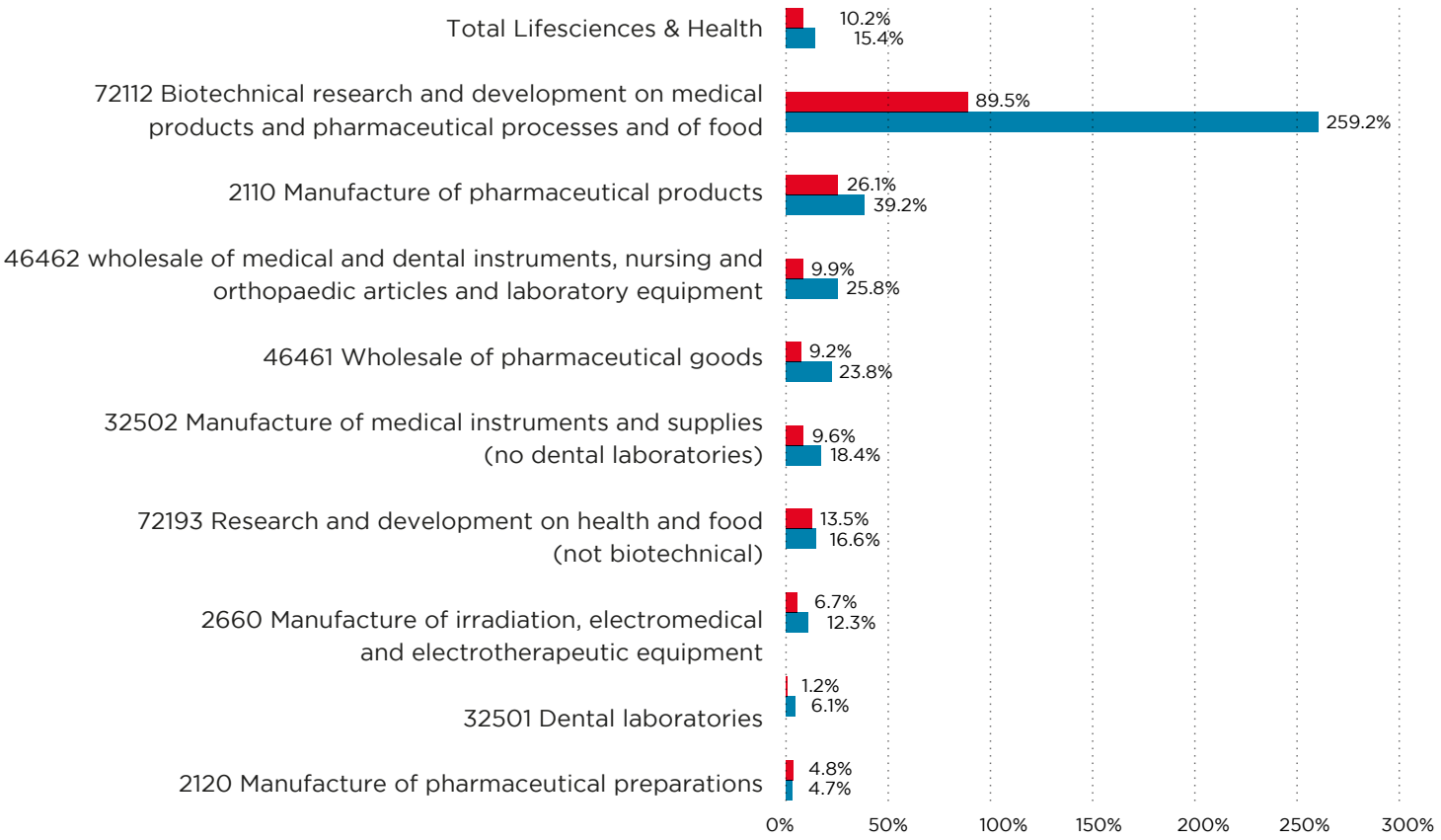
Source: Brabant Register of Companies 2014-2018, LISA 2014 and 2018

GROWTH OF LIFE SCIENCES & HEALTH COMPANIES, 2014-2018



Source: Brabant Register of Companies 2014-2018, LISA 2014 and 2018

GROWTH OF LIFE SCIENCES & HEALTH JOBS, 2014-2018



Source: Brabant Register of Companies 2014-2018, LISA 2014 and 2018

D. Other LS&H companies (not falling under the priority industry definition)

HIGH TECH MANUFACTURING IN LIFE SCIENCES & HEALTH

In addition to the companies discussed under section C, which carry an activity code exactly matching the boundaries set for the Dutch Life Sciences & Health Priority Industry, a significant number of companies are located in Brabant that are likewise active in Life Sciences & Health, but have been registered under a different Standard Industrial Classification (or SIC) code. This can be the result of a backlog in the Chamber of Commerce or the provincial registry or just because the company never changed its SIC code when it engaged in new activities.

The companies in question are generally tier 1 and tier 2 suppliers to the LS&H manufacturing chain, but there are also a number of OEM companies. A total of 87 companies in the production chain have been identified as closely related to medtech, biopharma and/or the healthcare sector. Examples include suppliers of high tech precision parts (both metal and plastics), bodywork, electronic modules, embedded software, measuring and control equipment, management software, air and water treatment systems and so on.

These companies have a total of 9,500 employees. By far the largest and most well-known is Philips Electronics Nederland (an OEM company). Philips has a 3,500-strong workforce at the High Tech Campus in Eindhoven, which is the company's global research headquarters and global research centre, with a predominant focus on healthcare. The Philips branch is still registered under the activities of its predecessor in Eindhoven – the consumer electronics company – and thus not considered an LS&H company under the priority industry definition. Philips management at the High Tech Campus in Eindhoven confirms that 80% of the work undertaken by Philips at the HTCE is healthcare-related.

THE 30 LARGEST COMPANIES (OEM, TIER 1 AND 2 SUPPLIERS) ACTIVE IN OR SUPPLYING TO THE HEALTHCARE INDUSTRY

Company	City	Main activities	Country of Origin	# of Jobs
Philips Electronics Nederland B.V.	Eindhoven	Research	The Netherlands	More than 1.000
Prodrive Technologies	Eindhoven	High quality medical equipment	The Netherlands	More than 1.000
Thermo Fisher Scientific (former FEI)	Eindhoven	Electron microscopes	United States of America	500 - 800
Applied Micro Electronics (AME) B.V.	Eindhoven	Electronic products	The Netherlands	200 - 500
Buvo Castings B.V.	Helmond	Casting Aluminum parts	The Netherlands	200 - 500
VDL Enabling Technologies Group	Eindhoven	Components and modules	The Netherlands	200 - 500
Omron Manufacturing of the Netherlands B.V.	Den Bosch	Measuring and control equipment	Japan	100 - 200
Neways Industrial Systems B.V.	Son en Breugel	Electronics / Electronic components	The Netherlands	100 - 200
Sioux Embedded Systems B.V.	Eindhoven	Integrated solutions software and systems.	The Netherlands	100 - 200
Kulicke & Soffa Netherlands B.V.	Eindhoven	Machine construction and printed circuit boards	Singapore	100 - 200
Neways Technologies B.V.	Son en Breugel	Electronics / Electronic components	The Netherlands	100 - 200
Frencken Mechatronics B.V.	Eindhoven	Mechatronics / Machine construction	The Netherlands	100 - 200
Stichting IMEC Nederland	Eindhoven	Research electronic products	The Netherlands	100 - 200
Siemens Industry Software B.V.	Den Bosch	Software solutions / embedded systems	Germany	100 - 200
Rols Machine-Onderdelen B.V.	Geldrop	Machine parts and components	The Netherlands	50 - 100
Thales Cryogenics B.V.	Eindhoven	High-quality cooling systems	France	50 - 100
TNO	Eindhoven	Research	The Netherlands	50 - 100
Total Support B.V.	Eindhoven	Mechatronic projects	The Netherlands	50 - 100
IGS GEBOJAEGEMA B.V.	Eindhoven	Plastic forms	The Netherlands	50 - 100
Adimec	Eindhoven	Scientific cameras	The Netherlands	50 - 100
VDL Apparatenbouw B.V.	Eersel	Systems and devices	The Netherlands	50 - 100
VDL Fibertech Industries B.V.	Hapert	Synthetic fiber materials	The Netherlands	50 - 100
TMC Mechatronics B.V.	Eindhoven	System architects	The Netherlands	50 - 100
Machinefabriek Frencken B.V.	Eindhoven	Mechatronics / Machine construction	The Netherlands	50 - 100
TMC Field Service Eindhoven B.V.	Eindhoven	System architects	The Netherlands	50 - 100
Parker Hannifin Manufacturing Netherlands	Etten-Leur	Components and parts	United States of America	50 - 100
Cematec Engineering B.V.	Roosendaal	Engineering advice	The Netherlands	50 - 100

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

Continued on next page >

THE 30 LARGEST COMPANIES (OEM, TIER 1 AND 2 SUPPLIERS) ACTIVE IN OR SUPPLYING TO THE HEALTHCARE INDUSTRY

Company	City	Main activities	Country of Origin	# of Jobs
Luminex B.V.	Den Bosch	Measuring and control equipment	United States of America	50 - 100
G.T.A. (Gear Technology Applications) B.V.	Someren	Precision parts	The Netherlands	50 - 100
Machinefabriek Kusters Goumans	Beek en Donk	Precision parts	The Netherlands	20 - 50
Jansen Machining Technology BV	Valkenswaard	Precision mechanical components and various parts	The Netherlands	20 - 50
Stirling Cryogenics	Son en Breugel	High-quality cooling systems	The Netherlands	20 - 50

SUPPLIERS TO THE BIOPHARMACEUTICAL SECTOR

Company	City	Main activities	Country of Origin	# of Jobs
Thermo Fisher Scientific (former FEI)	Eindhoven	Electron microscopes	United States of America	500 - 800
Siemens Industry Software B.V.	Den Bosch	Software solutions / embedded systems	Germany	100 - 200
Malvern Panalytical B.V.	Eindhoven	Spectrometers, X-ray equipment	United Kingdom	50 - 100
VDL Apparatenbouw B.V.	Eersel	Systems and devices	The Netherlands	50 - 100
Parker Hannifin Manufacturing Netherlands (Filtration & Separation)	Etten-Leur	Components and parts	United States of America	50 - 100
Luminex B.V.	Den Bosch	Measuring and testing equipment	United States of America	50 - 100
G.T.A. (Gear Technology Applications) B.V.	Someren	Precision parts	The Netherlands	50 - 100
Berson UV-techniek	Nuenen	UV treatment and disinfection	United Kingdom	20 - 50
eHealth Ventures Group	Oud Gaste	Digital solutions	The Netherlands	20 - 50
Robopharma B.V.	Waalwijk	Pharmacy/Drugstore automation	The Netherlands	10 - 20
Protechnicon Pharma B.V.	Eindhoven	Process rooms/Cleanrooms	The Netherlands	< 5
Orcapharma B.V.	Heesch	Software	The Netherlands	< 5

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

SUPPLIERS TO HOSPITALS, CARE INSTITUTIONS, GENERAL PRACTITIONERS AND DRUGSTORES (SELECTION)

Company	City	Main activities	Country of Origin	# of Jobs
Systemair B.V.	Waalwijk	Air treatment	Sweden	100 - 200
PharmaPartners B.V.	Oosterhout	Software for care	The Netherlands	100 - 200
VECOZO B.V.	Tilburg	Service organization	The Netherlands	100 - 200
Lubron Waterbehandeling BV	Oosterhout	Water systems	The Netherlands	50 - 100
Vega-Systems B.V.	Oss	Washing machines	The Netherlands	50 - 100
Epic Den Bosch B.V.	Den Bosch	Health software	United States of America	50 - 100
G2 Speech B.V.	Nuenen	Voice recognition	The Netherlands	20 - 50
IT&Care B.V.	Son en Breugel	Software / services	The Netherlands	20 - 50
H.P.S. Connectivity Solutions	Oss	IT	The Netherlands	20 - 50
Cleanlease Medical	Eindhoven	Laundry services	The Netherlands	20 - 50
Synergy Health Ede B.V., a STERIS Company	Etten-Leur	Disinfection / sterilization instruments	United Kingdom	20 - 50
PinkRoccade Healthcare B.V.	Den Bosch	Software / services	The Netherlands	10 - 20
(Axians) VCD Healthcare B.V.	Eindhoven	ICT / Services	The Netherlands	< 5
MGP eHealth B.V.	ICT / Services	Oirschot	Netherlands	< 5

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

SPECIALISED LOGISTICS SERVICES PROVIDERS TO LS&H COMPANIES

Also adding to Brabant's overall clout in the Life Sciences & Health industry is its abundance of specialised logistics service providers with dedicated systems and materials for biopharma and medical technology. Below we have included a select list of specialised, dedicated LS&H logistics companies with significant operations in Brabant. They have warehousing and transportation facilities and equipment specifically designed for biopharmaceutical purposes, i.e. temperature-controlled and condition-monitored. The large majority of these companies are GDP-certified.

3/4PL LOGISTICS SERVICE PROVIDERS TO THE BIOPHARMACEUTICAL AND MEDTECH SECTOR

Company	City	Country of Origin	# of Jobs
DB Schenker Logistics Nederland (Healthcare Hub contract logistics)	Tilburg	Germany	500 - 1,000
Rhenus (7 establishments)	Tilburg, Eindhoven, Son, Etten-Leur, Best	Germany	500 - 800
DSV	Moerdijk/Zevenbergen	Denmark	200 - 500
E. van Wijk Logistics B.V.	Giessen	Netherlands	200 - 500
Van Rooijen Logistiek B.V.	Eindhoven	Netherlands	200 - 500
Alloga	Veghel	United Kingdom	100 - 200
Brocacef Healthcare Logistics	Boxtel/Eindhoven	Germany	100 - 200
O&M-Movianto Nederland BV	Oss	United States	50 - 100
Base Logistics B.V.	Klundert	Netherlands	50 - 100
Healthlink Europe	Den Bosch/Waalwijk/Tilburg	United Kingdom	50 - 100
CEBAN	Breda	Netherlands	20 - 50
I&L Logistiek	Berkel-Enschot	Netherlands	20 - 50
Nassau Medicool Transport	Breda	Netherlands	20 - 50
Otentic Logistics B.V.	Oosterhout	Netherlands	20 - 50
Yusen Logistics Benelux	Moerdijk	Japan	20 - 50
ARCO Transport & Logistics B.V.	Breda	Netherlands	10 - 20
Quality Transports B.V.	Best	Netherlands	< 5

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

E. The complete LS&H value chain is both present and well-developed

When one adopts an all-in perspective of the complete Life Sciences & Health industry in the province of Brabant in the Netherlands, one can rightly conclude that the full industrial value chain is in place and very well-developed. The following graphic provides a good illustration of this fact.

THE INTEGRATED VALUE CHAIN LIFE SCIENCES & HEALTH BRABANT – A SELECTION OF COMPANIES

INBOUND LOGISTICS	FUNDAMENTAL RESEARCH	PRODUCT DEVELOPMENT	HEALTH, SAFETY & EFFICACY RESEARCH	PRODUCT APPROVAL	MANUFACTURING	MARKETING & SALES	OUTBOUND LOGISTICS
• AMGEN • Abbot Logistics	• Cytura Therpeutics • ImmunoPrecise • Citryll • Certara • Acerta Pharma (AstraZeneca)	• Glycostem • Lead Pharma • Synnafix • NTRC • Acerta Pharma (AstraZeneca)	• Charles Rivers Laboratories • BioFacilities, Landerd Campus • Janssen-Cilag • Venn Life Sciences • Edwards Life Sciences • Ardena	• InnSense • Janssen-Cilag • Zwiers Regulatory Consultancy • MSD (Merck) Biologicals & Pharmaceutical Operations • MSD (Merck) Animal Health	• Aspen • MSD (Merck) Biologicals & Pharmaceutical Operations • MSD (Merck) Animal Health • AMGEN • Agglomix • Dechra Pharmaceuticals	• AMGEN • Janssen-Cilag • Covetrus Animal Health • MSD (Merck) Animal Health • Brocacef • Centrafarm/STADA	• AMGEN • Abbot Logistics • Thermo Fisher Scientific / Pantheon Softgels • Alliance Healthcare • Brocacef
• Thermo Fisher Scientific • Medtronic • Zimmer Biomet Global SSC • Hollister	• Philips Healthcare • Thermo Fisher Scientific Electron Microscopy Solutions • DEMCON • GE Healthcare Life Sciences Core Imaging • VanBerlo Agency • Hendrix Genetics • MicroSure • Preceyes	• Philips Healthcare • VDL ETG, Enabling Technologies Group • Thermo Fisher Scientific Electron Microscopy Solutions • DEMCON • GE Healthcare Life Sciences Core Imaging • Össur • MicroSure • Preceyes	• Philips Healthcare • GE Healthcare Life Sciences Core Imaging • Bambi Medical	• Philips Healthcare • Thermo Fisher Scientific Electron Microscopy Solutions • GE Healthcare Life Sciences Core Imaging	• Philips Healthcare • Thermo Fisher Scientific Electron Microscopy Solutions • GE Healthcare Life Sciences Core Imaging • Össur • DEMCON	• Philips Healthcare • Medtronic • Össur • Illumina • Adimec • Ventinova Medical • Blue Medical Devices/ Wellinq • MedEye	• Zimmer Biomet Global SSC • Hollister • B. Braun Medical • Boeren Medical • Illumina • Malvern Panalytical • GCX Corporation

SUPPORT INDUSTRY & SERVICES: HR, FINANCE, IP, IT, CERTIFICATION, PACKAGING, INFRASTRUCTURE ETC.

Systemair – Tjaopack – Sioux Embedded Systems – Omron – Neways Technology – Thales Cryogenics – IT&Care – STERIS / Synergy – Arnold & Siedsma – PerkinElmer / One Source

OUTSOURCED SERVICES: LOGISTICS (3PL, 4PL); RESEARCH (CRO); MANUFACTURING (CMO); SALES (AGENTS & DISTRIBUTORS)

BioConnection – Rhenus – Ardena – O&M Movianto – Pivot Park Screening Centre – DB Schenker Healthcare Hub – ImmunoPrecise – HealthLink – Eurofins / Spinnovation Analytical

UNIVERSITIES & KNOWLEDGE INSTITUTES

Radboud University Medical Center (Nijmegen) – TU/e. Eindhoven University of Technology – JADS, Jheronimus Academy of Data Science (a.o. Den Bosch)
Avans University of Applied Sciences (a.o. Breda) – Fontys University of Applied Sciences (a.o. Eindhoven, Den Bosch) – Holst Centre (Eindhoven)

Source: Engel – Een Heldere Blik helder@benengel.nl – +31 (0)652612671

■ (Bio)Pharma
■ MedTech or MedTech and (Bio)Pharma

F. Distribution of LS&H production value across the Netherlands

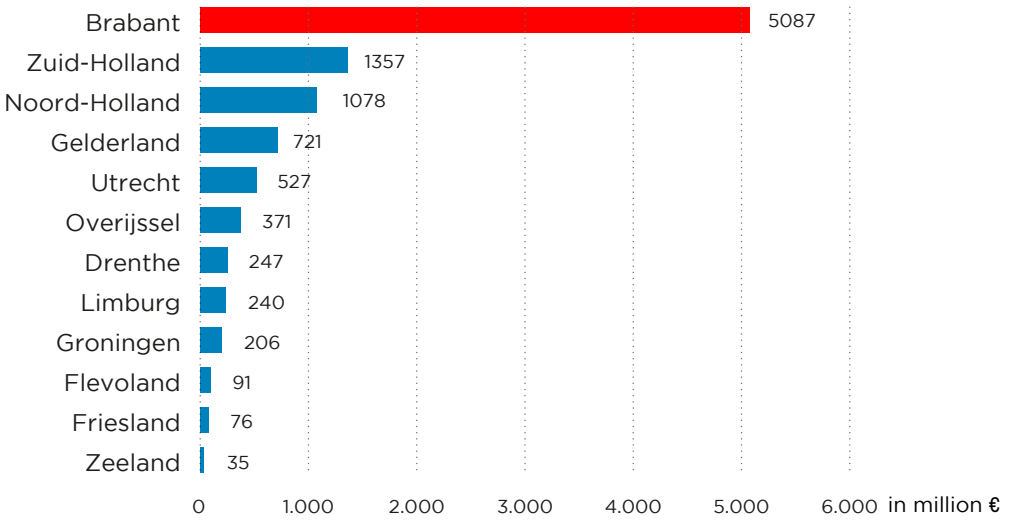
PRODUCTION VALUE (EXCLUDING WHOLESALE)

Brabant is a major contributor to the production value of the Life Sciences & Health industry (wholesale excluded) in the Netherlands. In 2014, Brabant's production value in the industry stood at over €5 billion, more than the production value of all the other eleven provinces combined.

The principle reason for that achievement is, of course, the number of large multinational companies based in Brabant, such as Philips Health Care, MSD, MSD Animal Health, Aspen, VDL ETG and Thermo Fisher Scientific.

The south-eastern region of Brabant (Eindhoven for medtech) and the north-eastern region (Den Bosch/Oss/Boxmeer for pharmaceuticals) are the province's hotspots. Other hotspots in the Netherlands include the Leiden and Utrecht regions.

PRODUCTION VALUE OF THE LS&H PRIORITY INDUSTRY (WHOLESALE EXCLUDED) BY PROVINCE, 2014 (PUBLISHED IN 2017)



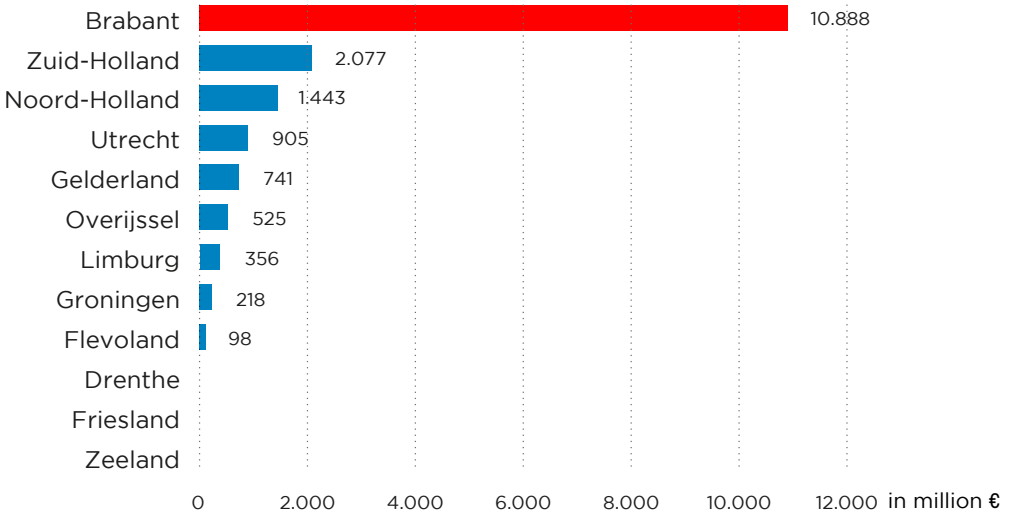
Source: Monitor Top Sectoren 2017, Statistics Netherlands, adapted by Fanion Onderzoek & Advies

PRODUCTION VALUE IN 2013, INCLUDING WHOLESALE

In 2017, the figures for the Life Sciences & Health production value in 2013 were modified to exclude wholesale activities. In the 2016 version of those figures, wholesale was still included. They are presented below, and it is evident here that the difference between Brabant and rest of the Netherlands in terms of production value is then even more dramatic.

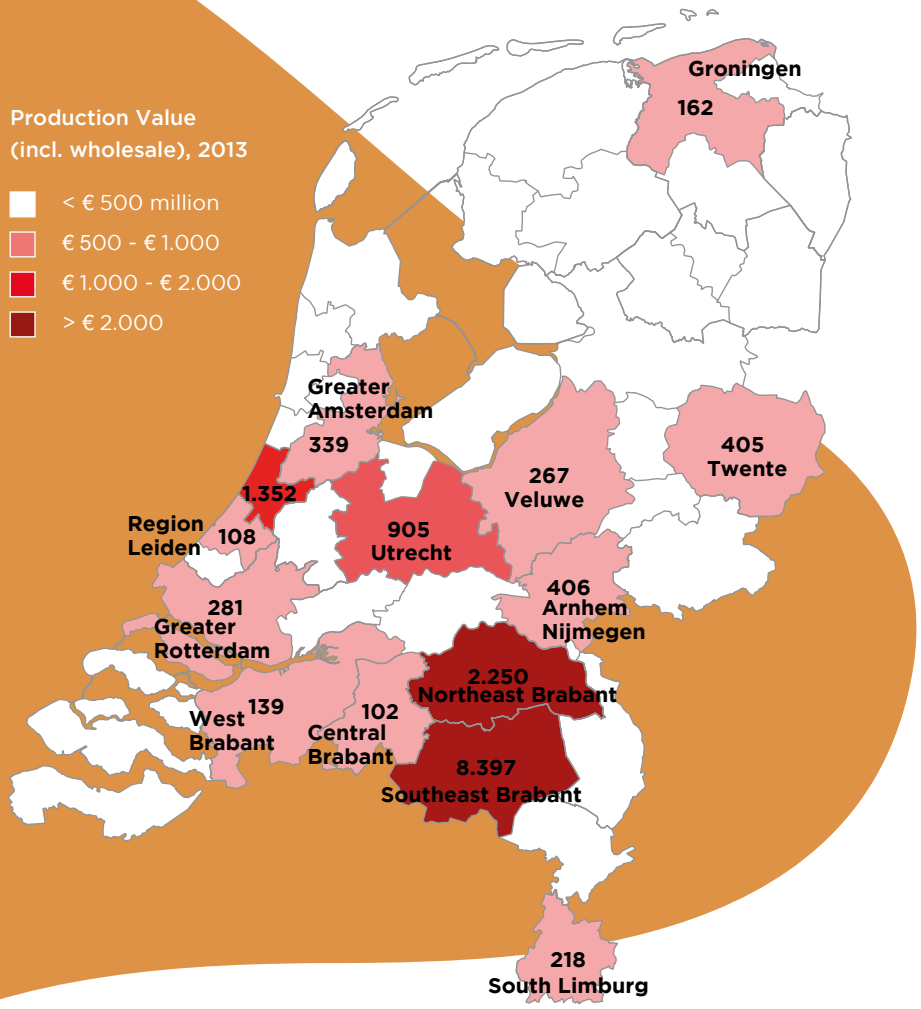
This was the last time Statistics Netherlands collected national and regional production value data, and later information is no longer available. Since that time Brabant's high tech industrial R&D and manufacturing capabilities became even stronger, including in medtech and biopharmaceuticals, and so it is safe to assume that the proportion of production value held by Brabant and the other Dutch regions has not changed significantly since 2014.

PRODUCTION VALUE OF THE LS&H PRIORITY INDUSTRY (WHOLESALE INCLUDED) BY PROVINCE, 2013 (PUBLISHED IN 2016)



Source: Monitor Top Sectoren 2016, Statistics Netherlands, adapted by Fanion Onderzoek & Advies

PRODUCTION VALUE IN LS&H BY REGION IN 2013 (INCLUDING WHOLESALE)

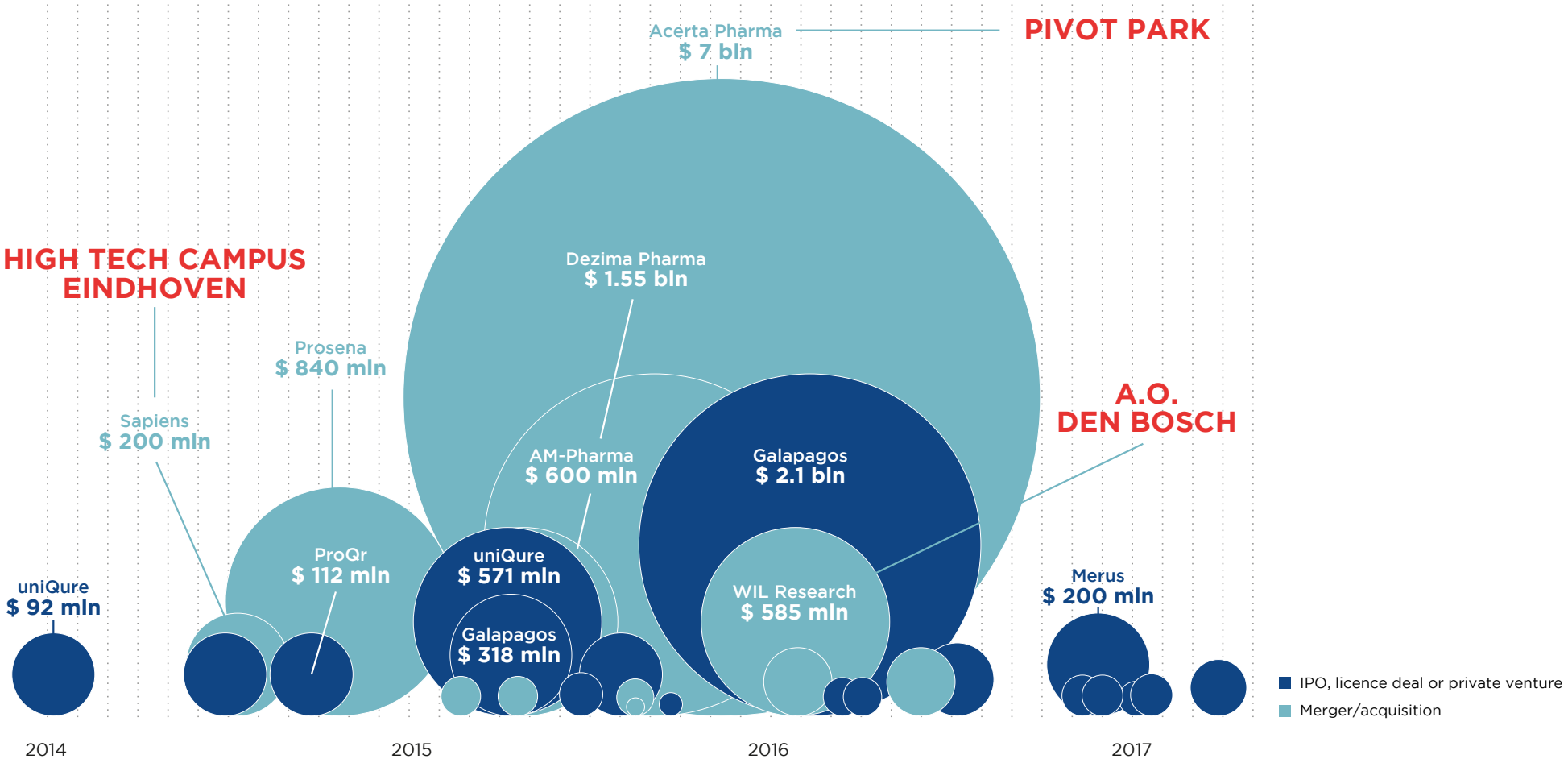


Source: Monitor Top Sectoren 2016, Statistics Netherlands, adapted by Fanion Onderzoek & Advies

G. Significant LS&H mergers and acquisitions in the Netherlands

Brabant was the scene for the largest acquisition by far (AstraZeneca's takeover of Acerta Pharma) as well as two other top-10 M&As in the past decade in the Netherlands.

MERGERS AND IPO'S



Source: Health~Holland, adapted by Engel – Een Heldere Blik

H. Regional distribution of LS&H activities within Brabant

Brabant is administratively divided into four subregions: the Den Bosch region, which in reality makes up the whole north-eastern part of the province, including Oss and Boxmeer, the Eindhoven/Helmond region, which covers all of south-eastern Brabant, the Tilburg region, being the central part of the province, and the Breda region, which covers the western part of Brabant.

With these geographic boundaries in mind, the Den Bosch and Eindhoven/Helmond regions have the largest concentration of companies and highest employment figures in Life Sciences & Health. The profiles of these two regions are quite different. In the Den Bosch area – Oss and Boxmeer in particular – many companies are active in the discovery, development and production of (bio)pharmaceuticals (both human and veterinary). Examples include MSD, MSD Animal Health, Aspen, BioConnection, Acerta Pharma and Lead Pharma.

The Eindhoven/Helmond area, meanwhile, is a global leader in the field of medical technology, thanks to companies like Philips Healthcare, Philips Research, VDL ETG, Thermo Fisher Scientific (formerly FEI Company), Illumina and GE Healthcare Life Sciences Core Imaging.

The Breda area also exhibits a concentration of activities and jobs, especially those related to wholesale and support services in medtech and pharmaceuticals. Both AMGEN and Abbott have large-scale European distribution centres here, while marketing and sales operations and customer-oriented support services for IT, purchasing, contact centres and other services are also present. AMGEN performs GMP-certified manufacturing activities in Breda.

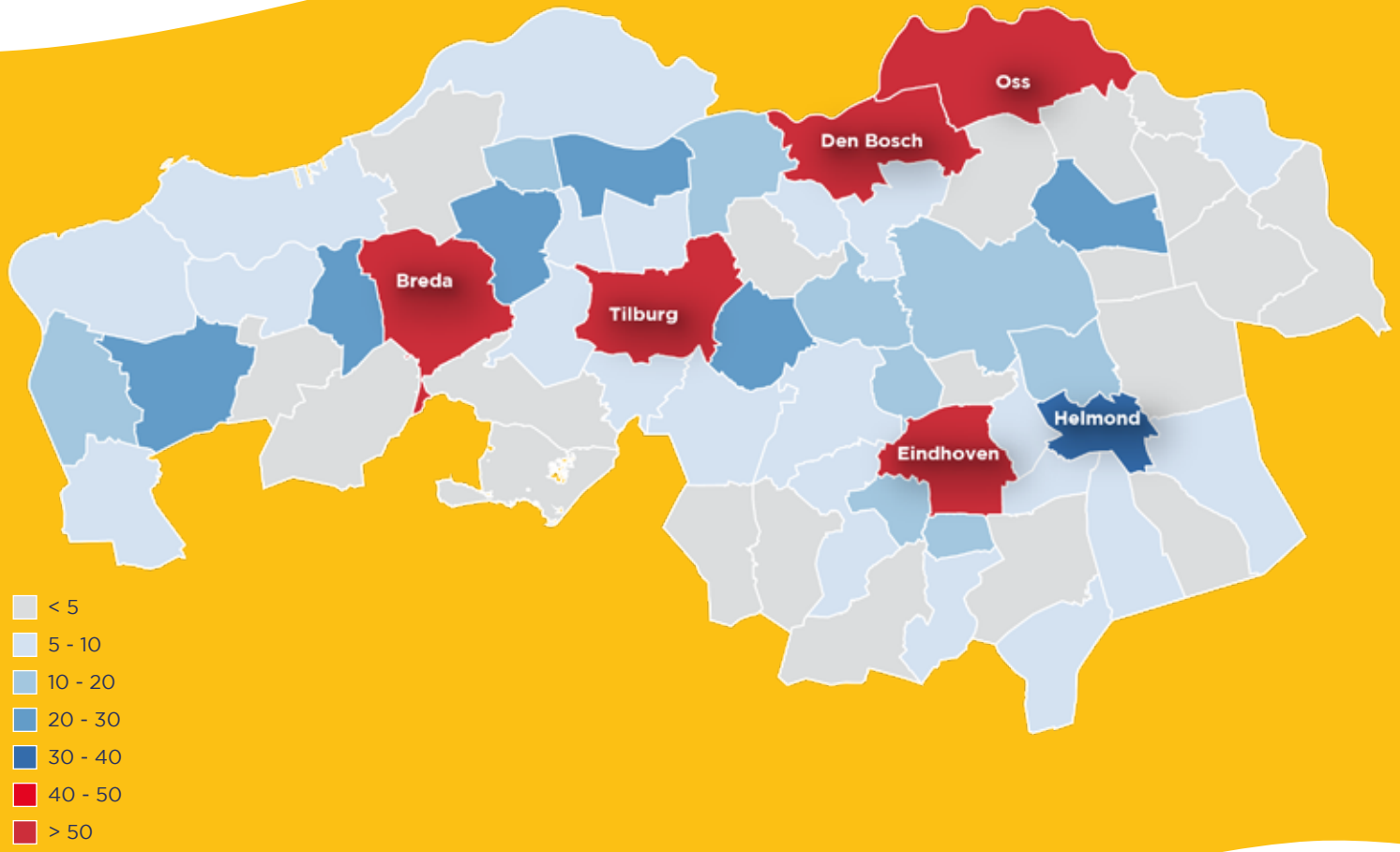
NUMBER OF LS&H COMPANIES AND JOBS BY REGION IN BRABANT

Number of	Breda area	Tilburg area	Den Bosch area	Eindhoven/ Helmond area	Brabant	The Netherlands
Companies	240	165	235	275	915	5.850
Jobs	3.710	1.590	7.400	5.470	18.160	77.380

Share regions in NL	Breda area	Tilburg area	Den Bosch area	Eindhoven/ Helmond area	Brabant	The Netherlands
Companies	4,1%	2,8%	4,0%	4,7%	15,6%	100,0%
Jobs	4,8%	2,1%	9,6%	7,1%	23,5%	100,0%

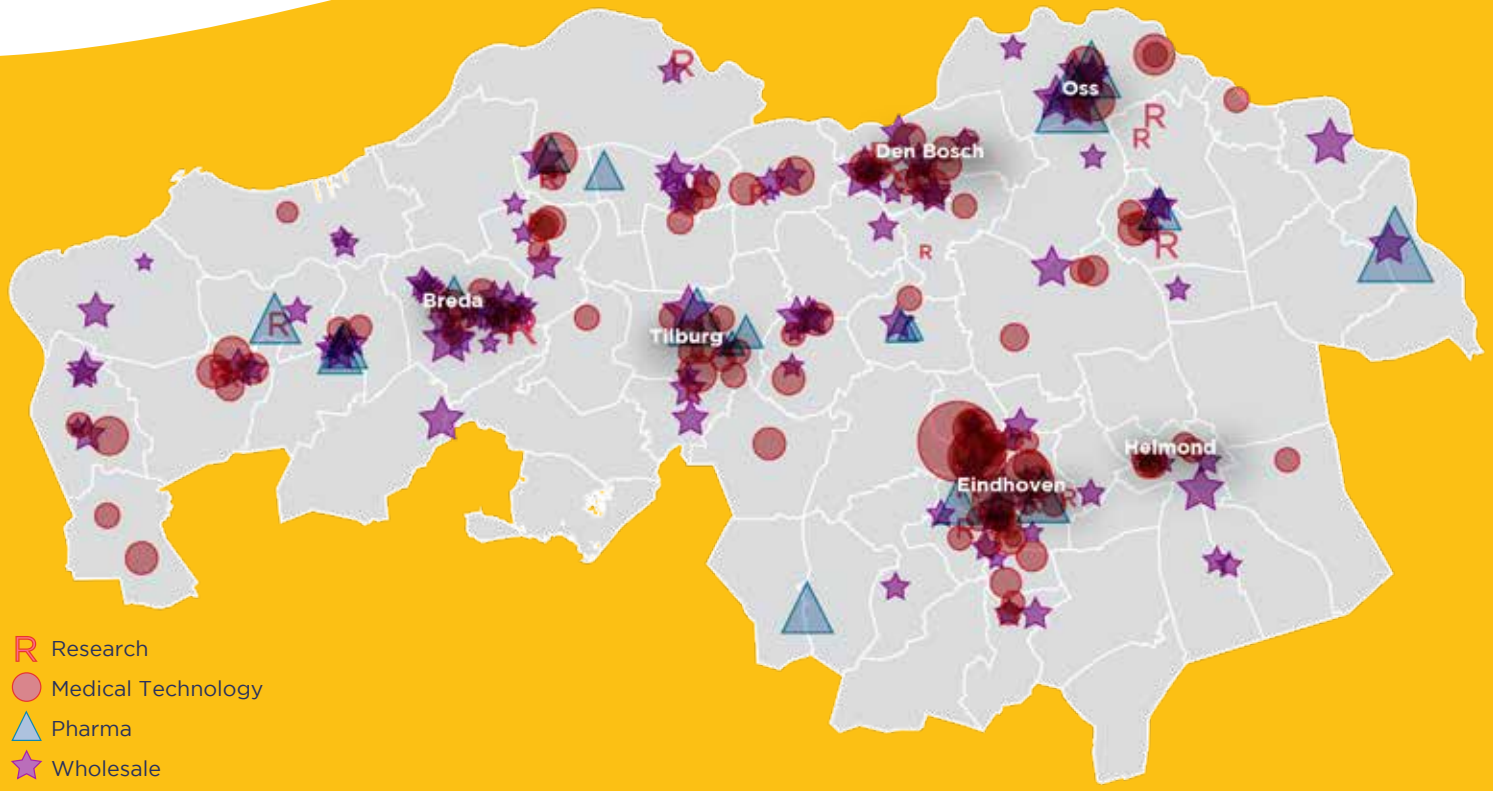
Source: Brabant Register of Companies/LISA 2018, adapted by Fanion Onderzoek & Advies

NUMBER OF LS&H COMPANIES BY MUNICIPALITY



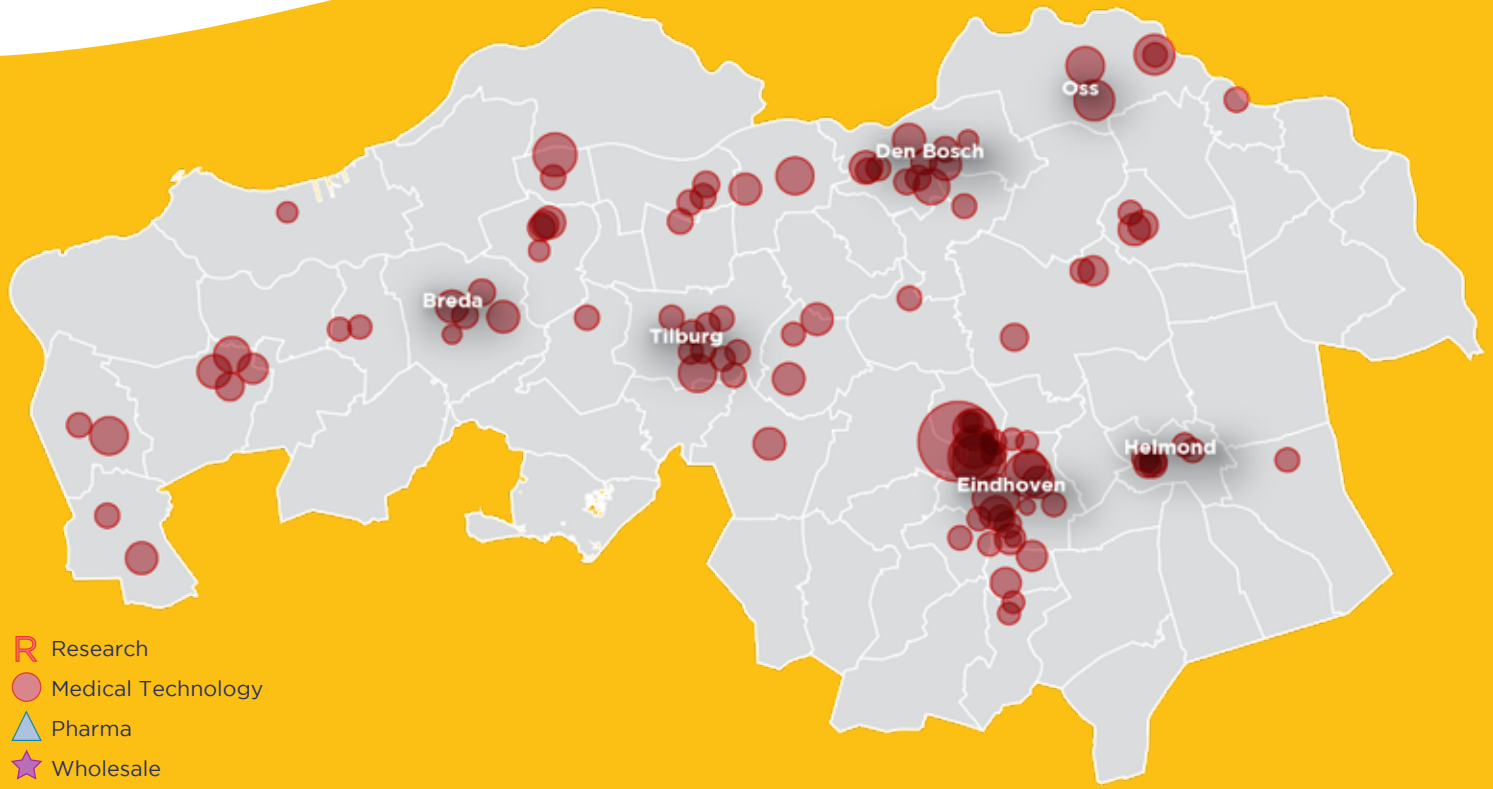
Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

HEATMAP OF LS&H COMPANIES IN BRABANT BY TYPE OF ACTIVITY, 2018



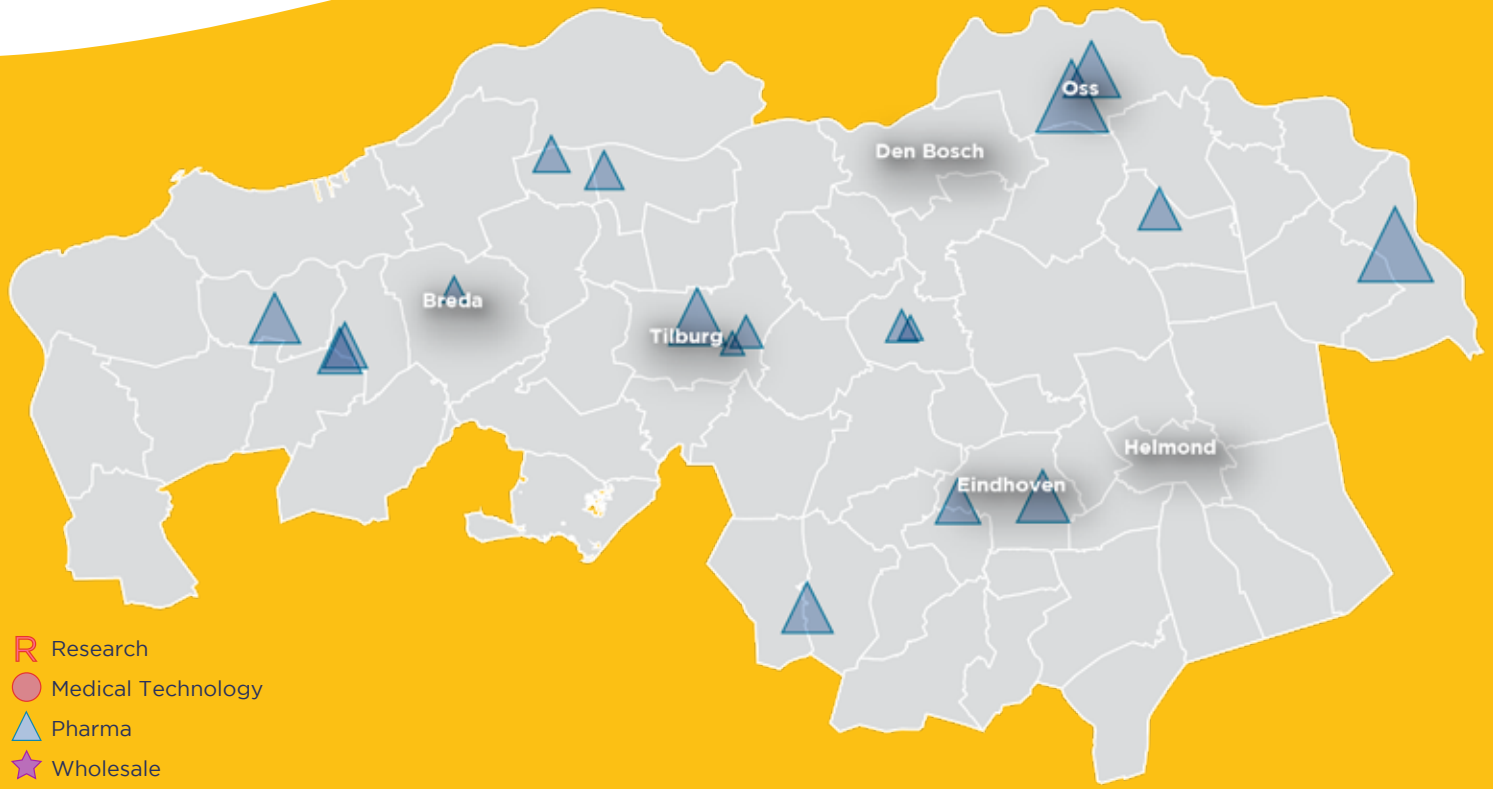
Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

MEDICAL TECHNOLOGY MANUFACTURING FACILITIES



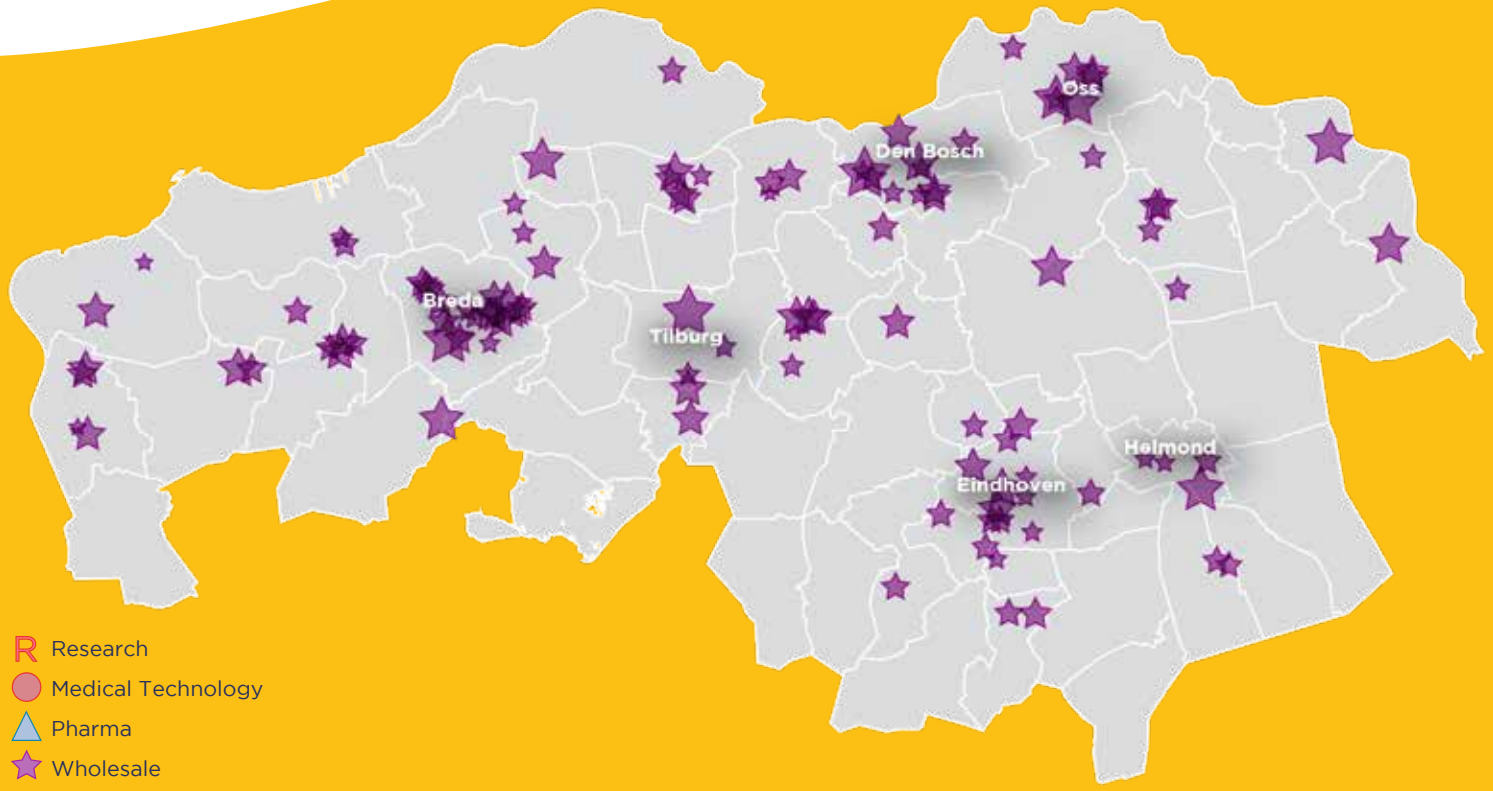
Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

MANUFACTURING OPERATIONS IN (BIO)PHARMACEUTICALS



Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

LS&H WHOLESALE (INCLUDING LOGISTICS AND SUPPORT SERVICES) OPERATIONS

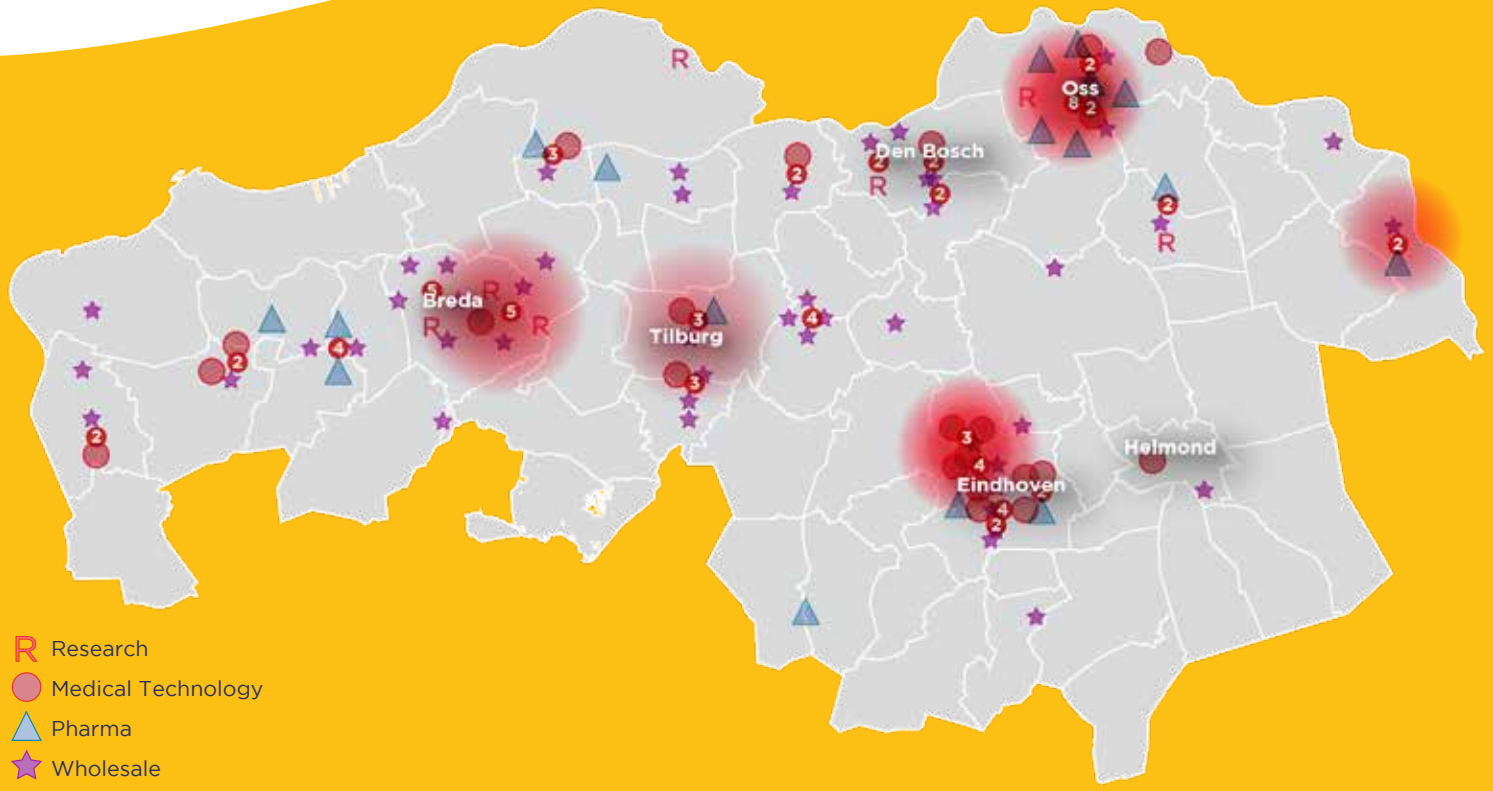


Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

LS&H R&D OPERATIONS

Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

LS&H COMPANIES EMPLOYING MORE THAN 20 PEOPLE



Source: Brabant Register of Companies 2018, QGIS, adapted by Fanion Onderzoek & Advies

THE FOLLOWING CITIES MAKE UP THE TOP FOUR IN BRABANT IN TERMS OF EMPLOYEE NUMBERS

City	# of jobs	Main companies
Eindhoven / Best	4,610	Philips Healthcare, Philips Research, GE Healthcare Life Sciences Core Imaging, Thermo Fisher Scientific (former FEI), Medtronic, Össur, Illumina,
		VDL ETG, Brocacef
Oss	3,990	MSD, Aspen, B. Braun Medical, Pivot Park (home to 60 start-ups & scale-ups)
Breda	2,340	Amgen, Thermo Fisher Scientific, Zimmer Biomet, Janssen-Cilag (Johnson & Johnson), Abbott Logistics
Boxmeer	1,520	MSD Animal Health, Hendrix Genetics

INTERESTING FACTS

- Oss can be characterised as the **(bio)pharmaceutical centre of excellence** for the southern Netherlands

- The cities of Eindhoven and Best are adjoining municipalities, and the two cities fall under the same de facto metropolitan area. If one were to take this into consideration with regard to the employment figures in the table above, the joint Eindhoven/Best metropolitan area hosts 4,610 professionals in Life Sciences and Health, mostly in the field of **advanced medical technology**

- Breda has the greatest concentration of **European logistics** operations in biopharmaceuticals and nutraceuticals, including significant **marketing and sales** operations and **support functions**, such as purchasing, IT services, customer support services and support for healthcare professionals

- Boxmeer is a global powerhouse in **animal health and animal nutrition**

Source: Brabant Register of Companies 2018/Fanion Onderzoek & Advies

4. UNIVERSITIES, KNOWLEDGE INSTITUTES AND HOSPITALS

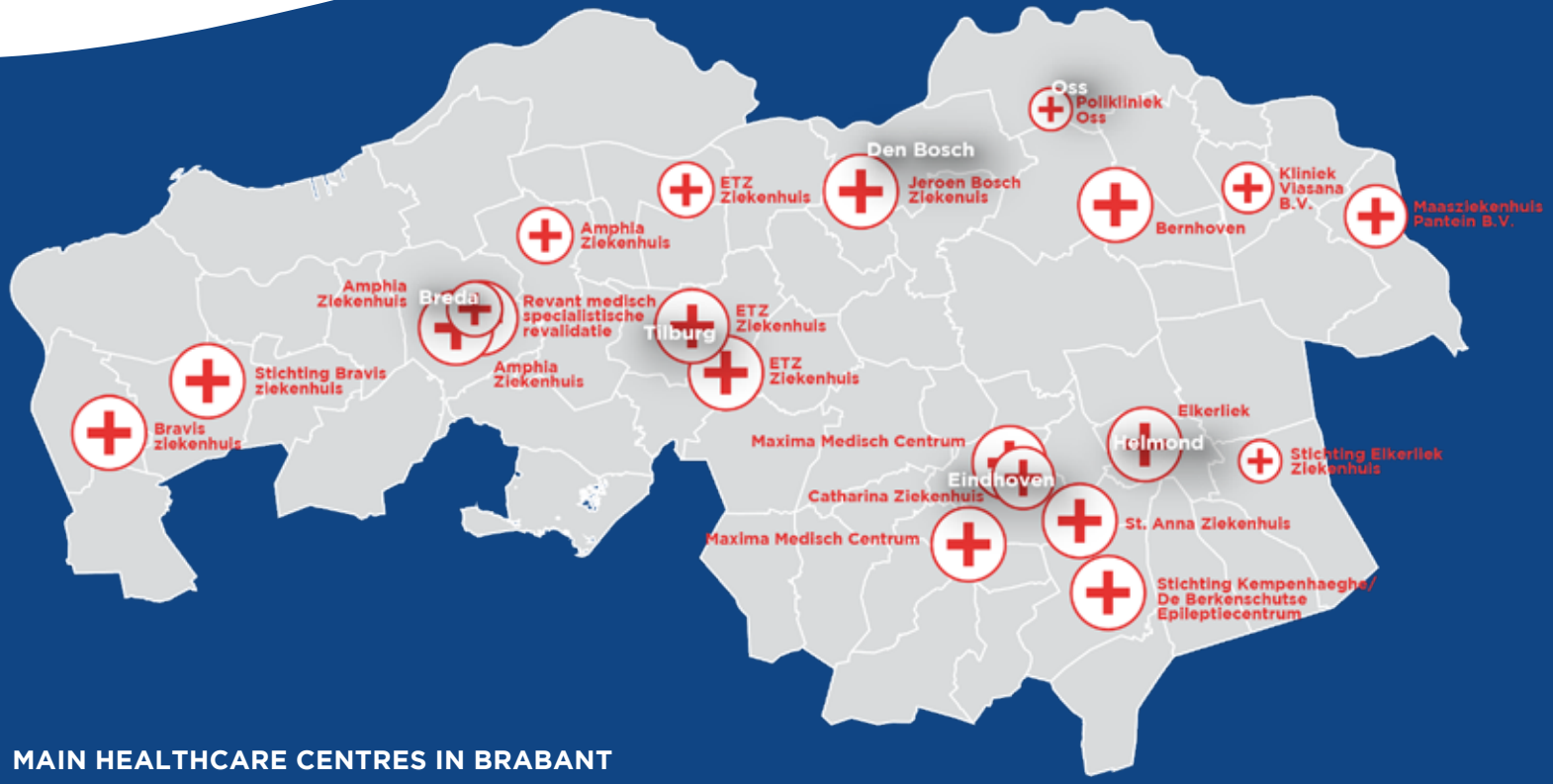
The Netherlands is home to ten universities, eight university medical centres and three universities of applied sciences that are active in R&D for biotechnology and medical technology. In Brabant, the Eindhoven University of Technology is the most renowned Life Sciences & Health institution, but the HAS (Den Bosch), Fontys (Den Bosch) and AVANS (Breda) universities of applied sciences offer a number of courses that also focus on Life Sciences & Health.

ABBREVIATIONS

Amsterdam Academic Medical Centre (AMC), Erasmus Medical Centre (EMC), Erasmus University Rotterdam (EUR), Leiden University (LU), Leiden University Medical Centre (LUMC), Radboud University Nijmegen (RU), Radboud University Medical Centre (RUMC), Delft University of Technology (TUD), Eindhoven University of Technology (TU/e), University of Groningen (RUG), University Medical Centre Groningen (UMCG), Maastricht University Medical Centre (MUMC+), University Medical Centre Utrecht (UMCU), University of Twente (UT), University of Amsterdam (UvA), Utrecht University (UU), VU University Amsterdam (VU), VU University Medical Centre (VUmc), Wageningen University and Research (WUR), Wageningen Bioveterinary Research (WBVR).

Source: The Netherlands Antibiotic Development Platform

A. Hospitals in Brabant



MAIN HEALTHCARE CENTRES IN BRABANT

Brabant has a widespread network of healthcare centres. The larger hospitals, located in the largest cities of Breda, Den Bosch, Tilburg, Eindhoven and Helmond, provide a full range of treatments.

Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies, QGIS

EMPLOYMENT FIGURES FOR HOSPITALS AND CLINICS IN BRABANT

HOSPITAL AND / OR CLINIC	LOCATION	# JOBS
Jeroen Bosch Hospital	's-Hertogenbosch	3.903
Catharina Hospital	Eindhoven	3.596
ETZ Hospital	Tilburg	3.315
Amphia Hospital (location Molengracht)	Breda	3.090
Maxima Medical Center	Veldhoven	2.494
Elkerliek	Helmond	2.116
Bernhoven	Uden	1.938
ETZ Hospital	Tilburg	1.920
Bravis Hospital	Bergen op Zoom	1.626
St. Anna Hospital	Geldrop	1.493
Amphia Hospital (Location Langedijk)	Breda	1.402
Foundation Bravis Hospital	Roosendaal	1.385
Foundation Kempenhaeghe/De Berkenschutse Epilepsy Center	Heeze	1.228
Maas Hospital Pantein B.V.	Beugen	748
Maxima Medical Center	Eindhoven	710
Revant – specialized medical revalidation	Breda	370
ETZ Hospital	Waalwijk	287
Amphia Hospital	Oosterhout	281
Clinic Viasana B.V.	Mill	141
Outpatient Clinic Oss	Oss	97
Foundation Elkerliek Hospital	Deurne	91
TOTAL NUMBER OF JOBS IN BRABANT		**32.231**

Source: Brabant Register of Companies 2018, adapted by Fanion Onderzoek & Advies

STZ HOSPITALS - SPECIALISED CLINICAL CARE

Five of these centres are what are known as STZ hospitals, members of the association of tertiary teaching hospitals providing specialised clinical care. This is healthcare that is not offered by every hospital, and these STZ hospitals all have full inhouse diagnostics and treatment expertise, deal with many patients and are centrally located in the regional healthcare networks. Every STZ hospital has its own departments for specialised clinical care and the approach is always multidisciplinary. Specialists in a field work together with nurses, paramedics and other support professionals to provide this specialised clinical care. Several forms of scientific and other research, often in partnership with the healthcare industry, are performed in order to maintain and bolster the high level of specialised care.

JEROEN BOSCH HOSPITAL, DEN BOSCH	• Top clinical HPV cervical cancer expertise centre. Specialises in pathology • Breast cancer. Specialises in surgery • Cognitive disorders, Alzheimer's, limbic encephalitis, primary progressive aphasia, frontotemporal dementia, young-onset Alzheimer's. Specialises in geriatrics • Overweight children, morbid child obesity. Specialises in paediatrics • Polypharmacy, issues arising from the simultaneous use of multiple drugs. Specialises in clinical pharmacology • Reproductive issues, subfertility. Specialises in gynaecology and obstetrics • Mobility and/or exercising issues. Sports medicine and paramedical care
MÁXIMA MEDICAL CENTER, VELDHOVEN & EINDHOVEN	• A well-known institute thanks to its VMK (Woman Mother Child) centre, pre-rehabilitation and cancer centre. Adrenal cortex carcinoma, adrenal cancer. Specialises in internal medicine • Abdominal pain due to nerve compression, abdominal wall pain, groin pain, anterior cutaneous nerve entrapment syndrome (ACNES). Specialises in general surgery • Chronic exercise-dependent pain syndromes of arms and legs. Specialises in surgery • Epilepsy due to vitamin B6 deficiency, pyridoxine dependent epilepsy (PDS). Specialises in paediatrics • Knee instability, cruciate ligament injuries, collateral band surgery. Specialises in orthopaedics • Vascular problems in athletes' leg arteries. Sports medicine/vascular surgery
AMPHIA HOSPITAL, BREDA	• Complex disorders of elbow, forearm. Specialises in orthopaedics
ETZ HOSPITAL, TILBURG	• Disorders of the spine, including vertebral fractures and metastases, spinal surgery. Specialises in orthopaedics • Allergy, food allergy, insect poison allergy, drug allergy. Specialises in allergology • Trauma-related injury, accidental injury, trauma injury, multi-trauma injury. Specialises in surgery • Disease(s), multiple sclerosis. Specialises in neurology • Infertility, impaired fertility, infertility or subfertility in women, infertility in men, severe male subfertility, azoospermia, IVF. Specialises in reproductive medicine • Brain tumours, bridge angular tumours, acoustic neuroma, vestibular schwannoma, Gamma Knife. Specialises in neurosurgery
CATHARINA HOSPITAL, EINDHOVEN	• Uterine cancer, high grade and recurrent endometrial carcinoma. Specialises in gynaecological oncology • Pinched vascular nerve bundle in the shoulder region, TOS (thoracic outlet syndrome) expertise centre. Specialises in vascular surgery

HOW HEALTHCARE IN BRABANT MAKES DIRECT USE OF ITS HIGH TECH CAPABILITIES IN A TIME OF A REAL CRISIS – THE COVID-19 PANDEMIC

nu.nl 01 April 2020

TILBURG ETZ HOSPITAL PRODUCES VALVES FOR OXYGEN MASKS USING A 3D PRINTER

The Elisabeth-TweeSteden Hospital (ETZ) in Tilburg has started printing valves for oxygen masks that are being used in the treatment of coronavirus (COVID-19) sufferers, the hospital announced on its website. Trauma surgeon Mike Bemelman spoke of the risk of an 'impending shortage'.

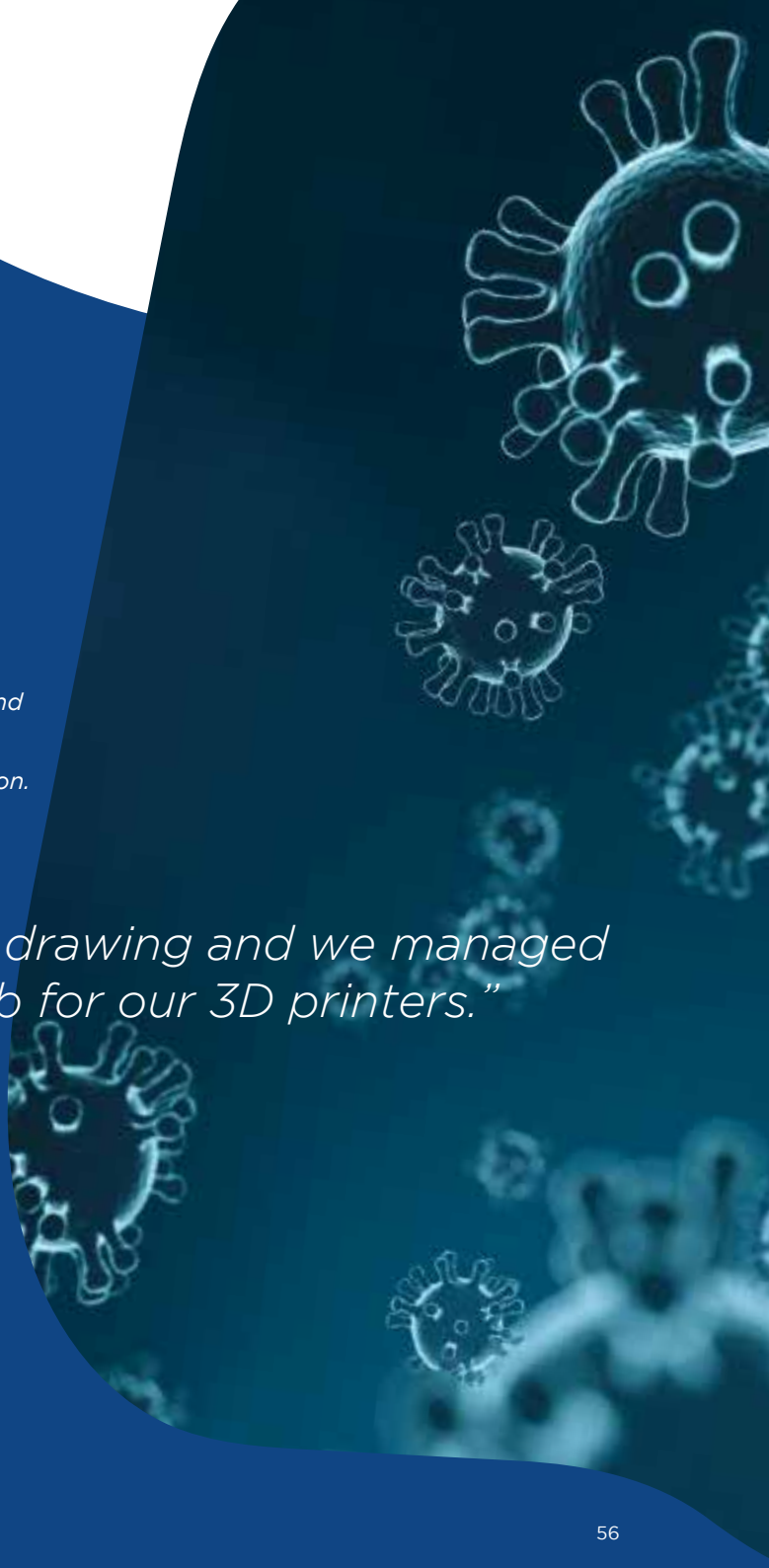
The ETZ uses Venturi oxygen masks for its coronavirus patients. Using special valves attached to the masks the concentration of the oxygen inhaled can be controlled and adjusted. But the valves cannot be re-used and, thanks to the international pandemic, there is a backlog of new orders.

'That's why I searched the internet for technical information about the valve,' said Bemelman. 'I quickly found the digital drawing and we managed to convert it into a print job for our 3D printers.'

This can solve the impending shortage. According to the surgeon, 60 to 80 valves are used daily. With the three available printers, over a hundred can be made per day. The printed valves have been approved by the hospital's Medical Technology department and meet all requirements. Bemelman is now sharing the print designs with others, so that they can also produce the valves.

Author's note: *the ETZ Hospital has been using 3D printing and VR/AR in its 3D LAB for some time already. Surgeons prepare for complex operations by practicing and testing the procedures in a VR environment in the 3D lab. The models are produced by 3D printers. The trauma surgeons at the Brabant hospital print anatomical models of bones and joints. They can immediately identify exactly where the fracture is and how to best treat it. They can also bend metal plates to the exact size, while the screws are produced at the exact length needed for the operation.*

"I quickly found the digital drawing and we managed to convert it into a print job for our 3D printers."



UNIVERSITY MEDICAL CENTRES (UMCS) IN THE NETHERLANDS

There are a large number of university medical centres (UMCs) in the Netherlands, and LS&H companies in Brabant work closely with almost all of the eight UMCs. Given that the Netherlands is a small country, every UMC is within a radius of 120 miles. UMCs fulfil a wider range of tasks than regular hospitals, and patients with rare or complex diseases are often referred to them. The UMCs also serve as educational institutions and research centres, offering bachelor and master courses for medical students, training for physicians specialising in a particular medical fields and both basic and advanced nursing courses.

8 university medical centres
12 universities engaged in biomedical research

1. Erasmus MC
2. UMC Utrecht
3. Leids Universitair Medisch Centrum
4. umcg
5. Radboudumc
6. Amsterdam UMC
7. Maastricht UMC+

Source: The Netherlands, Europe's most attractive and innovative biopharmaceutical environment, Health-Holland

B. Universities

EINDHOVEN UNIVERSITY OF TECHNOLOGY (TU/E)

TU/E HAS 10 RESEARCH DEPARTMENTS

I. Biomedical Engineering
II. Built Environment
III. Electrical Engineering
IV. Industrial Design
V. Industrial Engineering & Innovation Sciences
VI. Chemical Engineering and Chemistry
VII. Applied Physics
VIII. Mechanical Engineering
IX. Mathematics and Computer Science
X. Eindhoven School of Education

TU/E HAS 10 STRATEGIC RESEARCH AREAS

1. Artificial Intelligence
2. Smart Mobility
3. Energy
4. Engineering Health
5. Integrated Photonics
6. High Tech Systems
7. Complex Molecular Systems
8. Data Science
9. Humans and Technology
10. Smart Cities

The Department of Biomedical Engineering is wholly focused on Life Sciences & Health, but several of the other departments also have research groups devoted to LS&H matters.

A CLOSER LOOK AT THE ENGINEERING HEALTH STRATEGIC RESEARCH AREA

Today the Engineering Health strategic research area is being driven by over 400 PhD and PDEng students, supervised by seven professors in seven focus areas. The research is:

- demand-driven - based on patient or doctor needs
- innovative - breakthrough technologies drive the research
- collaborative - all research is done in close collaboration with general and academic hospitals, industry (healthcare, medtech and biopharma) and patient organisations
- target-based - researchers aim to achieve real, positive improvements in health and healthcare

TU/e research aims to develop healthcare technology that is human-focused, i.e. self-explanatory and user-friendly. A crucial part of this strategy is the organisation of the care provided and the development of associated IT systems. At TU/e this revolves around making patients more independent – rendering technology more accessible and so making selfcare easier.

TU/E'S ENGINEERING HEALTH RESEARCH IS AIMED AT SEVEN CORE AREAS ACROSS NINE TU/E RESEARCH DEPARTMENTS

I. Bio-molecular sensing
II. Data science in health
III. Healthy daily living
IV. Medical imaging & Monitoring
V. Monitor, diagnose and present
VI. Regenerative medicine
VII. Robotics

I. BIO-MOLECULAR SENSING

The overall goal in this research area is to develop technologies for measuring biomolecular markers, or biomarkers, in bodily fluids and tissues. Biomarkers are biochemical substances that are strong indicators of health and disease. The challenge for the future is to enable testing at any place (hospital, GP's practice, at home) and at any time.

TU/e develops sensing technologies for point-of-care testing (measuring fluids outside of the body) and for continuous patient monitoring (measuring performed inside the body by means of a catheter on or in the skin or by being implanted in the body). These sensors are not yet available for biomarkers such as hormones, drugs, electrolytes, peptides, proteins and DNA.

This highly multidisciplinary work at TU/e is currently being done on topics such as optical detection methods, sensing with single molecule resolution, engineering protein and nucleic-acid based molecular constructs, use of nanoparticles for signal generation and micro-fluidic device technologies.

II. DATA SCIENCE IN HEALTH

Advances in information technology (IT), IoT, cloud computing, big data and high-performance computing are having a significant impact on health services:

- Advances in sharing medical knowledge results in better diagnoses and treatments
- Information management is affected by trends such as increased patient-centricity (including shared decision-making), self-care and integrated care delivery
- Delivery of health services is being fundamentally altered through the sharing and integration of data across organisational boundaries

TU/e performs research in close collaboration with leading healthcare institutes and industrial companies on decision-support for better health, visual health analysis and on healthcare process and environment innovation. Some of TU/e's partners include Catharina Hospital, Jeroen Bosch Hospital, Maastricht University Medical Centre, Utrecht University Medical Centre, Zhejiang University, Philips Healthcare and the Jheronimus Academy of Data Science (JADS).

III. HEALTHY DAILY LIVING

Today's society is faced with a number of major challenges including health-related ones, such as aging, obesity, cardio-vascular diseases or social isolation. When looking at the field of public health, society faces the risk that an increasing number of people will ask for an increase in quality of life while having to rely on increasingly expensive healthcare paid for by a decreasing number of people, up to a point that it is no longer suitable and maintainable.

Technology can provide support in addressing societal challenges. It can stimulate certain behavior and discourage other behavior, as well as amplify or reduce specific aspects of reality, thus providing support to improve health. However, addressing these major societal challenges often requires systemic change and active involvement of many different stakeholders.

The Healthy Daily Living research area aims at empowerment for wellbeing and healthy living: from prevention to care. It aims to bring about systemic change and support quality of life by developing and optimizing personal and value-centered complex health systems. The idea is to integrate personal, contextual and technological elements with innovative complex health systems.
Healthy Daily Living targets three areas:

1. Human vitality and technology
2. Healthy cities and smart societies
3. Interactive technologies and health continuum

The TU/e develops devices, systems and living environments, as well as related theories, methods and tools to support quality of life in these three areas. The aim is to develop solutions for healthy daily living through design, system thinking and co-creation in real-world environments. For this, Fieldlabs and Experiential Design Landscapes are used to explore, use, test and validate new innovative processes and systems in real-world situations. In this way, the systemic character of challenges and solution scan be addressed as well.

IV. MEDICAL IMAGING AND MONITORING

TU/e is part of the world-renowned electronics hotspot of Brainport Eindhoven. Eindhoven developed into this hotspot thanks to the fact that the city was the birthplace, more than 120 years ago, of Philips Electronics and to this day it remains the innovation home base for Philips Healthcare, one of three industry giants ruling the world of medical imaging.

And so it is no surprise that TU/e has been exceptionally active in all related research areas since its inception in 1956

- Screening to detect diseases early (a large population analysis using computer aided image analyses, automatic triage of patients and second opinions)
- Making accurate diagnoses and prognoses: determining the specific type of disease, its causes, progress and the outlook for the patient
- Determining the best treatment: using imaging to create patient-specific treatment plans, such as helping to define the outlines of a tumour that is to be removed or irradiated and determining the safest, least invasive pathway to that tumour.
- Helping guide the clinicians in medical operations to perform minimally invasive therapy
- Helping measure the efficacy of a medical procedure and switching treatment policies more rapidly where required
- Medical monitoring of a person's health: in a hospital setting during (or after) a medical procedure, but also in a home setting, for example in order to study sleep disorders

A selection of TU/e's research (sub) areas in this domain

Diagnosis and treatment

- Ultrasound imaging
- Automatic precise determination of pathology boundaries
- Visualisation of big data
- Neuro-engineering

Image-guided therapy

- Cardiac catheter detection and tracking in 3D ultrasound
- Neurosurgical guidance

Monitoring

- Neonatal monitoring
- Alarm enhancement for neonatal monitoring
- Sleep disorders

V. MONITOR, DIAGNOSE AND PRESENT

An increasing amount of health data concerning an individual patient/person is becoming available (thanks to, for example, new sensors, new imaging technologies, etc) and can be used for diagnosis and research. The results can be presented in many different ways and at various levels of specialisation.

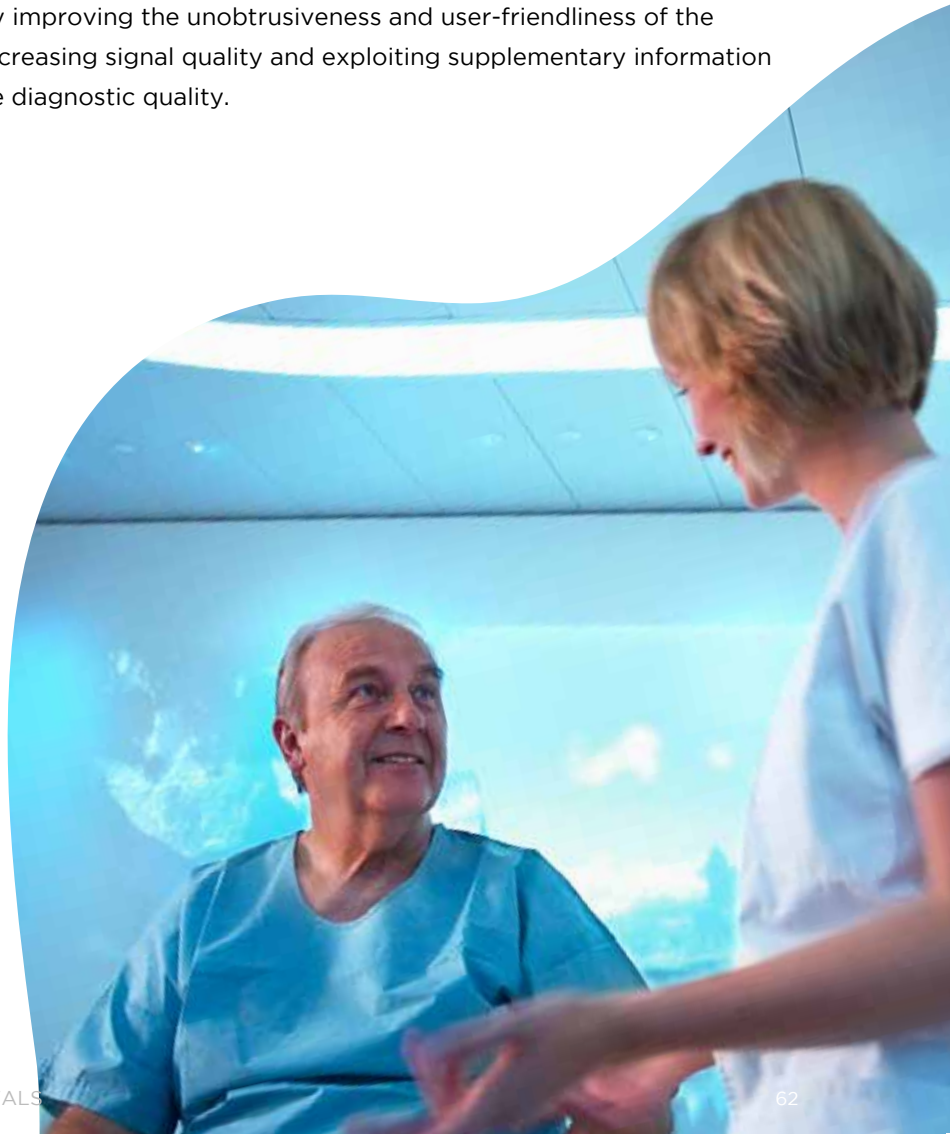
New electronic devices – smartphones in particular – greatly enhance the possibilities for a partial or full diagnosis and/or collecting research input and communicating with the patient. And that brings us to e-Health: an online platform where patient data is collected from numerous sources for diagnostic or even disease-prevention purposes. These new and advanced health monitoring opportunities are helping healthcare specialists look for more advanced and better monitoring, diagnosis and presentation methods.

The four main therapeutic areas TU/e is focusing its research efforts on in monitoring, diagnosing and presenting are:

- **Cardiology**. For example, the Ambulatory Cardiac Monitoring project, a new monitoring approach based on a smart watch with embedded wrist photoplethysmography (PPG) for long-term home monitoring. New signal processing methods for the PPG-based detection of atrial fibrillation (AF) will pave the way for unobtrusive, cost-effective and long-term AF screening and prevention of AF-related stroke.

- **Neurology**. For example, neuro-engineering research such as the Neu3CA project, which is based on neuro-imaging using MRI. Functional MRI and diffusion weighted imaging are used to find imaging biomarkers for diseases and to gain a better understanding of disease mechanisms in order to improve treatments (and prevention).

- **Oncology**: using contrast-enhancing ultrasound dispersion imaging (CUDI) in prostate cancer diagnoses to reduce the number of unnecessary biopsies and increase the use of minimally invasive focal treatment.
- **Perinatology**: TU/e is working on several projects for enabling unobtrusive long-term monitoring of pregnancies and foetal well-being through both sensor/circuit technologies and smart signal processing. The EWAM (Enabling Widespread Ambulatory Monitoring for Improved Pregnancy Outcome) project, for example, is developing technologies for reliable continuous pregnancy monitoring (of the foetal heart rate) in ambulatory settings by improving the unobtrusiveness and user-friendliness of the sensors, increasing signal quality and exploiting supplementary information to improve diagnostic quality.



EINDHOVEN SCIENTIST YOURI VAN DER BURGHT SELECTED BY MIT AS ONE OF THE TOP "INNOVATORS UNDER 35" OF 2019

20 December 2019

Yoeri van de Burgt of TU/e wins Innovators Under 35 Europe award from MIT Technology Review. Mr. van de Burgt combines neural networks with microfluidic sensors to help detect cancer metastasis earlier, more efficiently and non-invasively: https://lnkd.in/ekRS5Xh

The functioning of the human brain has inspired the creation of neural networks capable of translating languages, classifying images and facilitating autonomous driving, among many other applications. These computational models also open up a range of possibilities in the medical sector, as they could improve our understanding of the emergence and evolution of diseases such as cancer. The algorithms with which these networks operate, however, require an enormous amount of computational resources associated with high energy consumption.

The brain is much more efficient. It acts with a network of neurons that communicate with each other through synapses, that is, through the transmission of electrical impulses between them. In order to imitate these biological synapses and approach the energy efficiency of the brain, devices called memristors have emerged. In them, the algorithms of a neural network, which are traditionally implemented in software, are directly integrated into hardware, on a chip that emulates not only the function, but also the efficiency of the brain.

This is what the researcher Yoeri van de Burgt tries to take advantage of in his BIOMORPHIC project, which aims to apply these technologies in the monitoring of cancer metastasis and the guiding of effective and personalised cancer treatments.

Thanks to this technology he has become one of the winners of Innovators Under 35 Europe from MIT Technology Review.

VI. REGENERATIVE MEDICINE

Regenerative medicine is where engineering meets life sciences and exploits the properties of living cells, in combination with biomaterials, drugs or genes, to repair or replace living tissues and organs. In other words, 'Coaxing the body to repair itself'.

Building on its expertise in biomaterials and biomedical engineering, the TU/e principally focuses on:

- Materials-based in-situ tissue engineering for cardiovascular and orthopaedic applications and for functional organ repair, where 'instructive materials' are being used to stimulate the regenerative capacity of the human body itself
- In conjunction with this, TU/e uses its engineering skills to design computational models and in-vitro engineered tissue models that deepen the understanding of tissue development, malformation (including cancer), degeneration and regeneration

The research is performed by highly creative, multidisciplinary teams that operate at the cross-section of bio-engineering, materials science and cell and tissue biology. These teams collaborate with patient organisations, clinical partners and industry to develop regenerative strategies that can outrange existing therapies in terms of costs and effectiveness.

This focus area has won support from various individual and consortium research grants (including ERC, FP7, Horizon 2020, NOW and CVON) and many projects are public-private-patient partnerships. Members participate in large regional and cross-border initiatives, such as Chemelot-InScite, RegMed-XB and hDMT.

TU/E SPINOFF: XELTIS

In cardiovascular regeneration, the group has developed a synthetic supramolecular, biodegradable heart valve implant that 'coaxes' the body to create a new living heart valve at the site of the implantation by recruiting cells from the environment. Initial clinical trials employing the technology started in 2016 under the guidance of the group's spinoff company Xeltis. Xeltis' cardiovascular implants are made of bioabsorbable polymers based on Jean-Marie Lehn's Nobel Prize-winning work on supramolecular chemistry. Today Lehn is one of Xeltis' scientific advisors. The clinical trials were a success, and 18 children have received a new Xeltis biodegradable heart valve

VII. ROBOTICS

The robotics research group, part of the faculty of Mechanical Engineering, focuses on both healthcare *(care robotics)* and surgical robotics *(cure robotics)*.

Cure robotics: robotics technology used in surgery to create innovative assistive devices that enable new surgical procedures. Present-day examples include the Sophie robot for minimally invasive abdominal surgery, an eye-surgery robot that maximises surgical precision and a micro-surgery robot for treating lymphedema, while a robot for automated CNC jawbone milling surgery and a robot for deep-brain stimulation surgery are also in their final stages of development.

The medical spinoffs of this group, Preceyes and Microsure, have had world-firsts in eye surgery and the clinical treatment of lymphedema and Eindhoven Medical Robotics is preparing for clinical trials involving bone and brain surgery.

Care robotics: technology developed to allow elderly people or people with physical impairments to live independently at a sustained level.

The ageing population means that an increasing number of people will require nursing care in the near future, whereas the number of available caregivers is declining. It is anticipated that robotics will help to decrease the physical demands on caregivers (through devices such as people-movers and automated lifting devices) and also assist people living in their own homes. Examples include robots retrieving items from the refrigerator, providing walking assistance and opening doors. The focus of TU/e research is on creating robots that can function in unstructured, dynamic environments, can physically and safely interact with people and can also communicate so that patients can put them to good use.

TU/E'S DEPARTMENT OF INDUSTRIAL DESIGN

One research department that must be mentioned when it comes to Life Sciences & Health research in Brabant is TU/e's Department of Industrial Design.

TU/e is located in a highly industrialised region of the Netherlands that is known as Brainport Eindhoven. It is internationally recognised as a top technology area with a special focus on the integration of design and technology. Around the year 2000, the creative industries voiced the need for a new type of academic engineer, one that brings together knowledge from different fields, as the integrator of visions and as a problem-identifier. In essence, these people should be the designers of intelligent systems, products and related services in a societal context, addressing aspects such as adaptive behaviour, context awareness and highly dynamic interaction.

These systems meet the needs of today's users or, even better, offer new, breakthrough possibilities leading to societal transformations. It was on these grounds that the Department of Industrial Design (ID) settled on a specific new field within industrial design that matches the development, expertise and interests of both the nearby and the internationally-operating industries.

FACTS AND FIGURES

Education

- Bachelor's programme (BSc): Industrial Design
- Master's programme (MSc): Industrial Design
- Designer's programme (PDEng)
- User System Interaction (USI) – two-year postgraduate programme

Student numbers (2020)

- 635 bachelor's students
- 176 master's students

Staff numbers (2020)

- 15 full professors
- 6 associate professors
- 21 assistant professors
- 53 support staff (non-teaching, administrative and technical support staff)
- 20 other research and teaching staff
- 89 PhD students
- 14 USI postgraduate students

The department has two research clusters

1. The Future Everyday cluster investigates everyday interactions between individual people and the highly interconnected technology that surrounds them. TU/e measures, models and designs on the basis of the user-experience when individuals interact with social-technological networks in their homes, at work, while commuting, exercising or engaging in recreational activities.

2. The Systemic Change cluster focuses on designing innovations that impact upon systemic structures and groups of people, ultimately aiming to address large-scale issues such as urban health, future mobility and sustainability. Field data is used in novel iterative and circular research-through-design processes involving strategic alliances of stakeholders.

EXAMPLES OF PROJECTS
NEONATAL MONITORING - DEVELOPING ALGORITHMS USING CONTINUOUSLY-MONITORED VITAL SIGNS

Around the world, 10% of babies are born premature – a gestation period of less than 37 weeks. Premature birth increases the chances of mortality and lifelong morbidities and its incidence is rising globally, affecting both developed and developing countries alike. The most vulnerable infants, often weighing as little as 500 grams at birth, are placed in neonatal intensive care units (NICU) where their vital signs are continuously monitored so that nurses can rapidly stabilise any life-threatening deteriorations.

The neonatal monitoring project aims to develop algorithms using the continuously monitored vital signs recorded in the NICU in order to produce predictive monitoring that will either entirely eliminate clinical incidents – both acute deteriorations and diseases – or detect them at an early stage. An increased window of opportunity for clinical action increases the likelihood of timely intervention, which can potentially have a large impact over the course of the life of a preterm infant and also reduce the physical, emotional and financial toll on families and society at large.

Partners: Philips Research and Máxima Medical Center

MEDICAL SIMULATION FOR TEAM TRAINING - RESEARCH ON MANUFACTURING NEONATAL MANIKINS FOR TRAINING MEDICAL TEAMS

The Industrial Design department is researching the manufacture of neonatal manikins for the purpose of training medical teams. These manikins are highly realistic and allow teams to *suspend their disbelief*.

'Highly realistic' covers both the visual and the tactical aspects of the manikins. Tactical realism is required to, for instance, train staff to perform ABC (airway breathing and circulation) procedures. The manikin must also be physiologically realistic. For example, if blood oxygen levels are low, the manikin must automatically exhibit realistic symptoms of cyanosis, and once the oxygen levels restored the manikin must once again revert to 'normal' symptom-free characteristics.

The neonatal manikins are created using MRI scans, physiological models, microprocessors, sensors, advanced rapid prototyping and other manufacturing techniques.

Partners: Máxima Medical Center

08 OCTOBER 2019 - MULTIMILLION EURO GRANT BRINGS ARTIFICIAL WOMB A STEP CLOSER

The construction of an artificial womb has come one step closer, thanks to a new €2.9 million grant awarded to researchers in Eindhoven under the Horizon 2020 EU programme. The purpose of an artificial womb is to increase the survival chances of extremely premature babies outside of the body. [...] Thanks to this grant, scientists will be able to create a working prototype within five years. Professors Frans van de Vosse and Loe Feijs of Eindhoven University of Technology (TU/e) and Professor Guid Oei of the Máxima Medical Centre (MMC) and TU/e founded the European consortium that received the grant.

An artificial womb serves as a replacement for an incubator and artificial respiration and is a much more natural environment, given that it more closely resembles conditions in an actual womb. 'Our goal with the artificial womb is to help extremely premature babies get through the critical period of 24 to 28 weeks,' said Guid Oei, a gynaecologist at MMC and part-time lecturer at TU/e. The chances of survival for extremely premature babies are low, and approximately half of infants born at 24 weeks die while those that do survive often suffer from lifelong chronic disorders such as brain damage, respiratory problems and/or retinal conditions that could lead to blindness. 'With each day that a 24-week-old foetus of continues to develop in an artificial womb, the chances of survival will increase. If we are able to prolong the foetal development of these children in the artificial womb to 28 weeks, we will have reduced the most serious risk of premature mortality to 15%,' said Oei.

SUPPORT IN DECISION-MAKING

'We will use different technologies to create the artificial womb,' said Frans van de Vosse, project coordinator and Professor of Cardiovascular Biomechanics in the Department of Biomedical Engineering at TU/e. 'Premature babies are placed in a fluid-based environment, just like in the natural womb. In this environment, there is no artificial respiration via the lungs. Instead, oxygen and nutrients are provided via an umbilical cord using an artificial placenta. The system that makes this possible constantly monitors the baby's condition. This includes the heart rate and oxygen supply as well as brain and muscle activity. Smart computer models that simulate the baby's conditions provide the doctor with immediate support in the decision-making process when it comes to the artificial womb's settings.'

The Industrial Design of Embedded Systems group, under supervision of Loe Feijs, is also playing a role in the project. The group is developing a foetal mannikin that can accurately simulate the conditions of extremely premature babies in an intensive care ward so that the artificial womb can be evaluated in a realistic test setting before being employed in clinics.

EUROPEAN CONSORTIUM

[...] The European consortium was initiated by TU/e and MMC, in partnership with LifeTec Group, Nemo Healthcare, Politecnico di Milano and Universitätsklinikum Aachen. The partners of this consortium have the different areas of expertise required to develop the artificial womb. By sharing expertise and combining forces, they aim to bring the construction of the artificial womb a significant step closer. [...]

Prof. Guid Oei presenting an artist's impression of the artificial womb. Photo: Bart van Overbeeke

DUTCH DESIGN WEEK, DDW

The annual Dutch Design Week (DDW) is hosted in Eindhoven in October. This, the biggest design event in northern Europe, presents work and ideas by over 2,600 designers to more than 350,000 visitors from the Netherlands and further afield. The DDW arranges and facilitates exhibitions, lectures, awards ceremonies, networking events, debates and festivities in over 110 locations around the city.

While every imaginable discipline and aspect of design is on offer during the event, the emphasis is on experimentation, innovation and crossovers. Special attention is devoted to the work and development of young talent.

The DDW focuses on the *design of the future* and the *future of design*, and aims to demonstrate how designers from around the world are shaping a positive future and as well as to enhance the position and significance of Dutch designers.

The DDW was born in 1998, when the designer cooperative Vormgeversoverleg hosted the very the first Day of Design with the objective of introducing businesses to designers. The event, an annual Eindhoven highlight, attracted increasing levels of interest each year and grew exponentially until the Day of Design eventually became the Week of Design in 2002 and ultimately in 2005 was renamed Dutch Design Week (DDW).

DUTCH DESIGN WEEK

THE TU/E AND ARTIFICIAL INTELLIGENCE (AI) IN HEALTH

I. THE EINDHOVEN ARTIFICIAL INTELLIGENCE SYSTEMS INSTITUTE (EAISI)

The Eindhoven Artificial Intelligence Systems Institute (EAISI, pronounced 'easy') is the new institute of Eindhoven University of Technology in the field of artificial intelligence (AI). With the establishment of EAISI, the university wants to contribute to the growing importance of AI in society, business and science, and to meet the rapidly increasing demand for education, engineers and expertise in the field of AI. TU/e has been active in the field of Artificial Intelligence for decades, which gives the new institute an excellent starting position to build on. TU/e will invest 100 million euros in EAISI's education and research until 2025. In total, up to 150 people will be directly or indirectly involved in EAISI.

This money comes primarily from the university's own resources. EAISI also wants to attract an extra 30 million euros each year from so-called third tier grants (NWO, EU and other grants) and from industry directly. There are already about a hundred AI-scientists working at TU/e. On top of that, the university wants to recruit about 50 new researchers. In total, up to 150 people will be directly or indirectly involved in EAISI.

Unlike other AI institutes, EAISI will focus on the use of data and algorithms in machines, such as robots and autonomous cars, which has always been a strong point of TU/e and the Eindhoven Brainport region. The new institute will prioritize research into applications of AI in healthcare, the interaction between man and machine, and the moral and ethical aspects of AI.

In Health Applications, the institute will focus on the following topics:

a. Improved and explainable diagnostics capabilities
b. Personalized and wearable health systems with monitoring, health risk detection and adaptation capabilities
c. Causal and systemic understanding of individual states of health
d. Preventive health management
e. Process optimization in health care systems

TU/e has been active in the field of AI for years, with innovative research in the fields of intelligent machines, smart mobility and healthcare. With the Data Science Center Eindhoven and High Tech Systems Center, the university also has two leading institutes that are actively involved in research into and applications of AI.
Building on the traditionally close ties of TU/e with industry, EAISI has partnered with a number of relevant companies and organizations, both at a regional, national and European level. These include ASML, Philips Healthcare, NXP, Brainport Eindhoven, the AI NL Coalition, 4TU.Federation and EuroTech.

TU/e
EAISI

II. WORKING GROUP ARTIFICIAL INTELLIGENCE (AI) FOR HEALTH

Within EAISI, the working group Artificial Intelligence for Health is the first research program line. Three leading universities and a leading university medical center in the Netherlands have decided to form an alliance in AI research to gain a competitive position.

The alliance partners are:

1. Utrecht University & Medical Center (UMCU)
2. Eindhoven University of Technology (TU/e)
3. Utrecht University (UU)
4. Wageningen University & Research (WUR)

Goal of the alliance: create synergies, develop a roadmap and common agenda for research and education, stimulate new and facilitate ongoing AI projects within the alliance, ensure more effective use of resources and implement joint research and development.

All four partners in the alliance have unique track records, resources and contributions in terms of expertise in AI:

TU/e

The TU/e has its expertise in many technical areas, including HighTech systems. In addition the TU/e has launched the EAISI, the Eindhoven AI Systems Institute (EAISI), focusing on three AI application areas: HighTech systems and robotics, Health Applications and Smart Mobility. The High Tech Systems Centre and the Data Science Centre Eindhoven will be merged into EAISI to further integrated all available expertise.

UU

The UU launched the focus area Human-centered AI to foster interdisciplinary AI research at the university, connecting to related focus areas such as Governing the Digital Society and Applied Data Science, Complex Systems, Bioinformatics and Game research. This conglomerate of focus areas is likely to result in a new strategic theme with AI as the connecting factor. Characteristic for AI research at Utrecht University is that it aims to combine traditional symbolic or model-driven approaches with modern data-driven approaches, e.g. responsible AI, philosophy of AI, AI and law, logic-based knowledge representation, human-machine interaction, autonomy, reasoning, perception, computational linguistics, decision support, agent-based simulation and digital humanities.

UMCU

Within the UMCU a lot of effort is invested in the combination of healthcare, prevention and AI, e.g. in the Digital Health program, the Utrecht Exposome Hub, the gravitation program Exposome.NL and the EU BigData@Heart project. Furthermore, UMCU hosts important data collections, such as the Utrecht Cardiovascular Cohort, Julius Primary Care data, UPOD and EHR data. AI related research topics include clinical decision making, prognosis forecasting for Psychiatric and CVD patients, image recognition for food intake and environmental attributes, and high dimensional data analyses.

WUR

The development and application of AI in the entire research domain of WUR is one of the main objectives in the strategic plan. This applies to environment, society, plant, animal, food (safety) and health. In these domains, WUR both uses AI in fundamental research and integrates it in applications, aiming to research and demonstrate societal value of AI at higher TRL-levels. For this purpose, several strategic investment programs have started, such as Digital Twins and Data Driven & High Tech. These extend current knowledge and expertise.

The added value of the cooperation is obvious:

- Top Universities and clinics joining forces: all featuring in the World top 125
- Diversity and complementarity of AI knowledge and application areas across institutions
- The alliance presents a great framework to setup interdisciplinary collaborations, consortia and acquire grants
- The combined internal and external network of the four partners together has a very wide national and international reach
- Both model- and data-driven AI knowledge are available within the alliance. Combining these in an effort to achieve explainable AI is one of the main points within European and Dutch AI agendas
- AI talent is trained within the alliance, some collaborative education is already present which can be extended
- Synergy can lead to less wasted effort by the individual parties in, for instance, the applications for grants. Multiple initiatives on the same topics can be linked together and made stronger. Less work needs to be done twice

OTHER HEALTH-RELATED ACTIVITIES AND INITIATIVES AT THE TU/E

A. THE INTELLIGENT LIGHTING INSTITUTE (ILI)

The TU/e Intelligent Lighting Institute (ILI) was established in 2010 to investigate novel intelligent lighting solutions that will come within our reach by the large-scale introduction of LED technology, with a special emphasis on how these new solutions might affect people. In addition ILI aims at providing scientific evidence for the claims that go with these novel lighting solutions. At the campus of the Eindhoven University of Technology (TU/e), researchers at ILI are developing new concepts for interactive lighting solutions, as well as the requisite technology. This often requires combining the resources of various disciplines at the university.

Today, lighting systems are transforming into networked systems, offering a range of intelligent services and applications. The intelligent lighting technology allows many opportunities including autonomous lighting control, advanced user interaction styles and support for health and well-being through lighting.

PROJECT LIGHTCAP

An exciting example of the research and training work in this domain is project LIGHTCAP, a European Training Network under the Marie Skłodowska-Curie actions framework.

Light can make or break health, social and cognitive functioning. Given the rapid technological developments in light sources (LED, OLED) and the proliferation of intelligent infrastructures (IOT, data science), truly human-centered lighting can now be realized.

LIGHTCAP aims to address this challenge by providing a strong impulse to insight in the intricate and complex relationship between light, perception, attention and cognition. The goal of LIGHTCAP is to prepare the next generation of experts able to deliver on the promise of truly intelligent, human-centric lighting.

The 3 – 4 year training program is international, interdisciplinary, cross-sectional and translational. The project unites experts from neurobiology, cognitive neuroscience, chronobiology, psychology and lighting technology. It will train a generation of researchers who can look beyond the borders of their discipline and understand the implications of their findings for other fields.

In LIGHTCAP, 15 early stage researchers will be trained in a joint program between 7 academic European partners: The Human-Technology Interaction group and the Building Lighting group at Eindhoven University of Technology; the Centre for Biological Timing at the University of Manchester; the Lighting and Visual Perception group of the University of Sheffield; the GIGA-Cyclotron Research Centre-In Vivo Imaging of the University of Liège; the Centre for Chronobiology of the University of Basel; the Laboratory of Integrated Performance in Design of the Ecole Polytechnique Fédérale de Lausanne (EPFL); and the Lighting Technology group of the Technical University of Berlin. These groups will be working together intensively with each other and with the solid consortium of industrial and medical partners through secondments (research visits), consortium meetings and a joint training program.

B. THE DEMENTIA AND TECHNOLOGY CENTRE OF EXPERTISE

The Dementia and Technology centre of expertise is an initiative by the TU/e, initiated by the departments Industrial Design, Human Technology Interaction and the Built Environment. In this centre the researchers and developers aim to design, develop, evaluate and research non-pharmaceutical technological interventions for people living with dementia, and their caregivers.

Often technology is viewed as a solution for safety, efficiency or care management, however, technology can play a significant role in terms of quality of life as well. In this centre TU/e explores these possibilities in the context of for example social technology, effects of light, reminiscence technology, effects of sound and more.

RESEARCH PROJECTS (SELECTION)

DEMENTIA EMPATHIC HANDOVER

Development of a dementia simulator with help of the Empathic Handover approach. Effectively empathizing with people with dementia is challenging. Especially, when not all designers are able to encounter these vulnerable users themselves due to resource problems (time and budget) and ethical considerations (user burden, designers' capacity). Therefore, the research team developed the Empathic Handover approach. This approach supports multi-disciplinary design teams in transferring and translating user insights from a principal designer, who executed the user research with people living with dementia, to members of the design team who could not.

DESIGN WORK (SELECTION)

PAM

PAM is an agenda-buddy for people with dementia to follow a personal structured routine while they live by themselves. PAM can help people with dementia remember those small tasks again. PAM is located in the living room of the elderly. In the connected app, family members can plan daily activities, like breakfast and tea-time or add special events, like you can in a normal agenda-app. For each activity, they add a personal photo and record their own voice with a directive message, which the user will hear and see on PAM when it is time for the activity. When looking at PAM, the user can see how long it takes for the next activity to happen by looking at the progress of the lights until the last light becomes green.

UITVERTRAAGD

The Uitvertraagd installation challenges people with early-stage dementia to explore the beauty in simple activities by slow-motion videos, to trigger their intrinsic motivation to be active. The installation guides imagination and also functions as a catalyst for conversation between people with dementia, their family and caregivers. Caregivers can gain insight in the interests of a person with dementia by observing their interactions with the installation. The installation consists of a table with miniature representations of possible activities that can be engaged in at a care home (like painting or cooking). These representations help the person with dementia imagine their possibilities, as they often have difficulties when deciding upon an activity to participate in. The miniature activities can be used on one side of the table, while a small high speed studio is built on the other side of the table. This way caregivers can easily take slow-motion videos of the activities, which will be shown through projection. Enlarging a short action that does not require any skills or knowledge can create a beautiful output that people can feel proud of, which will stimulate and motivate them to be more active.

JHERONIMUS ACADEMY OF DATA SCIENCE (JADS)

The Jheronimus Academy of Data Science (JADS) is a unique concept in the Netherlands, which allows PDEng and others students to study, research and apply data science at three different Data Science Centres (TU Eindhoven, Tilburg University and Mariënburg Campus, Den Bosch) and to incorporate what they learn into existing ecosystems. The mission of JADS is to understand and further the value of data for solving complex societal and business challenges, with the academy serving as a linchpin between industry and the applied data science research conducted throughout JADS.

The Data Science and Entrepreneurship Graduate School turns out entrepreneurial and innovative data scientists who are just as good at performing cutting-edge scientific research as they are at applying it to the most pressing societal and business challenges. These graduates learn to operate in a collaborative ecosystem, fostering a stream of new scalable (or exponential) business models in Brabant and beyond.

The current JADS student body numbers 1,500-2,000 scattered across a range of programmes and three research centres.

APPLIED RESEARCH LABS

In the applied labs, research focuses on how data science can be used in specific industries, creating specialist knowledge that can be applied directly, is in-depth and relevant.

- **Data and Health**
  Data and Health aims to bridge the gap between technical possibilities and practical ambitions. Exploring innovative methods for disease prevention, detection, treatment and follow-up. Advancing and accelerating learning capabilities within the full healthcare ecosystem.
- **Data and AgriFood**
  Fourth paradigm research and innovative crossovers between AgriFood, data and engineering in all its forms will be essential for feeding the world by 2050 while simultaneously reducing the environmental footprint of current food production systems. Solutions will only be created by working together.
- **Data and Cities**
  Data and Cities focuses on providing a novel perspective on the complexity of cities (and urban areas) by developing new data-based envisioning methods for *cities4people*.
- **Data and Smart Industry**
  Data and Smart Industry uses data science to deal with the complex dynamics of production systems. Real-time, detailed information allows the right product to be delivered to the right customer at the right time and at a minimal cost. Data science helps to improve the daily planning and monitoring of operations, is the basis for optimising production systems, and enables new concepts in the design of products and services.
- **Data and Smart Mobility**
  Data and Smart Mobility aims to improve and perfect the way data is used from two perspectives – smarter connected vehicles and improved services surrounding mobility (such as *Maas*). The success and sustainability of these developments is greatly dependent on the quantity and quality of the underlying data.

RESEARCH SHOWCASE: THE ODDSPOT PROJECT

Data-driven diagnoses: OddSpot - Diagnosing suspicious skin spots to identify actinic keratoses and basal cell carcinomas

Scientific literature tells us that some decisions can be adequately supported by or even made by a computer model. This fact may take some getting used to (how can my phone be just as smart as a human expert?'), but in the world of data science this has been common knowledge for at least a decade. And it is no surprise either, given that today's computers excel at well-defined tasks such as playing chess and draughts and recognising faces.

To showcase this aspect, students at JADS implemented a decision-making model that is able to diagnose two kinds of suspicious spots on the skin with a high degree of accuracy – actinic keratoses (AK) and basal cell carcinomas (BCC).

Of all the suspicious spots that appear on a person's skin, AK and BCC are among the most common.

The team developed a smart phone app called OddSpot that employs the user's input to evaluate the likelihood of that small suspicious spot being a potential precursors to skin cancer, an actinic keratosis or basal cell carcinoma. Much work has been devoted to the methodology to ensure that predictions are accurate, but a rider is included that in the event of any doubts the user must consult a doctor.

The app was created by the Human-Technology Interaction group at Eindhoven University of Technology (TU/e) together with the Jheronimus Academy of Data Science (JADS) in Den Bosch.

FUNDAMENTAL LABS

The fundamental labs focus primarily on establishing and advancing the scientific side of data science.

- **Computational Personalisation**
  The Computational Personalisation Lab focuses on statistical and machine learning methods for personalised healthcare treatment and more. The lab endeavours to find the 'right treatment for the right person' by developing and analysing sequential allocation policies and building software to deploy those policies in field experiments.

- **Dynamic Organizational Networks**
  The Innovative Data Services Lab is focused on the transition of product-oriented companies towards becoming solution-providers through the application of data. The lab conducts research and supports companies through educational programmes for executives and company-tailored solutions.

- **Jheronimus Academy Data Engineering (JADE) Lab**
  Industry-level big data tech requires the systematic study, development and evaluation of methods, techniques and tools for big data-intensive software and data engineering. The JADE lab serves the JADS and EU research community in achieving excellence in this field by creating synergies with the most renowned academic researchers and practitioners from both JADS' parent universities, industry and other universities.

- **Recommender Lab**
  In the Recommender Lab the research focuses on how decisions can be supported by recommender systems. It includes fields such as movies, music, health-related decisions and energy-saving measures.

- **Digital Business Models and Ecosystems**
  In the DBM lab the research focuses on how to translate data and the outcomes of data mining and visualisation techniques into new business opportunities.

- **Ambitious Digital Entrepreneurship**
  The Ambitious Digital Entrepreneurship Lab is focused on teaching and conducting research on those intersections where data science and business meet in their quest to create value using big data and new technologies.

AVANS UNIVERSITY OF APPLIED SCIENCES

AVANS is located in Breda, Den Bosch, Roosendaal and Tilburg and offers two Life Sciences and Health programmes.

Active aging

The research focuses on health care innovations, particularly for providing care to the elderly. AVANS has developed a health and technology laboratory devoted to this group, the GET-LAB. Healthcare professionals are introduced in GET-LAB to new healthcare technologies and learn to implement healthcare innovations.

Analysis techniques in life sciences

The focus is on new developments in the field of metabolic profiling, allergen and biomarker research. Separation techniques such as liquid chromatography and its joint use with mass spectrometry play a prominent role. Biochemical and molecular-biological analysis techniques also play a major role.

To facilitate and support its research, AVANS has a well-equipped laboratory with spectrometry (UV/VIS, AAS, FTIR), liquid chromatography (HPLC), gas chromatography (GC) and mass spectrometry (GC-MS and LC-MS) instruments as well as biochemical analysis technology.

FONTYS UNIVERSITY OF APPLIED SCIENCES

Fontys University of Applied Sciences has campuses in Eindhoven, Tilburg, Den Bosch, Helmond and Veghel.
Fontys UAS focuses on five areas of research: high tech systems & materials, health, learning to learn, a smart society and the creative economy.

The following research groups are active in the field of healthcare:

Human and technology	The expertise in this research field concentrates on areas such as user-oriented design, playful interactions and influencing technology.
Health innovation and technology	Acceptance and implementation of technological innovations in healthcare, the development of new applications of technology in healthcare from the perspective of and in partnership with users: patients, loved ones, informal healthcare providers and healthcare professionals. Ethical aspects of the use of technology in healthcare. Accessibility of technology in healthcare and digital inequality.
Decision support: who cares	The added value of technological innovations for monitoring patients and gathering qualitative patient data that can improve decision making and improves the care process.
Interaction design	Interactive games, serious gaming to improve health
Move to be	Learn how to move, active lifestyle, exercise-friendly environment
Big data	Using big data to improve predictions, diagnoses, etc.
Self-direction	A sustainable change in health and exercise behaviour and integration of monitoring and eCoaching technology in physiotherapy/paramedical care to improve self-management, therapy compliance and (long-term) effectiveness of care.

FONTYS EGT

Fontys EGT is the institution's Healthcare and Technology Expertise Centre and consists of some 30 partners from the education, healthcare and the business communities in the Brainport region and North Limburg. The partners involved aim to improve the connection between healthcare practitioner demands and the range of technological solutions on offer, which they hope will accelerate healthcare innovations. This contributes to a better quality care and a higher quality of life.

Source: Fontys University of Applied Sciences

C. Knowledge institutions

HOLST CENTRE

The Holst Centre is an independent R&D centre that develops technologies for wireless autonomous sensor technologies and flexible electronics, in an open innovation setting and in dedicated research processes. A key feature of the Holst Centre is its partnership model with industry and academia, based on roadmaps and programmes. It is this kind of cross-fertilisation that enables the Holst Centre to balance its scientific strategy with industrial needs.

The Holst Centre was launched in 2005 by imec (Flanders, Belgium) and TNO (the Netherlands) and is supported by local, regional and national governments. Located on the High Tech Campus Eindhoven, the Holst Centre benefits from, and contributes to, the state-of-the-art on-site facilities. The Holst Centre has over 200 employees from some 28 nations and a commitment from more than 40 industrial partners. It concentrates on six areas of innovation, one of which is connected health solutions.

CONNECTED HEALTH SOLUTIONS

When it comes to connected health solutions, the Holst Centre is at the forefront of developments in personal health and biomedical sensing technologies. The ability to unobtrusively monitor our bodies and deliver medical-grade data in any setting will revolutionise healthcare. Instead of just managing diseases, the information gathered will allow people to manage their own health. By helping people identify early warning signs and providing them with feedback that encourages healthy behaviour and lifestyle choices, quality of life can be improved while healthcare spending remains under control.

Through advanced, low-power sensors and data-handling circuitry, Holst creates multifunctional solutions for wearable and non-contact monitoring coupled with ground-breaking autonomy and data quality. Moreover, highly sophisticated algorithms are developed to help analyse the data and extract meaningful and actionable information.

Together with dedicated R&D projects for individual clients, Holst also offers complete R&D prototyping including initial clinical trials. Together with Holst's ecosystem partners, the centre is also active in circuit design for reducing power consumption. The Holst Centre's extensive expertise in printed and flexible electronics is also helping to lower manufacturing costs and increase user-comfort.

Holst and partners are active in all areas of personal health, with a focus on managing chronic diseases such as heart failure and disease prevention through behavioural changes. From a different perspective, other research teams are exploring how physiological sensing technologies and insight can add value beyond healthcare, such as by enhancing virtual and augmented reality experiences.

SPINOFFS

The Holst Centre supports initiatives for spinning off applications of mature technologies. Initiatives by employees are allowed to incubate within the Holst Centre and are spun off after demonstrating proven viability. Where required, networks of startup accelerators are available for the entrepreneur-to-be to gain the knowledge required for launching a successful startup.

A selection of the Holst Centre's spinoffs:

Bloomlife

Bloomlife is a women's health company solving the most significant yet underserved global challenges of today in maternal health. In the future, it aims to provide evidence-based solutions combining connected devices with data analytics in order to improve access to care, provide personalised feedback to mothers and help doctors at an earlier stage in predicting and managing pregnancy complications. By addressing modifiable risk factors, detecting abnormalities, and predicting adverse events, Bloomlife aims to ensure that every family gets a healthy start.

Bambi Medical

Bambi Belt is a soft fabric, skin-friendly wireless monitoring device. It accomplishes the same functions as the wired adhesive electrode systems currently implemented in NICUs. The disposable belt is wrapped around a baby's chest and sensors integrated in the Bambi Belt measure critical data in a nonintrusive way, while a small sensor module sends the captured data to the systems portable monitor. The belt can either be used as a stand-alone device or in combination with existing patient monitors within the hospital infrastructure. The non-adhesive texture of the belt means that babies will not suffer from pain or stress, while its wireless features allow parents to remove their child from the incubator and perform kangaroo mother care.

5. TALENT AND EDUCATION INCLUDING LABOUR MARKET

General characteristics of the Brabant labour market

Brabant's workforce has proven to adapt easily to the cultures of foreign companies and multilingualism is the norm. Over 94% of the labour force has conversational knowledge of a second language, with English (90%), German (71%) and French (29%) being the most common. At least three-quarters of the population speaks two languages aside from Dutch and a third are competent in four languages. Two world-class universities (one offering technical studies, the other economics and law) and numerous universities of technology guarantee a steady influx of new talent into the province.

LABOUR FORCE BY GENDER AND AGE

Gender	Breda region	Tilburg region	Den Bosch region	Eindhoven region	Brabant	Participation rate
Male	180,000	139,000	191,000	226,000	736,000	76.0%
Female	157,000	119,000	164,000	187,000	628,000	66.3%
Total	**337,000**	**258,000**	**355,000**	**413,000**	**1,364,000**	**71.2%**

Age	Breda region	Tilburg region	Den Bosch region	Eindhoven region	Brabant	Participation rate
15-24 yr	54,000	45,000	57,000	65,000	221,000	72.1%
25 - 44 yr	130,000	102,000	135,000	167,000	534,000	89.0%
45 -74 yr	153,000	111,000	163,000	181,000	609,000	60.4%

LABOUR FORCE, 2018

Brabant 1,364,000 people (14.9% of total)

The Netherlands 9,125,000 people (100%)

Source: Statistics Netherlands, 2019

NUMBER OF STUDENTS ATTENDING SECONDARY AND HIGHER EDUCATIONAL INSTITUTIONS IN BRABANT (2018/2019)

	Secondary education (Prevocational or general secondary education)	Medium vocational education (Vocational secondary education)	Higher Professional education (University of technology)*	University BSc, MSc
Breda region	36,980	15,690	See Brabant total	70
Tilburg region	24,820	17,640	See Brabant total	15,730
Den Bosch region	36,950	22,880	See Brabant total	x
Eindhoven/Helmond region	43,420	22,280	See Brabant total	11,970
Brabant	**142,170**	**78,490**	**86,910**	**27,770**

** Data for universities of technology unavailable at sub-regional level due to mergers between these institutions. Data only available at provincial level. Universities of technology have institutions in all four sub-regions.*

QUALITY OF EDUCATION AND TRAINING SYSTEM

Unlike many other countries, the Netherlands offers multiple forms of secondary education, giving children the opportunity to choose their path based on their talents and interests. The Netherlands has an excellent system of lower, secondary, higher and professional education. The World Economic Forum's Global Competitiveness Report ranks the Netherlands third in the world, as evaluated by business leaders, based on the quality of education and training systems.

GRADUATE SKILLS LEVELS

RANKING		SKILLS OF GRADUATES
1.	Switzerland	81.4
2.	Finland	77.0
3.	**The Netherlands**	**74.4**
8.	Singapore	73.4
3.	United States of America	71.2
6.	Luxembourg	71.1
7.	Denmark	71.0
8.	Quatar	70.9
9.	Austria	70.8
10.	Iceland	70.1

Source: DUO, 2019, World Economic Forum, The Global Competitiveness Report 2019

The Brabant labour market for LS&H

A. Current employment
B. Education: students and graduates
C. Unemployment: registered jobseekers

REGIONS AND CITIES IN BRABANT WITH MORE THAN 500 LIFE SCIENCES & HEALTH JOBS

A. Current employment

As mentioned in Chapter 1, 18,160 people are currently employed in the life sciences industry in Brabant. The Den Bosch region (being north-east Northeast Brabant, which includes the cities of Oss and Boxmeer) has the largest workforce with 7,400 people, followed by the Eindhoven/Helmond region (south-east Brabant). The fact that Life Sciences & Health is a knowledge-intensive industry is evident from the large proportion of highly educated personnel – over 40% of the workforce is highly educated, with that figure rising to 47% in the Den Bosch region. The average level of education of the workforce in the Tilburg (central Brabant) and Breda regions (western Brabant) is a bit lower, possibly reflecting the fact that the Life Sciences & Health activities in these regions are focused more on wholesale rather than R&D.

EMPLOYMENT ACCORDING TO LEVEL OF EDUCATION IN LS&H

Education level	Total	low	medium	high
Breda region	3,710	1,020	1,560	1,090
Tilburg region	1,590	450	680	450
Den Bosch region	7,400	1,240	2,650	3,480
Eindhoven/Helmond region	5,470	1,050	2,090	2,300
Brabant	**18,160**	**3,760**	**6,970**	**7,320**

Shares education levels	Total	low	medium	high
Breda region	100.0%	27.6%	42.2%	29.5%
Tilburg region	100.0%	28.1%	42.5%	28.1%
Den Bosch region	100.0%	16.8%	35.8%	47.0%
Eindhoven/Helmond region	100.0%	19.2%	38.2%	42.0%
Brabant	**100.0%**	**20.7%**	**38.4%**	**40.3%**

Source: Brabant Register of Companies 2018, Statistics Netherlands 2018, adapted by Fanion Onderzoek & Advies

B. Education: students and graduates

STUDENTS AND GRADUATES IN BRABANT

Graduates form the largest group of new people entering the labour market. The Eindhoven University of Technology (TU/e) offers several programmes in the Life Sciences & Health industry, and in 2018 some 670 students followed the Biomedical Technology bachelor's degree programme and 540 students followed a master's degree programme.

Over the past five years the number of students in Life Sciences & Health at the Eindhoven University of Technology has been steadily rising, and more students means more graduates. In 2013 there were 230 graduates in life sciences-related courses, and that number had increased to 340 by 2018.

In 2018 2,820 students followed a programme that matches the requirements of the Life Sciences & Health industry at Brabant's Fontys, AVANS and HAS universities of applied sciences (UAS). Fontys, with 220 students in this field in 2018, had the lion's share. The universities of applied sciences are also seeing a rise in life sciences students, with 530 more students (a rise of 23% over 2013) taking a Life Sciences & Health-related course in 2014. Here again, more students mean more graduates, with 230 bachelor's degrees awarded in 2013 and 340 handed out in 2017.

Approximately 290 students graduated in 2018 with a mid-level vocational diploma in a specific Life Sciences & Health-related course. Most of them – 180 – graduated in the Den Bosch region. This is a relatively small group in comparison with the much larger group of students who obtained a vocational education diploma in Health and Welfare (care). In Brabant, 4,640 students graduated from such a course in 2018.

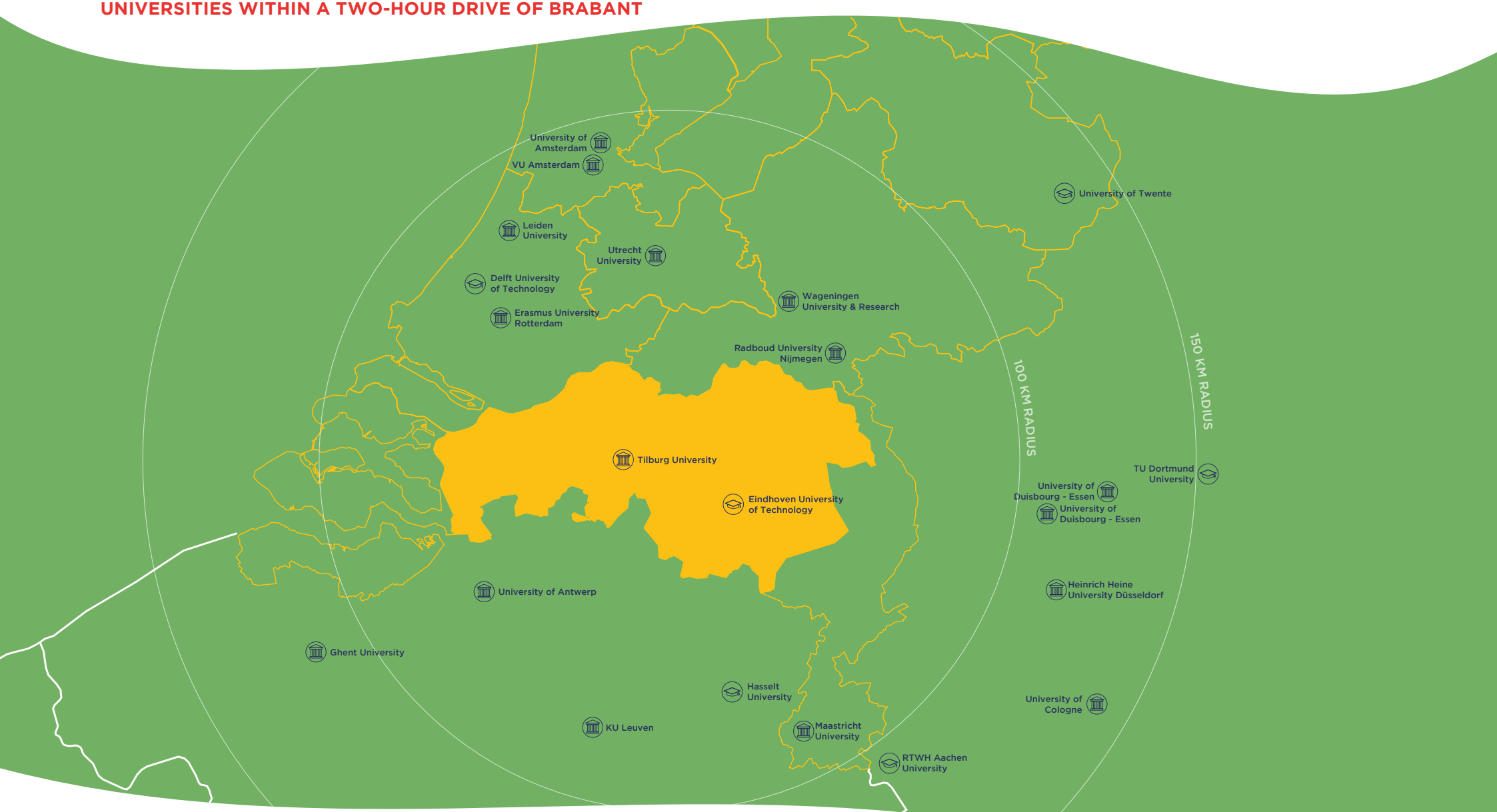
Education centres that offer healthcare and life sciences vocational studies at secondary and higher level are widespread across the country and Brabant. In Brabant there are seven large institutions that offer life sciences and health education at secondary level: ROC West-Brabant, ROC Tilburg, De Rooi Pannen, Koning Willem I College, ROC De Leijgraaf, Summa College and Sint Lucas.

Moreover, 6,250 students follow secondary education related to Life Sciences & Health, taking courses that prepare them for further education in Nature & Health or Nature & Technology studies. These students mostly continue their education at a higher level at a UAS or university.

STUDENTS AND GRADUATES WITHIN A 150 KM RADIUS

There are 22 universities in three countries within a radius of 150 km (approximately a two-hour drive) of the centre of Brabant. Eleven of these institutions have a general focus, five are universities of applied sciences and six specialise in other fields. A total of 605,340 students study at these universities, with at least 255,680 majoring in an environmental, health or technology field.

UNIVERSITIES WITHIN A TWO-HOUR DRIVE OF BRABANT



Source: DUO, Dataloep Vlaanderen, DEStatis/Statistisches Bundesambt (2019), adapted by Fanion Onderzoek & Advies

NUMBER OF STUDENTS FOREIGN UNIVERSITIES

Netherlands			**Total Netherlands**	**260,140**	**111,250**
City	**University**	**Driving distance**	**Type of university**	**Number of students**	**Students in Nature, Health and Technology**
Tilburg	Tilburg University	0	Specialized University	15,730	460
Eindhoven	Eindhoven University of Technology	0	Technical University	11,970	11,900
Nijmegen	Radboud University Nijmegen	80 km	Broad University	21,680	7,090
Utrecht	Utrecht University	90 km	Broad University	31,800	13,580
Rotterdam	Erasmus University Rotterdam	90 km	Specialized University	26,960	3,830
Delft	Delft University of Technology	110 km	Technical University	24,510	23,900
Wageningen	Wageningen University & Research	110 km	Specialized University	11,940	11,840
Maastricht	Maastricht University	110 km	Specialized University	17,190	5,590
Leiden	Leiden University	130 km	Broad University	29,050	6,390
Amsterdam	VU Amsterdam	130 km	Broad University	24,570	10,060
Amsterdam	University of Amsterdam	130 km	Broad University	34,070	8,960
Enschede	University of Twente	180 km	Technical University	10,670	7,650
Belgium			**Total Belgium**	**133,860**	**65,110**
City	**University**	**Driving distance**	**Type of university**	**Number of students**	**Students in Nature, Health and Technology**
Hasselt	Hasselt University	70 km	Specialized University	5,700	3,330
Antwerp	University of Antwerp	90 km	Broad University	20,220	9,310
Leuven	KU Leuven	110 km	Broad University	56,490	29,110
Ghent	Ghent University	150 km	Broad University	51,450	23,360
Germany			**Total Germany**	**210,350**	**79,320**
City	**University**	**Driving distance**	**Type of university**	**Number of students**	**Students in Nature, Health and Technology**
Duisburg	University of Duisburg - Essen	130 km	Broad University	15,870	.
Dortmund	TU Dortmund University	130 km	Technical University	33,810	33,810
Aachen	RTWH Aachen University	130 km	Technical University	45,510	45,510
Essen	University Duisburg - Essen	140 km	Broad University	26,600	.
Düsseldorf	Heinrich Heine University Düsseldorf	140 km	Broad University	35,560	.
Cologne	University of Cologne	170 km	Broad University	53,000	.
			Total number of students	**604,340**	**255,680**

Source: DUO, Dataloep Vlaanderen, DEStatis/Statistisches Bundesambt (2019), adapted by Fanion Onderzoek & Advies

1. University - TU/e, Eindhoven University of Technology

The crucial facts and figures for the TU/e are:

- 11,000 students
- 5,000 knowledge workers
- 90 nationalities
- 14 distinct laboratories

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

NUMBER OF STUDENTS IN LS&H

	2014	2015	2016	2017	2018
Bachelor	**550**	**630**	**710**	**740**	**670**
Biomedical Technology	550	630	710	740	670
Master	**410**	**490**	**580**	**660**	**740**
Human-technology Interaction	70	80	100	120	120
Medical Engineering	60	60	70	80	110
Biomedical Engineering	130	170	190	220	260
Chemical Engineering	150	180	220	240	250
Total	**960**	**1,120**	**1,290**	**1,400**	**1,410**

NUMBER OF GRADUATES IN LS&H

	2013	2014	2015	2016	2017
Bachelor	**70**	**80**	**100**	**130**	**150**
Biomedical Technology	70	80	100	130	150
Master	**160**	**150**	**150**	**160**	**190**
Biomedical Engineering	60	40	50	50	60
Human-technology Interaction	20	20	30	20	40
Medical Engineering	10	20	20	20	10
Chemical Engineering	70	70	50	70	80
Total	**230**	**230**	**250**	**290**	**340**

Source: DUO, 2019

NUMBER OF STUDENTS IN INDUSTRIAL DESIGN

	2014	2015	2016	2017	2018
Bachelor					
Industrial Design	462	498	514	293	581
Master					
Industrial Design	139	150	156	79	176
Total	**601**	**648**	**670**	**372**	**757**

NUMBER OF GRADUATES IN INDUSTRIAL DESIGN

	2013	2014	2015	2016	2017
Bachelor					
Industrial Design	92	80	117	92	130
Master					
Industrial Design	59	45	58	61	61
Total	**151**	**125**	**175**	**153**	**191**

Source: DUO, 2019

2. Universities of Applied Science - Fontys, AVANS, HAS

UNIVERSITY OF APPLIED SCIENCES/COURSES

	2014	2015	2016	2017	2018
Avans UAS	**770**	**780**	**860**	**940**	**930**
Human and Technology	180	210	230	230	250
Biology and Medical Laboratory Research	590	570	630	710	680
Fontys UAS	**1,000**	**990**	**970**	**950**	**1,070**
Medical Imaging and Radiotherapeutic Techniques	570	580	580	570	700
Human and Technology	200	210	200	210	210
Podiatry training	230	200	190	170	160
HAS	**520**	**570**	**670**	**750**	**820**
Applied Biology	520	570	670	750	820
Total	**2,290**	**2,340**	**2,500**	**2,640**	**2,820**

GRADUATES UNIVERSITY OF APPLIED SCIENCES

	2013	2014	2015	2016	2017
Avans UAS	**120**	**110**	**100**	**130**	**130**
Biology and Medical Laboratory Research	100	90	90	90	100
Human and Technology	20	20	10	40	30
Fontys UAS	**200**	**200**	**250**	**240**	**220**
Medical Imaging and Radiotherapeutic Techniques	90	100	120	110	100
Podiatry training	50	60	50	40	30
Teacher Biology (second degree)	30	20	30	30	40
Human and Technology	20	10	40	40	40
Teacher Biology	10	10	10	20	10
HAS UAS	**80**	**60**	**80**	**90**	**110**
Applied biology	80	60	80	90	110
Total	**390**	**380**	**430**	**460**	**460**

Source: DUO, 2019

OVERVIEW OF EDUCATIONAL INSTITUTIONS IN LS&H
AT SECONDARY VOCATIONAL EDUCATION LEVEL (GREEN) AND UNIVERSITIES OF APPLIED SCIENCES (RED)

SECONDARY VOCATIONAL EDUCATION

1. ROC West-Brabant
2. Koning Willem I College
3. ROC de Leijgraaf
4. ROC Ter AA
5. ROC Gilde Opleidingen
6. ROC Leeuwenborgh
7. Scalda
8. ROC Da Vinci College
9. ROC Albeda College/Zadkine
10. ROC Mondriaan
11. KAN DE NAAM NIET LEZEN OP DE KAART
12/13. Utrecht/Midden Nederland
14. ROC Rivor
15. ROC Nijmegen e.o.
16. ROC AVENTUS
17. ROC Graafschap College
18. ROC van Flevoland
19. Regio College
20. ROC Horizon College
21. ROC Kop v Noord-Holland
22. Deltion College/Landstede
23. ROC Drenthe College
24. ROC Friese Poort/ROC Friesland College
25. Alfa-college/Noorderpoort/ROC Menso Alting

UNIVERSITIES OF APPLIED SCIENCES

1. Avans Hogeschool
2. HAS
3. Fontys Hogescholen
4. Zuyd Hogeschool
5. HZ University of Applied Sciences
6. Hogeschool INHOLLAND/Hogeschool Rotterdam
7. Haagse Hogeschool
8. Hogeschool Leiden
9. Hogeschool Utrecht
10. Christelijke Hogeschool Ede
11. Hogeschool van Arnhem en Nijmegen
12. Hogeschool van Amsterdam
13. Saxion Hogeschhol
14. Christelijke Hogeschool Windesheim
15. NHL Stenden Hogeschool
16. Hanzehogeschool Groningen

Source: DUO, adapted by Fanion Onderzoek & Advies

3. Senior secondary vocational (MBO) education and secondary education

AN OVERVIEW OF SECONDARY (VOCATIONAL) EDUCATION GRADUATES, LIFE SCIENCES & HEALTH, TECHNOLOGY AND NATURE, 2018

	MBO	HAVO	VWO	Total
Breda region	80	750	820	1,650
Tilburg region	0	510	480	990
Den Bosch region	120	870	840	1,830
Eindhoven/Helmond region	90	1,020	950	2,060
Brabant	**290**	**3,150**	**3,100**	**6,540**

SECONDARY VOCATIONAL EDUCATION GRADUATES IN HEALTH AND WELFARE, IN 2018

	2014	2015	2016	2017	2018
Breda region	1,510	1,330	1,140	1,110	1,060
Den Bosch region	1,370	1,460	1,270	1,390	1,230
Eindhoven/Helmond region	2,050	1,820	1,500	1,570	1,410
Tilburg region	1,200	1,010	990	910	940
Brabant	**6,130**	**5,620**	**4,900**	**4,980**	**4,640**

OVERVIEW OF SPECIFIC LIFE SCIENCES & HEALTH COURSES AT SECONDARY VOCATIONAL EDUCATION LEVEL

- Laboratory employee (All-round laboratory technician) - Eindhoven, Etten-Leur, Veghel
- Advisor health technical facilities (Orthopaedic shoe technician/Manager) - Den Bosch
- Healthcare Facilities Advisor (Orthopaedic Technician) - Den Bosch
- Analyst (Analyst pathology) - Etten-Leur, Veghel
- Analyst (Biotechnology analyst) - Eindhoven, Veghel
- Analyst (Microbiological analyst) - Eindhoven, Etten-Leur
- Pharmacist's assistant - Eindhoven, Etten-Leur, Den Bosch
- Veterinary assistant/Para-veterinary - Etten-Leur, Den Bosch
- Employee, Sterile Medical Devices - Eindhoven
- Orthopaedic shoe technician - Den Bosch
- Orthopaedic shoe technician (Shoe technician) - Den Bosch
- Orthopaedic Technical Assistant -Den Bosch
- Test animals (Biotechnician) - Den Bosch
- Laboratory animals (Laboratory animal caretaker) - Den Bosch

Source: DUO, 2019

C. Unemployment - registered jobseekers

In 2018 there were 25,510 people registered as jobseekers in Brabant with technical training. Unfortunately, their professions (qualifications) are not further defined. About 70% of the jobseekers had a low education profile and are not qualified to enter the labour market. About a quarter had a secondary level education and only three percent of the jobseekers were highly educated.

REGISTERED JOBSEEKERS IN 2018

Jobseekers with technical qualifications	Education level				Share in total		
	low	medium	high	Total	low	medium	high
Breda region	4,600	1,350	330	6,280	70.7%	25.9%	3.3%
Tilburg region	4,630	1,000	220	5,850	73.5%	23.7%	2.8%
Den Bosch region	4,090	1,100	290	5,480	72.4%	25.1%	2.5%
Eindhoven/Helmond region	6,050	1,420	430	7,900	71.0%	25.2%	3.8%
Brabant	**19,370**	**4,870**	**1,270**	**25,510**	**71.8%**	**25.0%**	**3.2%**

Source: UWV, 2019, adapted by Fanion Onderzoek & Advies

6. LOCATION, FACILITIES AND CAMPUSES

A. Location

BRABANT, THE NETHERLANDS: YOUR GATEWAY TO EUROPE

In geographic terms the Netherlands – and Brabant in particular – has historically been the key port of entry to mainland Europe.

This is also true in a literal sense, as Brabant is part of the delta stretching between Rotterdam (Europe's largest port) and Antwerp (the continent's second largest port) and three of Western Europe's busiest airports: Amsterdam Schiphol, Brussels Airport and Dusseldorf International Airport. Excellent infrastructure (by road, rail, water and air) and IT and data communication networks that are second-to-none anywhere in the world are added bonuses.

This combination of strengths helps industry in the area to fluidly reach 170 million consumers in a radius of 500 kilometres (300 miles). These consumers with significant financial means (north-western Europe is one of the wealthiest markets in the world) are all within 24 hours of Brabant.

Efficient logistics services empowered by **INNOVATION & COLLABORATION**

#1 ENTRY POINT
In Europe for overseas products

#1 LOGISTICS
Hub in Europe

COMPETITIVE COST
for labour, real estate and transport

500 km proximiy to European markets
170 MILLION CONSUMERS

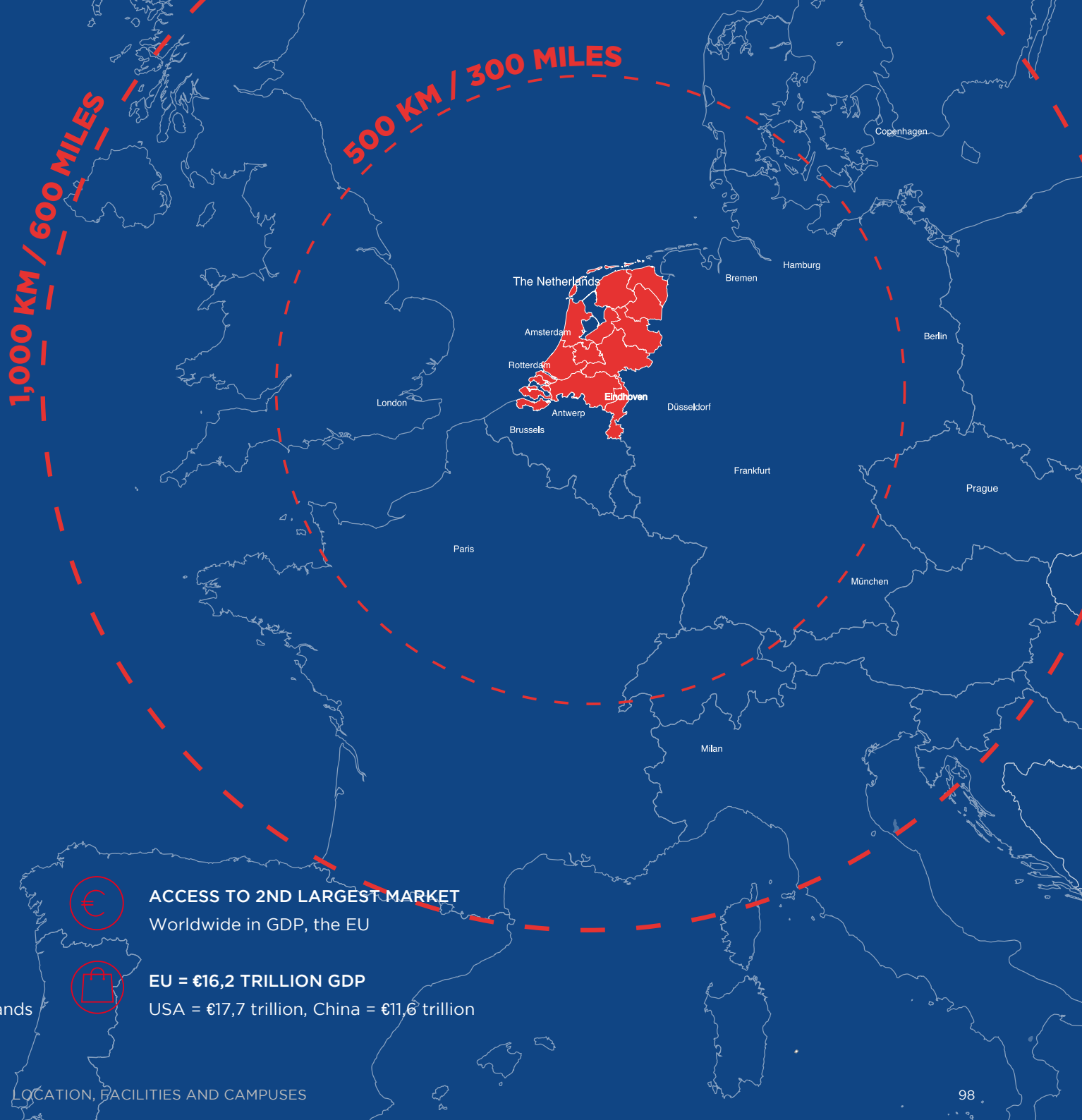
3 MAINPORTS
For air, data and sea

EXCELLENT CONNECTIVITY
To Europe and all continents

World class & competitive business environment
NO VAT PAYMENT AT IMPORT

BRABANT, THE NETHERLANDS: ACCESS TO THE SECOND LARGEST MARKET IN THE WORLD

Within a radius of 500 kilometres, businesses can reach 170 million consumers in Western Europe, and if that circle is extended to a radius of 1,000 kilometres (600 miles) – still within easy and rapid reach – this figure grows to 250 million people. The largest European economies – Germany, France, the United Kingdom and the Benelux region – are all within a day's reach. The rest of the European Union (the second largest market in the world in GDP terms) is just as accessible from Brabant, with an additional 24 to 36 hours in transit time.



170 MILLION CONSUMERS
Within a 500 km / 300 mile radius

250 MILLION CONSUMERS
Within a 1,000 km / 600 mile radius

PERFECT SPRINGBOARD
into European market

MAJOR EUROPEAN ECONOMIES
are within a day's reach of the Netherlands

Source: Invest in Holland, 2018

ACCESS TO 2ND LARGEST MARKET
Worldwide in GDP, the EU

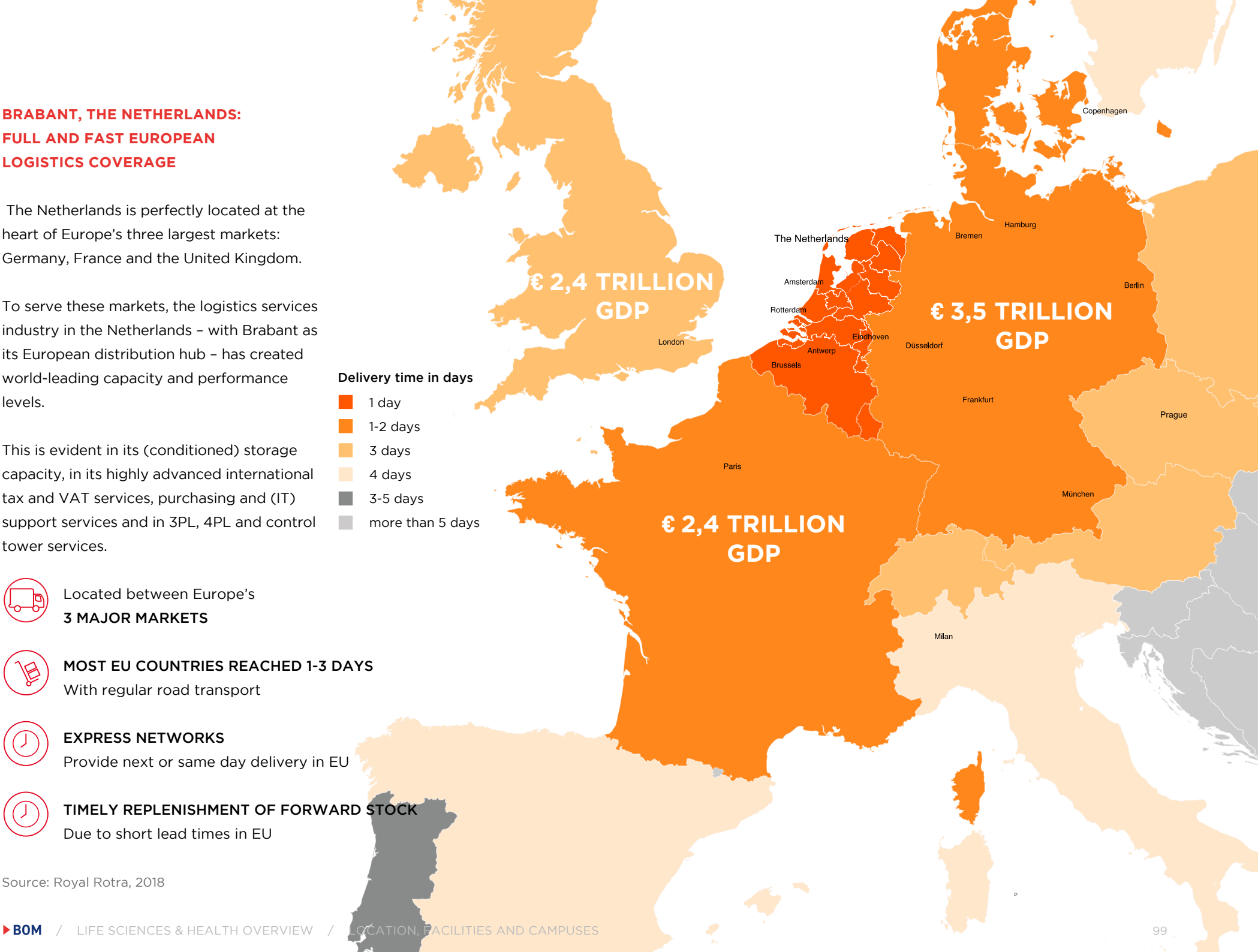
EU = €16,2 TRILLION GDP
USA = €17,7 trillion, China = €11,6 trillion

BRABANT, THE NETHERLANDS: FULL AND FAST EUROPEAN LOGISTICS COVERAGE

The Netherlands is perfectly located at the heart of Europe's three largest markets: Germany, France and the United Kingdom.

To serve these markets, the logistics services industry in the Netherlands – with Brabant as its European distribution hub – has created world-leading capacity and performance levels.

This is evident in its (conditioned) storage capacity, in its highly advanced international tax and VAT services, purchasing and (IT) support services and in 3PL, 4PL and control tower services.



Located between Europe's
3 MAJOR MARKETS

MOST EU COUNTRIES REACHED 1-3 DAYS
With regular road transport

EXPRESS NETWORKS
Provide next or same day delivery in EU

TIMELY REPLENISHMENT OF FORWARD STOCK
Due to short lead times in EU

Source: Royal Rotra, 2018

B. Pivot Park (Oss)

Pivot Park is a life sciences campus with a special focus on pharmaceutical innovation. The campus offers lab and office spaces of all sizes with access to high-quality pharmaceutical R&D facilities and infrastructure and expertise that give companies the chance to accelerate, grow and excel in the field of drug discovery and development.

Among the 60 startups and scaleups at Pivot Park there are also two GMP-certified pilot plants (gram-to-kilogram and fill and finish) and an ultra-high-throughput screening centre for accelerating drug discovery. Onsite analytical support (including NMR and LCMS) and a well-equipped open access laboratory significantly reduce the need to invest in your own equipment.

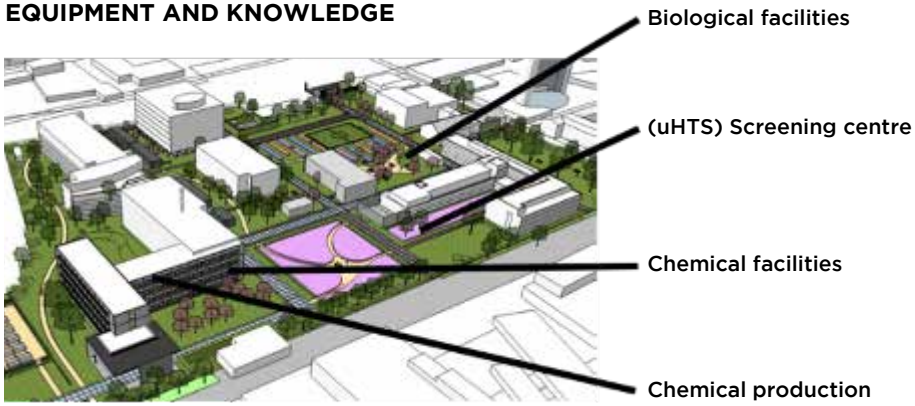
The Pivot Park ecosystem consists of an active and innovative pharma R&D community that acts as a hub within a broader international network. The campus is an incubator that connects knowledge and experience between established companies, startups and spinoffs. Pivot Park's business support in respect of access to grants, private investment and venture capital will provide startups with all the ingredients for launching their company in the best way possible.

Pivot Park is based in the heart of the city of Oss, the Netherlands, at a single site with an open character. Oss is perfectly situated in the middle of a triangle made up by the cities of Eindhoven, Nijmegen and Den Bosch, which means that companies in Oss benefit both from the universities, institutions and companies in those locations and can also take advantage of the highly qualified labour pool in the region. Oss is moreover easily accessible by car and public transport and through the various nearby international airports.

Source: Pivot Park

A life sciences culture is embedded in Pivot Park and its community, which makes it the hotspot for pharmaceutical innovation.

UNIQUE MAJOR PHARMACEUTICAL R&D FACILITIES, EQUIPMENT AND KNOWLEDGE



The whole value chain, from drug discovery, drug development, approval and registration through to manufacturing is present at Pivot Park

pivotpark

R&D FACILITIES, CONTRACT RESEARCH AND CONTRACT MANUFACTURING AT PIVOT PARK

Pivot Park has state-of-the-art core pharmaceutical R&D facilities that can be used by product developers, contract research organisations and service providers alike. The core facilities consist of cutting-edge biological and chemical laboratories and numerous modern chemical labs for synthesis and analysis, with a comprehensive range of services and utilities. Pivot Park also provides startups with a 'starter package', ranging from glassware to laboratory equipment. And fully-furnished and serviced offices, coffee corners, a meeting centre and a restaurant are also all available.

Leading examples of CROs, CMOs and service providers at Pivot Park:

- BioConnection, a company active in the field of contract services and GMP manufacturing aimed at developing and producing sterile (bio) pharmaceutical drug products.
- Ardena has expertise in active pharmaceutical ingredients and nanomedicines, which it uses to develop and validate manufacturing processes and analytical methods, as well as performing cGMP manufacture, quality control and stability studies.
- Pivot Park Screening Centre, with its open access lab for laboratory automation and high-throughput screening facility where drug discovery can be accelerated.

EQUIPMENT AVAILABLE AT PIVOT PARK

A growing list of equipment available through the Pivot Park Community and a well-equipped open access laboratory significantly reduce the need to invest in your own equipment. An overview of some of the available equipment:

- Agilent/Avantes UV-Vis spectrometer
- Biomek FX Lab Automation Workstation
- Bohle container mixer 5-10-20 L
- Bruker NIR MPA spectrometer
- Echo® 555 Liquid handler for high throughput screening
- EnVision Multilabel Plate Reader
- FACS Canto II, 3 lasers, 8-colour (4-2-2 configuration)
- Flashforge Dreamer
- Flipr Tetra High-Throughput Cellular Screening System
- IncuCyte® Zoom Live-Cell Analysis System
- Malvern Sapphire NIR Imager
- MESO Quickplex SQ 120 (Meso Scale Diagnostics)
- Odyssey
- Operetta High-Content Imaging System
- PlateLoc Thermal Microplate Sealer
- Plateprep Island
- Proxima 2850
- Screening Island
- Tecan Infinite M1000
- Thorlabs Telesto II OCT
- XPeel
- X-Ray
- Zeiss Stereo Microscope

Source: www.pivotpark.com

THE PIVOT PARK COMMUNITY (SEPTEMBER 2019)

Source: www.pivotpark.com

C. High Tech Campus Eindhoven

High Tech Campus Eindhoven is the smartest square kilometre in Europe, with over 200 companies and institutions, and 12,000 researchers, developers and entrepreneurs working on developing future technologies and products. The professionals on campus come from all over the world, with more than 85 nationalities featuring. The Campus helps companies to accelerate their innovations by offering easy access to high tech facilities and international networks. Campus companies (such as Philips, NXP, TomTom, Shimano, Signify, IBM and Intel) decide, on a strategic basis, what knowledge, skills and R&D facilities to share in order to achieve faster, better and more customer-oriented innovations in the fields of health, energy and smart environments. Located in the heart of the city, also known as Brainport Eindhoven, Campus companies account for nearly 40% of all Dutch patent applications.

OPEN INNOVATION

The High Tech Campus is famous for its system of open innovation, which sees companies working together and having shared access to high tech facilities and international networks.

HISTORY

The driving force behind the High Tech Campus Eindhoven was Philips. At the end of the 1990s, the company's R&D activities were spread across the city, and so in 1998 Philips decided to establish the Philips High Tech Campus which would serve as a single location for all its Dutch R&D activities. The approach proved extraordinarily successful and the atmosphere of openness and the concentration of high-end knowledge produced considerable interaction between company researchers working in different fields. Knowledge-sharing and mutual inspiration considerably boosted its innovative capacity and, to further bolster that process, in 2003 Philips decided to open up its Campus to other technology companies. The result was massive growth with many innovative companies – large and small alike – vying to become part of this R&D hotspot.

The Campus entered a new phase in March 2012 when High Tech Campus Eindhoven (HTCE) became an independent entity in the wake of its sale to Ramphastos Investments. In recent years the Campus has witnessed further growth with the arrival of new companies and the expansion of existing ones. Philips is still one of the principal HTCE tenants: Philips Research alone employs over 1,200 professionals from 50 different countries. Their professional healthcare services focus on diagnostic imaging and minimally invasive image-guided procedures, patient care and clinical decision-making support. Its personal health researchers are studying technologies and solutions that encourage a healthy lifestyle, optimised personal care and exploring ways to enhance a fulfilling home and interactive lifestyle.

One unique Philips facility is the ExperienceLab, where a natural setting is provided in which proposed new technologies and applications can be tested and actually *experienced*. The ExperienceLab involves multi-disciplinary teams, including psychologists, sociologists and designers, observing people and monitoring their behaviour and interaction with innovative concepts.

HIGH TECH CAMPUS EINDHOVEN

FACILITIES AND SERVICES

High Tech Campus Eindhoven provides numerous technical and research facilities and is also home to companies offering CRO and CMO services. Most of the technical research facilities are made available by Philips Innovation Services, Eurofins and other companies. Advanced innovation services, expertise and high tech facilities are available for the entire innovation process – concept creation, product development, prototyping and small series production right through to sustainability and industrial process-consulting. In practice, this means access to 25,000 m2 of multi-purpose labs (physical, optical and chemical) and cleanrooms, reliability testing and materials analysis, electromagnetic compatibility (EMC) testing and RF/DC measurement labs. Furthermore, equipment such as high tech water scanners, printers for printing electronics on ultrathin substrates and a high-end fibre data network for data exchange and rapid analysis are all available.

PHILIPS INNOVATION SERVICES (PINS)

Philips Innovation Services is a service provider in innovation. With 1,000 specialists in Eindhoven, the company acts as an advisor and partner in bridging gaps all the way from innovation concept through to market. The company's approach involves bringing together all the required experience, expertise, methods and tools, and it can boast of a tradition of innovation and entrepreneurship stretching back more than 125 years. And because it works both for Philips as well as for external medical and high tech companies, Philips Innovation Services' is always cutting-edge. PINS has the following areas of expertise in the world of medical technology:

Medical Devices Design & Engineering

- High-Precision Engineering
- Electronic Systems and IoT
- MEMS and Micro Devices
- Manufacturing Systems and Industry 4.0
- Design for Reliability Solutions
- Industry Consulting
- Environment, Health and Safety

Medical Device Development

- Medical tests and Verification
- Small Series Pilot Equipment Production

Medical Device Prototyping

- Process Development
- Technology Consulting and Implementation

SIGNIFY (FORMER PHILIPS LIGHTING)

Signify also remains highly active on the High Tech Campus Eindhoven. Signify is the world leader in lighting for professionals, consumers and lighting for the Internet of Things, with sales reaching €6.4 billion in 2018 and some 29,000 employees worldwide. Signify continues to innovate in the field of LED lighting and is leading the industry's expansion when it comes to lighting systems. Signify's global headquarter are located on the Campus, together with 550 employees in innovation and 1,400 employees in enabling services as well as a large IT and sales contingent.

LS&H COMPANIES AND INSTITUTIONS AT HIGH TECH CAMPUS EINDHOVEN

High Tech Campus Eindhoven is home to 38 companies and institutions that are active in Life Sciences & Health or work in a related sector in the supply chain.

Company	Type	Activities
Biotech Systems Platform	Institute	The Biotech Systems Platform (BSP) promotes innovation and cooperation between companies and knowledge institutions active in biotech. and High-tech.
Holst Centre	Institute	The Holst Centre is an independent open-innovation R&D centre that develops generic technologies for wireless autonomous sensors and flexible electronics.
ITRI	Institute	The Industrial Technology Research Institute (ITRI) is a non-profit RTO dedicated to spearheading emerging high tech industry and enhancing the competitiveness of existing industries.
AKKA Technologies	SME	International engineering consultancy.
Intrinsic ID	SME	World's leading digital authentication company and the inventor of SRAM Physical Unclonable Function or SRAM PUF.
Timpel	SME	Timpel is a leading provider of electrical impedance tomography, covering the needs of all HCPs involved in ventilation and respiratory care.
AMS	Multinational	AMS' products are aimed at applications that require extreme precision, accuracy, dynamic range, sensitivity and ultra-low power consumption. AMS' product range includes sensors, sensor interfaces, power management ICs and wireless ICs for buyers in the consumer, industrial, medical, mobile communications and automotive markets.
Cetas Healthcare	Multinational	A global firm specialising in customer insights and strategy for the medical devices industry.
FAULHABER	Multinational	FAULHABER offers the most extensive range of miniature and micro-drive systems currently available worldwide.

Source: High Tech Campus Eindhoven

Company name	Type	Activities
Hudl	Start-up	Hudl is an innovative startup focusing on automatic image improvement and analysis using cutting-edge camera technology and algorithms.
KeyTec	Multinational	KeyTec offers various metal stamping/bending/deep-drawing technologies and plastic/2K/insert injection moulding, including various painting, printing and (sub)assembly techniques, all under one roof.
ON Semiconductors	Multinational	ON Semiconductor (Nasdaq: ON) is a driver of energy efficient innovations, empowering design engineers to reduce global energy consumption.
Philips	Multinational	Royal Philips N.V. is a leading provider of health technology that focuses on improving people's health and achieving better health-care outcomes throughout the health continuum, from healthy living and prevention to diagnostics, treatment and home care.
Siemens	Multinational	High tech industries.
Teledyne DALSA	Multinational	Teledyne DALSA, a wholly-owned subsidiary of Teledyne Technologies since 2011, is an international leader in high-performance digital imaging and semiconductors.
Care IQ	Service company	Care IQ is a healthcare consultancy that works with care providers, health insurers and medtech companies to create innovative smart care concepts for patients and their families.
Gilde Healthcare	Service company	Gilde Healthcare is a transatlantic investor in fast- growing healthcare technology and healthcare services companies.
MD Squared	Service company	In a changing regulatory and commercial environment, MD Squared is clearly focused on driving value creation through a unique combination of marketing expertise, medical competence and regulatory support for medical devices.
TEN Flecs	Service company	TEN Flecs is a contract manufacturing facility for thin-film integrated circuits and backplanes based on IGZO and organic TFT technologies.
AirBliss+	Startup/Scaleup	Health tech hardware startup developing an anti-pollution mask for prolonged and daily usage.
Bloomlife	Startup/Scaleup	Bloomlife's mission is to empower women by delivering unprecedented insight into their health. With its smartphone-connected sensor and app, Bloomlife puts clinically validated information into the hands of expecting parents, starting with an improved method for visualising and tracking.
byFlow	Startup/Scaleup	byFlow is a company founded in 2009 that specialises in 3D printing and is an expert in the field of 3D food printing.
Chromodynamics	Startup/Scaleup	High-speed, real-time multispectral imaging systems for medical and industrial applications.
Emultech	Startup/Scaleup	Emultech is a high tech company that helps pharmaceutical companies with more efficient drug delivery in order to contribute to a better quality of life.
GTX Medical	Startup/Scaleup	GTX Medical is developing a therapy using a spinal cord implant to deliver task-specific electrical stimulation during training.
LifeSense Group	Startup/Scaleup	Wearable healthcare technology, including for urinary incontinence
Minicare	Startup/Scaleup	Next-generation point-of-care diagnostics. Minicare BV is an innovative company that is active in the emerging field of point-of-care diagnostics.

Source: High Tech Campus Eindhoven

Company name	Type	Activities
Montes Jura Medical Technologies	Startup/Scaleup	Montes Jura develops and produces devices that are used in interventional radiology, with the focus on stents to keep the bile duct open, microspheres loaded with cytostatics for the treatment of liver tumours and detachable coils to repair aneurysms.
Nikinc Group	Startup/Scaleup	The Nikinc Group strives to make a positive difference as an innovative company, primarily through the development of ingenious, practical and affordable medical and dental products.
Pharmi	Startup/Scaleup	Adequately educating patients on a new drug prescription is one of the most important aspects that predicts adherence and adequate drug use and thus improves patient results.
Plasmacure	Startup/Scaleup	Medtech startup Plasmacure is dedicated to helping people who suffer from chronic wounds, and will market an innovative treatment method to heal such wounds.
Reset Yourself	Startup/Scaleup	Reset Yourself helps people crack their secret code to a healthy lifestyle using the Reset Hair Analysis.
Salvia BioElectronics	Startup/Scaleup	Salvia develops electrical stimulation instruments. The company's mission is to deliver bioelectronic solutions that restore health for people suffering from chronic migraines.
Sirius Medical Systems	Startup/Scaleup	Sirius develops affordable solutions that enable the precise and efficient surgical removal of early-stage tumours.
Sparckel	Startup/Scaleup	Sparckel is a young, innovative organisation that successfully conceived and developed and now produces and markets the world's first free-standing biodynamic LED lighting concept.
Usono	Startup/Scaleup	Usono facilitates medical staff in their work to provide better care using smart ultrasound solutions.
UVisio	Startup/Scaleup	UVisio develops comprehensive solutions allowing individuals to control their physical exposure to external factors, such as UV rays, and personalise their entire sun-care and skin-care experience.

Source: High Tech Campus Eindhoven

Institute	Activity
Philips Innovation Labs: Electromagnetic Compatibility & Wireless Connectivity lab	Far-reaching and accurate testing, consultancy and certification in the fields of: • Electromagnetic Compatibility (EMC) • Wireless approbation • Wireless robustness (multipath performance, total radiated power, antenna diagrams) • Electrical Safety
Philips Innovation Services	• Laser job prototyping services • Product prototyping • Instrumentation services • Technical support and technology consultants
Eurofins: Material Analysis lab	The Material Analysis lab was purchased by Eurofins EAG in December 2018 and was formerly the Materials Analysis lab for Royal Philips and Philips Lighting (now Signify).
	Services: The Eurofins facility in Eindhoven specialises in the materials analysis and reliability testing of high tech materials and products. It also has specific expertise in the areas of: • Chemical analysis and physical inspection of materials and objects • Analytical methodology • Contamination control • Chemical compatibility • Material reliability • Glass characterization
	Analytical techniques • Compositional analysis GF-AAS, CV-AAS, ICP-OES, (LA-)ICP-MS, Elemental Analysis, FT-IR, Raman, GC-MS, HPLC, IC-MS, MALDI, NTM, XRF, Gravimetry, , Titrimetry, Thermal Desorption
	• Surface and thin film characterization Ellipsometry, SAM, ToF-SIMS, XPS
	• Advanced imaging FIB, Image processing and analysis, SEM-EDX, TEM, IR imaging, Optical interferometry, Profilometry, SPM / AFM, Thermal imaging / Thermography, X-Ray inspection

Source: High Tech Campus Eindhoven

Institute name	Activity
	• Physical characterization Materialography, mechanical testing, particle size analysis, permeability, physical properties of glass, rheology, sample preparation laboratory, specific area of powders, strain analysis, thermal analysis, thermo-mechanical analysis, XRD, electrochemical testing
Eurofins: Reliability lab	The EAG facility in Eindhoven was purchased by Eurofins EAG in December 2018 and was formerly the Reliability Lab for Royal Philips and Philips Innovation Services. The Reliability Lab offers a complete package in reliability testing services:
	Environmental simulation: • High/Low temperature • Temperature and humidity • Power temperature cycling (PTC) • Thermal cycling • Thermal shock • HAST/corrosion testing • Solar/UV simulation
	In-Situ test service: • LED lifetime (optical output) • Event detection (low resistance) •Monitor (I/V/L/R vs. time)
	Highly accelerated lifetime test (HALT): • HALT test • MEOST test
	Mechanical test service: • Bump and shock • Drop test and free fall (mechanical and simulation) • Surface affection • Waterproof pressure test • Drawbench and tensile test
	Water Vapour Transmission Test (WVTR): • Calcium test on thin-film barriers

Source: High Tech Campus Eindhoven

HIGH-LEVEL ACCOMMODATION FOR HIGH TECH STARTUPS – TWICE

TWICE offers a special stimulating environment for young, innovative technology companies with growth potential. Our shareholders – the Brabant Development Agency, the municipality of Eindhoven, the Eindhoven University of Technology, Brainport Development and Rabobank Eindhoven-Veldhoven – have joined forces in order to ensure that businesses can thrive at TWICE in the Brainport Eindhoven region.

TWICE has four accommodation formulas based on individual themes. Strategically located in the very heart of the high tech hotspots in the Brainport region, the Eindhoven University of Technology and High Tech Campus Eindhoven.

- Office space and laboratories from 25 to 500 m^2
- High-quality and well-equipped laboratories
- Server rooms with server boxes
- High-quality redundant IT infrastructure

Mμ - Growth in LS&H and new energy

Mμ was created for research and development companies that are focused on life tech and new energy. Accommodation is available for these next-generation high tech companies in flexible office spaces and laboratories.

Bèta - Growth in high tech R&D

βèta is the ideal location for young and innovative high tech companies working in research and development. βèta is fully equipped with modern office spaces and high-quality electrical engineering laboratories.

Mμ and βèta are part of the High Tech Campus Eindhoven (HTCE), a site that is home to over 12,000 technically like-minded people. The building is located at the foot of The Strip, the lively heart of the HTCE containing restaurants, a conference centre, a shopping centre and many other facilities. The HTCE is considered the smartest square kilometre in Europe.

Twinning - Growth in IT, (embedded) software and electronics

Twinning provides office space to companies active in IT, (embedded) software and electronics. Twinning is aimed at young tech companies with a flexible, proven formula for launching technology products, processes and services.

Catalyst - Growth in electrical engineering, mechanical engineering and (bio) chemistry

Catalyst consists of small-scale office and laboratory spaces on the TU/e campus and offers a stimulating environment for young, innovative technology companies within the themes of mechanical engineering, electricity, physics and (bio)chemistry.

Catalyst and Twinning are perfectly-sited on TU/e campus grounds: a preferred place for innovative activities. The companies in Catalyst and Twinning form an energetic network in the middle of the university, providing access to knowledge, specialist research facilities, potential business partners and clients.

D. TU/e Campus - University of Technology Eindhoven

The TU/e Campus is an open and accessible community for technology education, scientific research and commercialising knowledge. It is a lively hotspot in the Brainport Region of Eindhoven, bringing together students, researchers, entrepreneurs and high tech companies. The green TU/e campus is fast becoming an attractive hotspot for students, researchers, entrepreneurs, investors and high tech companies, thanks to its state-of-the-art offline and online facilities. The campus is a site under development, but is already a lively and green spot in the heart of Eindhoven.

- Company accommodation - Apart from the university, around a hundred companies and organisations are also located on the campus, from large research institutes to smaller startups. The TU/e campus aims to be a place where these parties connect, which is why a range of different spaces are available.
- Living on campus - The campus has 700 apartments for (international) students and people working on the campus.
- Congress and conferencing facilities - The campus has excellent facilities for hosting congresses, while different rooms can be rented for smaller meetings and for conferencing.

FACTS & FIGURES

- 11,000 students
- 5,000 knowledge workers
- 90 nationalities
- 14 unique labs

TU/E INNOVATION LAB

One of TU/e's greatest assets is the TU/e Innovation Lab, a proven concept that TU/e itself describes as follows:

'TU/e Innovation Lab - How can you bring knowledge to the market?

Where innovation starts - that is our slogan and it complements the growth of our knowledge and education. We turn our academic and technological discoveries into solutions that help tackle societal challenges. The successful commercialisation of knowledge places us at the very heart of the Dutch knowledge economy. But how can you bring knowledge to the market?

Business expertise centre – the commercialisation process is performed by our expertise centre through the conversion of knowledge into business. We have an enthusiastic and experienced team of coaches, advisors and supervisors available to help TU/e staff and students as well as external parties perform this task.

A proven track record – we have a proven track record in commercialising knowledge. In recent years our team has overseen:

- 115 spinoff companies
- 123 student companies
- 60 TU/e patents
- 60 patent license applications
- 500 third-party patents

Exploring opportunities together – we explore all opportunities together, compile the business case, track down suitable forms of funding, establish business models and seek out potential partnerships. This allows us to co-create solutions for societal and global problems in the fields of health and healthcare, energy and mobility.

Research Support Network – a new initiative is available for researchers who need help with external funding to conduct research and develop project proposals on a national and European level: the Research Support Network. This network also offers support in establishing contacts with relevant companies (setting up consortiums) and networks, and helps researchers with patenting inventions and creating contracts.

TU/e Campus - the TU/e campus is growing in leaps and bounds, as can be seen in the activities and the growth of the campus. It is a meeting place for students, researchers, entrepreneurs, investors and high-tech companies. The campus is place of national significance and international allure with state-of-the-art research facilities. And there is plenty of scope for R&D-driven (startup) companies, no longer on the basis of closed but instead based on open multidisciplinary innovation processes, with all the associated benefits for startups, companies and investors alike.'

E. Máxima Medical Centre (MMC) Incubator

A number of startups are located in the MMC Incubator on the Máxima Medical Centre's campus in the heart of Brainport. It is an open workspace for businesses that not only want to be part of the MMC Innovates network, they also want to have a physical presence in an international community focused on high tech and innovation. The fact that they are in direct contact with the (medical) experts of the MMC means that MMC Incubator residents can rely on their support when it comes to launching and growing a company.

Examples of this support include:

- the (further) development of the concept
- testing innovations within a living lab
- conceiving a business plan
- arranging funding
- marketing and communication
- preconditions, such as applying for patents, trademark law and privacy

An extensive network of experts, directly or indirectly connected to the hospital, provides support to MMC Incubator residents in all these matters as a consultant, sparring partner, coach or service provider. In addition, the MMC Incubator offers a large number of practical benefits and services.

The following healthcare-related startups, organisations and companies are currently located in the MMC Incubator:

- **Bambi Medical**
  Bambi Medical is currently developing the Bambi Belt. The Bambi Belt is an alternative to the conventional method for monitoring (breathing, heartbeat and ECG) premature babies.
- **Nemo Healthcare**
  Nemo Healthcare develops innovative technology for monitoring pregnancies in a hospital environment.
- **Eindhoven Medtech Innovation Center (e/MTIC)**
  A regional and highly innovative ecosystem has been created within the e/MTIC research programme, which is a partnership between Philips, the Eindhoven University of Technology, Máxima Medical Centre (MMC), Catharina Hospital and the Kempenhaeghe academic centre. In this context, there are several projects ongoing at the MMC that are focused on improving the quality of perinatal care for both mother and child. An important part of this is the NICU (neonatal intensive care unit).
- **Ereva**
  Ereva has developed a secure and anonymous link between the hospital system and a personal patient-specific information page. Participants can use this website to grade the most frequently asked questions and compare them to people who have previously suffered from the exact same affliction.

máxima mc

F. BIC - Brainport Industries Campus

THE FACE OF THE HIGH TECH MANUFACTURING INDUSTRY - THE FACTORY OF THE FUTURE

The most innovative and successful companies and institutions in the Brainport region come together as one on the Brainport Industries Campus. The campus is where the innovative and competitive strengths of the high tech manufacturing industry take shape.

Leading knowledge institutions and renowned companies work together at the Brainport Industries Campus in order to accomplish ideas and develop business cases. This is where the next generation of professionals in the high tech manufacturing industry is trained in a state-of-the-art working and learning environment. Brainport Industries Campus is the place to be for far-reaching partnerships between suppliers, specialist companies and innovative education and knowledge institutions.

Brainport Industries Campus is the very first location where high tech suppliers innovate and manufacture together, where the most successful companies share high-quality facilities, such as cleanrooms, flexible production areas, warehouses and other advanced facilities, and where they present themselves as a unified force that they can showcase to their national and international customers.

Brainport Industries Campus

BRAINPORT INDUSTRIES CAMPUS NOW

- Over 20 companies
- 2,000 high-level staff
- 1,500 students
- 105,000 m2
- 6,000 m2 of shared facilities
- 6,000 m2 of shared logistics

Just some of the present tenants are KMWE, Siemens, Yaskawa, Ceratec, Brainport Industries, Fujitsu, Anteryon, Festo, Procureon and Hightech Software Cluster.

7. PARTNERSHIPS AND NETWORKS IN BRABANT (BUSINESS, SCIENCE, GOVERNMENT)

A. Partnerships in Brabant - history, culture, past and present

INTRODUCTION

Brabant has a distinctly strong culture, history and tradition of informal constructive partnerships that are based on trust and 'open innovation'. This is particularly evident in the following respects, along with numerous others:

- The fact that some of Brabant's largest companies (VION, Cosun/SuikerUnie, FrieslandCampina) have a history of working together
- The century-old roots of some of the region's industrial giants and the fact that these companies are completely intertwined with the development of the region, the cities, the universities, the schools, housing, leisure, the football clubs, and so on (Philips in Eindhoven, MSD via Organon in Oss, MSD Animal Health through Akzo/Intervet and Hendrix in Boxmeer)
- The fact that Philips decided, 17 years ago, to open up its originally hermetically-sealed NatLab research site in Eindhoven and began to invest in 'open innovation' by inviting other companies to join in. The company invested hundreds of millions of euros in further developing the campus and facilities to optimise joint research, the result being the Philips High Tech Campus. The site, located in the middle of Eindhoven and home to 12,000 researchers from over 200 companies and institutes from around the world, is now owned by a property investor and named the Eindhoven High Tech Campus (HTCE). Key tenants remain Philips Healthcare, Philips Research and Signify (formerly Philips Lighting) as well as NXP, ASML, Holst Centre and Xeltis.
- The concept (joint research, shared facilities, intensive cooperation and significant outsourcing when it comes to drug discovery and development) and success of the Pivot Park biopharmaceutical campus in Oss.

The advantages of this culture are that cooperative ventures, both informal and highly intensive, are ingrained in the area. Many CEOs in the region, the mayors and councillors of the cities and knowledge institution academics are regularly cited as saying 'the door is always open, so don't hesitate to drop by', 'we make the best decisions sitting at the kitchen table' and 'we know each other's mobile phone numbers and we pick up the phone whenever we see a friend is calling'.

In short: building partnerships in the region is a quick and fluid process – and faster than anywhere else in the Netherlands. Outsiders who wish to join the club and make an actual contribution will quickly and easily reap the rewards.

CONNECTING GLOBAL GIANTS: BRABANT'S INDUSTRIAL ICONS

In Brabant a number of key ingredients have been fruitfully mixed together for over a century, creating one of the strongest high tech systems regions in the world:

- Entrepreneurship
- Corporate social responsibility
- Cooperation and open innovation
- Roots in AgriFood and Health
- Strong regional pride and loyalty, but with a
- Focus on a global market

The growth of three remarkable Brabant business families in the past century exemplifies and characterises how this region developed to attain its current strong position and open approach to working and partnerships. Three extraordinary individuals started businesses here that developed into three connected clusters of companies, consisting of specialised SME Tier 1 and 2 suppliers, dedicated logistics service providers and renowned research centres all the way through to certification bodies and a number of global multi-billion dollar OEM companies.

These three individuals were Frederik Philips, Saal van Zwanenberg and Wim Hendrix.

- In 1891, Frederik Philips built a modest light bulb factory in Eindhoven
- Saal van Zwanenberg founded a slaughterhouse for export in 1887 in Oss
- Wim Hendrix started off selling chickens in Boxmeer in 1916

They all started out small, some of them on their own. But their businesses grew, flourished, diversified and have been entering new markets ever since. And, in the process, the parent companies have bred hugely successful subsidiaries and spinoffs:

- Frederik founded Philips, today's Royal Philips (Healthcare), a global 18 billion euro-company with 74,000 employees that also gave birth to other icons, such as ASML, FEI Company, Thales and NXP, all of them still headquartered in the region or with their global research centres based in the province
- Saal started Zwanenberg, which became Organon and then Chefaro, and is part of today's MSD (Merck) that focuses on human health and specialises in pharmaceutical and biological research and manufacturing, including one of the world's latest cancer treatments, Keytruda (pembrolizumab)
- Wim started selling chickens to farmers, after which his entrepreneurial spirit saw companies born that grew to become Hendrix Genetics, MSD (Merck) Animal Health (formerly Intervet), Nutreco and Marel Poultry

Today these companies are still leading the way, with crossovers found between the domains of Life Sciences and Health and High Tech Systems and Materials. New solutions are being developed in areas such as

Today these companies are still leading the way as cross-overs are found between the domains of Life Sciences and Health and High Tech Systems and Materials. New solutions are developed in areas such as:

- Imaging, monitoring and guided surgery
- Big data and smart algorithms in animal husbandry
- Vision and sensor technology for monitoring welfare
- Needle-free, intradermal vaccination devices

A SUCCINCT OVERVIEW OF PHILIPS' GROWTH OVER THE LAST CENTURY CAN BE FOUND IN THE 'PHILIPS TREE' (DATING FROM 2016)

Some of these companies have grown to similar sizes and with a greater stock market value than their parent company, such as ASML (with a turnover of €10.9 billion), FEI (now Thermo Fisher Scientific) and NXP (with a turnover of $9.4 billion), to name just a few.

The tree gave rise to a new branch in 2019 – Signify (formerly Philips Lighting) has now gone public and is a separate entity with a workforce of 29,000 people and a turnover in 2018 of €6.4 billion.

B. Successful networks and public-private partnerships (PPPs)

1. REGMED XB

RegMed XB stands for Regenerative Medicine Crossing Borders. It is a virtual institute of Dutch and Belgian public (universities and governments) and private (health foundations and companies) partners that intend to work together to develop regenerative medicine solutions for health challenges.

In the Netherlands, five health foundations (Nierstichting, Diabetes Fonds, Diabetes Onderzoek Nederland, Hartstichting, and ReumaNederland) have given shape to the ambitious RegMed XB moonshots: treating kidney, osteoarthritis, cardiovascular, and diabetes-related issues. Today, scientists from four universities (Leiden University, Utrecht University/Hubrecht Institute, the Eindhoven University of Technology and Maastricht University) are contributing through technology and expertise to the fulfilment of their objectives.

REGENERATION OF THE HUMAN HEART MOONSHOT

One of the four projects/therapeutic fields of RegMed XB is the regeneration of the heart. Cardiovascular diseases are the leading cause of death worldwide and responsible for 17.9 million fatalities every year. In the Netherlands 103 people die every day from cardiovascular diseases, making this second-most prevalent cause of death in 2018 in the country. The situation is similar in Flanders, where cardiovascular disease likewise takes second place for fatalities, responsible for 28% of all deaths in 2016.

RegMed XB's cardiovascular moonshot consists of a comprehensive programme based on the concept that the participants should be able to create a cardiac (re)generative therapy that best suits the individual patient. One approach is to restore the heart's functioning outside of the body (ex vivo). The advantage of this method is that the healthcare professionals can then treat the heart on its own and assess cardiac function during treatment. The patient's body is connected to a heart-lung machine while the heart is removed.

After treating the heart, it will be re-implanted. This approach also means that gene therapy can be used to treat hereditary diseases. The researchers aim to stimulate the body's own regenerative capacity by, for example, improving the contractility and perfusion of the heart muscle and repairing or replacing coronary arteries and heart valves. The cardiovascular moonshot is divided into different steps, or milestones. The first milestone focuses on keeping a beating heart healthy and functioning for up to seven days in a bioreactor outside of the body, during which time the heart can be repaired. The main goal is to repair the damaged heart using regenerative medical solutions, which can range from, for instance, restoring its muscular functioning through to treating atherosclerotic damage.

Brabant organisations are playing a significant role in this project, with TU/e, Eindhoven University of Technology and the companies LifeTec Group, Xeltis, SupraPolix, IME Medical Electrospinning and SyMOChem all aboard. They are working closely with the three university medical centres of Utrecht, Leiden and Maastricht.

TOWARDS A BIO-ENGINEERED JOINT MOONSHOT

Knee osteoarthritis affects 250 million people worldwide. It involves the degeneration of knee joint cartilage and the underlying bone. Patients can experience severe pain accompanied by a decreased range of motion and reduced mobility. There is no cure for osteoarthritis, so treatment involves reducing and managing pain or surgical interventions such as replacing the entire joint. Regenerative medicine is able to offer a new treatment, such as a bioengineered replacement joint. The RegMed XB partners are coming together to take the first steps towards a bioengineered joint as a treatment and possible cure for osteoarthritis of the knee.

Brabant is home to two companies that are very closely involved in this project, Osteo-Pharma and Fujifilm. Osteo-Pharma develops novel pharmaceuticals and medical devices to improve the local healing of bone fractures and defects and has recently successfully completed a large preclinical study that demonstrates that its OsteoActivator coated collagen membranes effectively promote new bone formation.

Fujifilm has developed a recombinant peptide for healthcare applications as a synthetic alternative to animal-sourced material. The CellnestTM recombinant peptide is an animal-free matrix, based on human collagen type I and enriched with extra RGD groups to enhance cell adhesion. Because of its chemically-defined composition, cell adhesive characteristics and its highly reproducible quality, CellnestTM is particularly suitable for use in cell culturing or in regenerative medicines, such as bone regeneration.

2. E/MTIC - EINDHOVEN MEDTECH INNOVATION CENTER (E/MTIC)

Improving value-based healthcare by creating and expanding an ecosystem to enable fast-tracking high tech health innovations. Taking technical innovations all the way from initial research through to implementation and commercialisation can often take a long time and, especially in healthcare innovation, this lost time often equates to lost lives.

The goal of the Eindhoven Medtech Innovation Center (e/MTIC) is to create and develop an ecosystem that dramatically accelerates the speed of high tech health innovation, maximising value for patients.

PARTNERS

e/MTIC is a large-scale research partnership between the Catharina Hospital (CH), the Maxima Medical Centre (MMC), the Kempenhaeghe epilepsy and sleep centre (KH), the Eindhoven University of Technology (TU/e) and Royal Philips Eindhoven (RPE) in the fields of cardiovascular medicine, perinatal medicine and sleep medications. This partnership has evolved over several decades, has a strong scientific and commercialisation track record and currently involves around a hundred PhD students, supervised by a similar number of experts from the various partners.

E/MTIC DEVELOPMENTS AND SPINOFFS

- **MEDSIM:** the Máxima Medical Centre is working with Medsim and Nemo Healthcare to provide simulation training using the world's most lifelike childbirth simulator, called Victoria. She is anatomically accurate and contains state-of-the-art pregnancy monitoring technology. Over 60% of Dutch obstetricians have been trained using her, and the consortium hopes it can also be used to contribute towards reducing maternal and perinatal mortality in Africa, the Americas and Asia.
- **Smart baby bottle:** the Smart Baby Bottle is a sensor-equipped sleeve that tracks bottle-feeding routines and provides parents with personalised advice regarding their baby. This data-intensive sleeve was developed in collaboration with end-users, first exploring what data will be of value and then validating the design using prototypes. Philips AVENT is currently developing the bottle for product launch.
- **Smart Monitoring:** Hypertension, obstructive sleep apnoea and atrial fibrillation are highly prevalent (affecting over 30%, 9% and 2% of people respectively) and underdiagnosed conditions. If left untreated, patients are at elevated risk of developing further incapacitating medical conditions such as strokes and heart failure. The e/MTIC partners are developing self-monitoring solutions for patients using unobtrusive wearable sensing technology integrated in watches or patches for timely detection.
- **3D Needle:** Ultrasound (US) imaging is widely used to visualise and guide needle and catheter procedures, but is very challenging and the failure rates are considerable (between 25% and 50%) while complications frequently arise (in between 5% and 15% of cases). The key problem is that the field of view is limited by the US beam width, requiring the probe to be extensively and manually repositioned. This is complex and error-prone, because of imaging artifacts and low signal-to-noise ratio. A new solution using a 3D US probe overcomes these problems to a radical extent by automatically detecting and visualising the entire instrument. This enables the physician to be fully focused on a procedure, while easily and accurately guiding the instrument.
- **TraceBook:** TraceBook is an innovative clinical decision-support system that provides a digital insight of a patient's individual care process for care providers. It helps prevent medical errors by making the entire care process transparent and unambiguous. The system tracks and records the characteristics of individual patients using several electronic medical databases, whether hospital or other databases. Thanks to the use of smart dynamic checklists, TraceBook also helps improve compliance with local and national guidelines.

3. ICMS - INSTITUTE FOR COMPLEX MOLECULAR SYSTEMS

The TU/e research conducted in the field of complex molecular systems is dedicated to a fundamental understanding of complexity in molecular systems. It addresses research challenges and pushes the boundaries of science by unifying the basic principles of chemistry, biomedical sciences, engineering, physics and mathematics. The knowledge gained serves as the foundation for the development of future technologies in materials science, energy, mobility and health.

In particular, the ICMS pursues two major goals:

- the design and synthesis of smart materials for creating molecular devices
- unravelling the molecular complexity of living systems and transforming biology into an engineering science.

The study of complex molecular systems highlights the research performed by TU/e scientists in seven focus areas:

1. Polymer Science and Technology
2. Chemical Biology
3. A grip on Complexity
4. Advanced Analysis of Complex Molecular Systems
5. Molecular Devices
6. Materials for Regenerative Medicine
7. Functional Supramolecular Systems

SCIENTIFIC EXCELLENCE

The ICMS includes both senior researchers with an excellent track record (including three winners of the prestigious Dutch Spinoza Award and six members of the Royal Dutch Academy of Arts and Sciences, two of whom have been awarded Academy professorship) and young talent (including three NWO-VIDI Award winners in 2017 and four ERC laureates).

They have combined their strengths to push back the frontiers of complex molecular systems, for example by jointly applying for funding for research projects and/or infrastructure. Collectively, they have been awarded over ten ERC grants. Furthermore, academics and industry players from around the world approach the Institute seeking partnerships for inspiring academic and industrial challenges.

FACTS AND FIGURES

> 240 researchers: Nagoya Gold Medal, Chirality Medal 2018, three Spinoza Award winners, seven KNAW members, three NWO-VIDI Award winners in 2017, 16 ERC grants, four NWO-Gravitation grants

PARTNERING WITH INDUSTRY

The relationship with industry has been bolstered through the ICMS Industrial Consortium – where science meets innovation. The aim of the Industrial Consortium is to develop and foster productive partnerships that become lasting alliances.

CERES HOME BASE ON THE TU/E CAMPUS

The Ceres building is the home base of the ICMS. Located at the heart of the TU/e campus, the former university boiler house was renovated to give the Institute a dedicated workspace. The modern, highly transparent building perfectly fits the informal and interdisciplinary ICMS atmosphere. It contains state-of-the-art laboratories, offices, meeting rooms and a conference hall. The sociable common room encourages informal discussions and gives rise to future collaborative ventures.

THE ICMS LABORATORIES

ICMS/Lab is the research lab of the TU/e's ICMS Research Institute. The Lab facilitates the development and characterisation of innovative materials from a molecular perspective. When it comes to constructing, measuring and, where necessary, improving innovative materials in molecular terms, the laboratory offers cutting-edge instruments. While many laboratories focus on one of these discrete steps, the ICMS/Lab provides researchers with the tools required for the entire development process.

Among its facilities, the laboratory offers high resolution microscopy, light and X-ray scattering, various systems for surface analysis and microreactors. In such microfluidic reactors, chemical reactions occur at the microscale, as is the case when testing blood samples for diabetes in a lab-on-a-chip.

THE INSTITUTE'S X-RAY SCATTERING INSTRUMENT

The laboratory's X-ray scattering apparatus (SAXS) enables researchers to zoom in on the structure of both organic and synthetic materials. This allows them to examine how the material is structured and they can assess whether it meets the intended requirements. This instrument is not available at any other university in the Netherlands.

4. EUROPEAN LEAD FACTORY (ELF)

The European Lead Factory is a collaborative public-private partnership aiming to deliver innovative drug discovery starting points. Having established the first European Compound Library and the first European Screening Centre, the European Lead Factory now offers free access to up to 550,000 novel compounds, a unique industry-standard uHTS platform and much more.

State-of-the-art facilities
The European Lead Factory revolves around its ultra-high-throughput screening (uHTS) activities, which are performed for the wider European scientific community by the European Screening Centre (ESC). Some of the most advanced compound management, screening and hit to lead (H2L) testing capabilities in the whole of Europe are available at the European Screening Centre.

Management
Managed by Lygature, the ESC offers world-class compound storage-and-retrieval, screening and laboratory facilities.

Compound Storage
World-class compound logistics facilities of 1,100 m2 are provided by BioAscent Discovery Ltd using their automated compound store in Newhouse, Scotland. Both solids and DMSO solutions can be stored, retrieved and delivered with minimum turnaround time.

Ultra-high-throughput screening (uHTS)
The Pivot Park Screening Centre (PPSC) acts as a pivot for screening activities. Located in Oss on a site dedicated to open innovation and housing the latest generation in robotics, it provides automated cellular and biochemical in-vitro screening expertise. The centre builds on decades of experience in assay development, automation and screening. Opportunities for networking and partnerships are extensive.

Hit to lead
BioAscent, formerly the Newhouse group of the University of Dundee, provides biological data, medicinal chemistry, informatics analysis and modelling to the European Lead Factory's screening programmes.

Protein production
The biotechnology group of the Structural Genomics Consortium (SGC) at the University of Oxford provides protein production to the European Lead Factory programmes.

Photo: Pivot Park Screening Centre

EUROPEAN LEAD FACTORY

5. MÁXIMA MEDICAL CENTER (MMC) INNOVATION PROGRAM AND INCUBATOR

The Máxima Medical Center (MMC) is the largest healthcare provider in the Eindhoven region, serving the local and international community through two campuses The centre has over 600 beds and has 3,000 employees and 210 medical specialists responsible for providing care, cures and conducting research in 24 therapeutic fields.

The MMC is located on two campuses – MMC Eindhoven and MMC Veldhoven. Maxima Medical Centre Eindhoven is the location for many outpatient clinics, planned care, and the outpatient care centre. Maxima Medical Center Veldhoven handles acute care, critical care, child and neonatal intensive care, intensive care, outpatient clinics and the renowned Woman, Mother & Child Centre, as well as accident and emergency services.

The MMC has an intensive innovation programme (MMC Innovates). Using this platform for care innovation, medtech innovation and research, entrepreneurs, healthcare professionals and knowledge institutions work closely with the hospital on the healthcare innovations of tomorrow.

MÁXIMA MEDICAL CENTER INCUBATOR

The MMC has an Incubator centre where startups can have a physical presence in an international community focused on high tech and innovation and be a part of the MMC Innovates Network.

máxima mc

The following healthcare-related startups, organizations and companies are currently located in the MMC Incubator:

Bambi Medical
The company is currently developing the Bambi Belt. The Bambi Belt is an alternative to the conventional method for monitoring (breathing, heartbeat and ECG) premature born babies. This solution offers the advantage that the adhesive electrodes that cause pain and stress are no longer needed.
www.bambi-medical.com

Nemo Healthcare
Nemo develops innovative technology for pregnancy monitoring in a hospital environment. The PUREtrace™ technology created by Nemo Healthcare uses the most direct measure of contraction activity – the electrical activity of the uterine muscle – for foetal monitoring, both before and during delivery. Nemo is currently working on a new application of this technology that will make it possible to register the vital heart activity of both the mother and the unborn child in addition to the contraction activity. Nemo Healthcare is a spinoff company that originated from a partnership between the Eindhoven University of Technology and Máxima MC. The (further) development of PUREtrace™ technology underscores the importance of partnerships between universities, hospitals and businesses in application-oriented research.
www.nemohealthcare.com

Eindhoven Medtech Innovation Center (e/MTIC)
A part of the e/MTIC research programme - a partnership between Philips, the Eindhoven University of Technology, Máxima Medical Centre (MMC), Catharina Hospital and the Kempenhaeghe academic centre. In this context, there are several projects ongoing at the MMC that are focused on improving the quality of perinatal care for both mother and child. An important part of this is the NICU (neonatal intensive care unit).
www.tue.nl/en/research/research-groups/eindhoven-Medtech-innovation-center

6. LIFETECZONE

LifetecZONe is a network devoted to life sciences and medical technology businesses. The majority of them are SMEs and are located in the south of the Netherlands. The network is also open to knowledge institutions, healthcare providers, governments and organisations in and outside the region.

LifetecZONe encourages new partnerships by bringing the value chain in medical technology and life sciences together. The members bolster their ties during interactive network meetings and knowledge sessions. LifetecZONe is hosted by the Brabant Development Agency (BOM) in Tilburg.

8. GOVERNMENT SUPPORT

A. Government support structure

On a national level, the Dutch national and regional authorities work together through the Invest in Holland consortium to help foreign companies to establish themselves in the Netherlands. The national investment agencies NFIA (the Netherlands Foreign Investment Agency), HIDC (the Holland International Distribution Council) and all Dutch provinces, regions, and metropolitan areas work together under the Invest in Holland brand.

In the province of Brabant, a broad support structure has been developed by regional and local governments for Life Sciences & Health companies. The provincial government and the municipal authorities of all the larger Brabant cities generally have a positive, practical and supportive attitude towards the industry and want to see it prosper in the region. Teams of professionals exist in many organisations for providing operational and strategic support to LS&H, including BOM, Brainport Development, REWIN, the Pivot Park team, the High Tech Campus Eindhoven team, the TU/e team, and many others.

Three operational government agencies in Brabant have been specifically established to support industry:

- **BOM - Brabant Development Agency**
- **Brainport Development Eindhoven**
- **REWIN West Brabant**

INVEST IN Holland

Holland International Distribution Council

BOM

BRAINPORT EINDHOVEN

REWIN

1. Invest in Holland

Under the name of Invest in Holland (IiH), the Netherlands Foreign Investment Agency (NFIA) – an operational branch of the Ministry of Economic Affairs – has joined forces with the Ministry of Foreign Affairs and several regional partners in the Netherlands. This network represents and promotes the Netherlands abroad as an attractive location for investments or establishing businesses. It also provides support to foreign companies that are setting up or expanding their international activities in the Netherlands.

THE NFIA – NETHERLANDS FOREIGN INVESTMENT AGENCY

SERVICES

- The NFIA provides information, practical assistance and advice to foreign companies
- It was founded 40 years ago as an operational unit of the Dutch Ministry of Economic Affairs
- It is responsible for identifying and attracting direct investments (green field or expansion) from companies that could be made in various countries, including the Netherlands
- It provides access to a broad network of business partners and government agencies
- It is headquartered in The Hague and has a staff of 35
- NFIA initial support is provided abroad through its 27 offices and representatives around the world, staffed by around 75 people
- The NFIA works closely with embassies, consulates and other organisations that represent the Dutch government around the world, as well as with a broad network of partners in the Netherlands

www.investinholland.com

2. BOM - BRABANT DEVELOPMENT AGENCY

SERVICES

When companies are in the process of relocating, setting-up a new subsidiary or expanding their operations, they need the essentials to be taken care of quickly and comprehensively. BOM Foreign Investments was established to be the industry's partner for every one of those steps, providing a wide range of services and support that save on both time and money. BOM has a local team of experts available that provide free support for a wide range of matters – whether it be issues with building permits, finding new premises or sites for development, questions on employment law, understanding tax incentives or help with business development and networking.

Based in Tilburg, BOM Foreign Investments is part of the Brabant Development Agency (BOM), which is staffed by a hundred highly specialised professionals. In order to facilitate foreign investment in Brabant, the team combines its services with the unique expertise and support of their colleagues working in complementary fields within BOM, expertise that includes managing R&D programmes, initiating innovative industrial cooperative projects and venture capital funding.

1. SUPPORT FOR FOREIGN COMPANIES - THE STRENGTH OF BRABANT: A WORLD-CLASS ECONOMY

Located centrally in one of the world's largest markets and with a supply industry and a world-class knowledge economy, Brabant is an attractive location for many foreign companies. BOM Foreign Investments highlights the strengths that Brabant offers and assists newcomers and established foreign companies alike to fully utilise the province's opportunities as a business location.

BOM always works closely with the Netherlands Foreign Investment Agency (NFIA) and the Holland International Distribution Council (NDL), the country's logistics agency, in order to provide potential investors with the following essentials:

- Information: national and regional regulations are demystified by BOM's team of experts, and provides information on taxes and the business climate in the investor's industry.
- Network: a business and supply-chain network and talent acquisition are key to a company's success and often prove to make all the difference. BOM and partners introduce newcomers to Brabant (or companies looking to expand) to their extensive network of contacts in industry, academia and government, ensuring that investors immediately have the best possible contacts.
- Location and site selection: where and when – both crucial decisions in the investment process. BOM can function as a potential investor's guide and advisor from start to finish and help look for suitable sites until a perfect fit has been found

2. DOING BUSINESS ABROAD

BOM International Trade offers those businesses that have outgrown their Dutch roots hands-on support for growing successfully in foreign markets. BOM establishes relevant business and government contacts abroad and provides targeted information on markets and available funding. The International Trade team focuses on three of Brabant's Priority Industries: High Tech Systems & Materials, Life Sciences & Health and AgriFood.

BOM is a public agency that brings companies, knowledge institutions and public bodies together. As BOM has no commercial interests, its independent standing opens doors that often remain closed to commercial ventures. In this respect BOM's goal is to help to create a strong Brabant economy and guarantee that Brabant businesses play a leading role on the world stage. Current target markets for BOM International Trade include China (Jiangsu region), southern Germany (Baden-Württemberg and Bavaria regions) and the United States (Midwest and Texas). BOM International Trade works closely with partners such as the Netherlands Enterprise Agency, the Chamber of Commerce and embassies and consulates around the globe.

3. DOING BUSINESS IN BRABANT - EXPERTISE AND VENTURE CAPITAL FOR STARTUPS AND SCALEUPS

As a growth accelerator with over 35 years of experience, BOM Brabant Ventures helps ambitious Brabant companies to grow in a future-proof manner. Through its knowledge and risk capital, the agency focuses on startups and scaleups in Brabant's Priority Industries: High Tech Systems & Materials, AgriFood, the Biobased Economy, Life Sciences & MedTech and Maintenance & Supply Chain.

4. CREATING ENERGY PROJECTS - CONTRIBUTING TO ENERGY TRANSITION IN BRABANT

BOM Renewable Energy facilitates energy conservation and sustainable energy generation. The team works with businesses, property owners and citizens' initiatives to create sustainable energy projects. BOM Renewable Energy encourages energy conservation in the property market and industry and provides advice and assistance for cost-effective solutions that will help make Brabant energy-neutral.

BOM Renewable Energy advises on project organisation and structuring and can also invest in the projects and use its network to kick-start projects. The team's focus is on major projects, such as wind farms and solar parks, and on connecting and bringing smaller projects together. Smaller projects are supported through BOM's EsCo (energy service company) partners, who are active in specific markets, such as solar panel manufacturing or social housing and energy conservation for SMEs.

www.brabantisbright.nl

3. BRAINPORT DEVELOPMENT EINDHOVEN

SERVICES

Brainport Development, a part of Brainport Eindhoven, is the association that concentrates on innovation and economic development. Brainport Development fosters economic growth in the region by attracting international high tech and manufacturing companies and providing them with local support. From startups and scaleups to large multinationals, Brainport shares knowledge and advises on issues such as funding, putting them in touch with other companies and with local and international talent. It is also responsible for implementing the economic strategy defined by the Brainport Foundation, on the grounds of which Brainport Development partners with companies, knowledge institutions and public agencies as an independent body.

The region's philosophy is that 'we can grow faster when we grow together', and that businesses only require occasional guidance or additional assistance. And this is what Brainport Development offers to both foreign and local companies. In reality, it is an economic development association and is funded by all 21 municipalities within the Brainport region.

www.brainporteindhoven.com/en/

4. REWIN WEST-BRABANT

REWIN West-Brabant, the regional development agency for the western region of Brabant province, works to boost the regional economy by encouraging business investment. REWIN provides support for establishing and/or relocating both branch offices and entire companies, and it has a special interest in the following key industries: Logistics, Maintenance, AgriFood/ Biobased Economy and Creative services.

SERVICES

REWIN provides help and guidance on a wide range of issues, including:

- Advice on availability and the pricing of business locations in the western part of Brabant, including advice on locations and viewing properties together with you
- Support for legal and tax issues, such as incorporating a business or appealing a tax assessment
- Information on the regional business climate, labour market and residence and work permits
- Guidance on the availability of financial assistance, grants, venture capital and private investment opportunities
- Assistance with grant and permit applications
- Information on staff recruitment and training, current labour and salary conditions

REWIN will assist newcomers to western Brabant through introductions to its network of local authorities, educational institutions, knowledge networks and technological expertise and business networks throughout the region. Companies can also participate in a range of business development programmes in the key economic industries of logistics, maintenance and the biobased economy.

www.rewin.nl/en

5. Life Sciences & Health Priority Industry

The Dutch Life Sciences & Health (LS&H) industry is one of nine 'Priority Industries' in the Netherlands. The Priority Industries are designated by the Dutch Ministry of Economic Affairs and Climate Policy and are selected based on their ability to contribute substantially to global societal challenges.

The LS&H Priority Industry entails a broad scope of disciplines, from pharmaceuticals to medtech, from healthcare infrastructure to vaccination. In order to fulfil its mission – the vital functioning of citizens in a healthy economy – the Priority Industry builds on the strengths of the Dutch Life Sciences & Health industry to address the biggest societal challenges in prevention, cure and care: improving the quality of life (vitality) while keeping the costs of healthcare down.

The LS&H Priority Industry initiates and encourages multidisciplinary public-private partnerships (PPPs) to bring innovation to the market. By attracting funding, sharing best practices and the univocal Health~Holland industry communication, the Priority Industry stimulates a productive infrastructure.

MANAGEMENT OF THE LS&H PRIORITY INDUSTRY

The LS&H Priority Team is responsible for the daily management of the Priority Industry. The Priority Team consists of representatives of the three PPP partners: industry, academia and government. The Priority Team builds on the in-depth expertise of an Advisory Board that in which all the LS&H stakeholder groups have a voice. A dedicated Executive Office supports the LS&H Priority Industry and acts as the central point of contact.

PUBLIC-PRIVATE PARTNERSHIPS

Partnerships are embedded in the genes of the Dutch, as can be seen in the country's centuries-old war with water – a way of life that has produced innovative and smart solutions, like the famous dikes, as well as a cooperative mindset. And Dutch public-private partnerships (PPPs) also receive worldwide acclaim in the Life Sciences & Health industry, especially in the fields of oncology, medical technology, bio-banks and vaccines. In these PPPs researchers, businesses, government and patients work closely together to maintain and improve the high standards of healthcare. That's because the Dutch approach is: 'It's not what we do for you, it's what we do with you, that counts.'

PUBLIC-PRIVATE PARTNERSHIPS IN R&D

The LS&H Priority Industry encourages, facilitates and finances a variety of PPPs in order to achieve its overarching mission 'the vital functioning of citizens in a healthy economy.' There are currently more than 200 PPPs in the Dutch LS&H industry of varying shapes and sizes. Most of them have a project-based approach when it comes to making a significant contribution to R&D. Brief summaries of these R&D projects can be found on the Health~Holland website.

STRATEGIC PUBLIC-PRIVATE PARTNERSHIPS

There are also a number of strategic, thematic and long-term partnerships that strive for innovative moonshots within large, national consortiums. These consortiums are referred to as 'strategic public-private partnerships' by the LS&H Priority Industry. Based on their societal relevance, scientific quality and economic potential, the LS&H Priority Industry will support and facilitate these strategic PPPs, and at present the Priority Industry is in contact with around 30 of them.

Several of these strategic PPPs are built with Brabant companies and institutions that play a leading role: Cluster Medical Robotics, e/MTIC and RegMed XB. Two of these partnerships are discussed in greater detail in section C. Successful public-private partnerships.

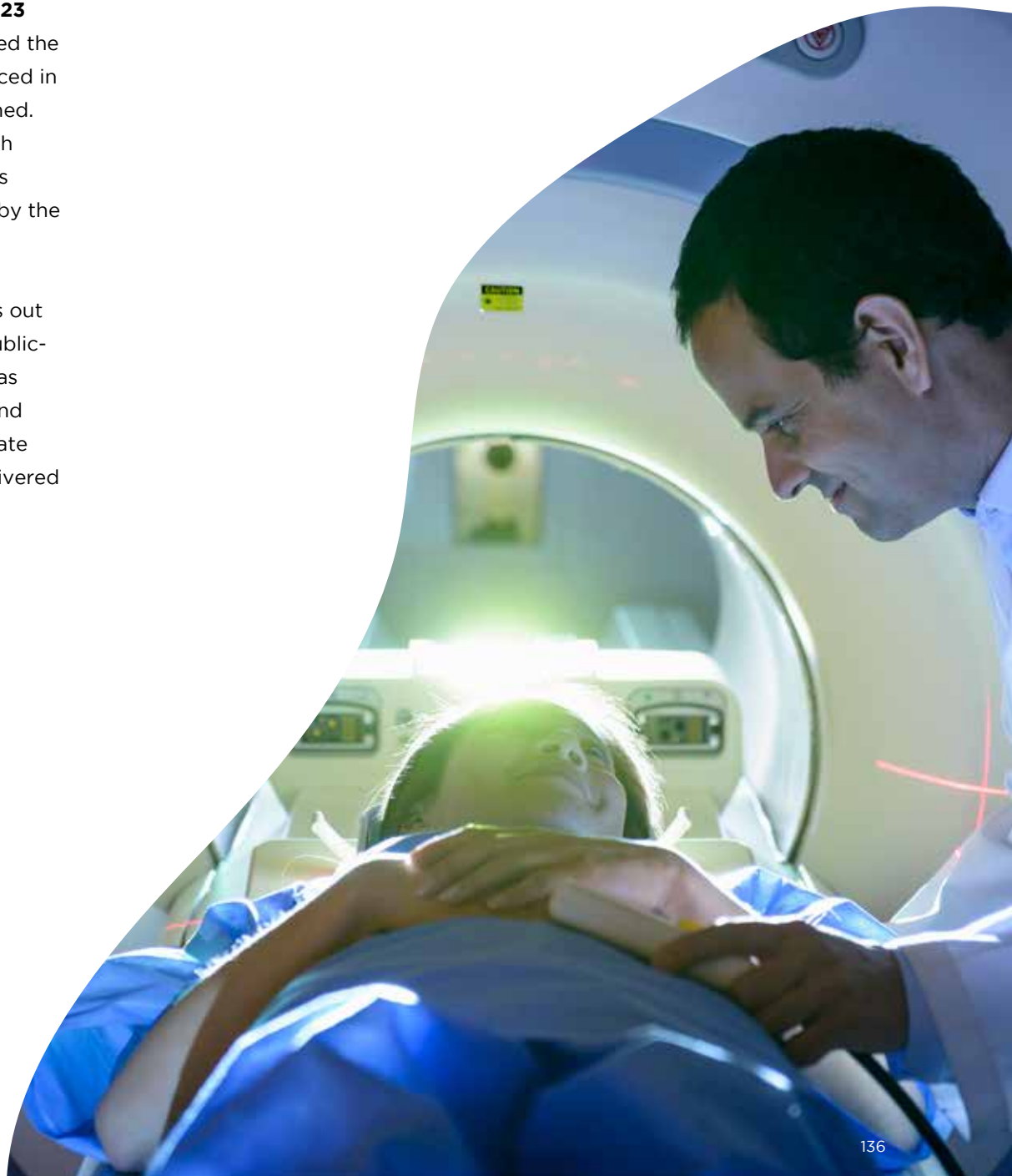
HEALTH & CARE KNOWLEDGE & INNOVATION AGENDA FOR 2020-2023

The Dutch Ministries of Economic Affairs and Public Health have designated the theme Health & Care as one of the four global societal challenges to be faced in the next decade. Addressing this theme, five missions have been determined. The one overarching mission is the goal of living longer in good health with reduced disparities in the health of higher and lower socioeconomic-status citizens. The other four missions contribute to achieving that overall goal by the year 2040.

The Knowledge & Innovation Agenda for 2020-2023, or KIA 2020-23, sets out the goals and objectives of the five Health & Care missionsin respect of public-private partnerships. The Life Sciences & Health Priority Industry – acting as a 'quartermaster' – has drafted the KIA in consultation with many public and private stakeholders, and it builds on a powerful ecosystem of public-private partnerships (PPPs) that have developed in recent years. The KIA was delivered to the Ministry of Economic Affairs on Tuesday, 15 October 2019.

The KIA 2020-23 is discussed in greater detail in Chapter 9, International Trends and Developments.

www.health-holland.com



6. HOLLAND EXPAT CENTER SOUTH

Holland Expat Center South is a non-profit governmental agency that is a joint initiative of the participating municipalities (almost every municipality in Brabant), the Netherlands' Immigration and Naturalisation Services (IND), Brainport Development, and the province of Brabant.

SERVICES

The Holland Expat Center South compiles the procedures and provides information that helps expats and their families to settle into their new living (and working) environment. Expats can obtain information about the region from the Expat Center and learn more about events organised specifically for the expat community. Its main purpose is to help expats feel welcome and at home.

The Expat Center helps companies employing expats and expats themselves to fulfil the formalities required for residing in the Netherlands, such as acquiring the compulsory BSN (Citizen Service Number), help with visa/residence permits, work permits (if required), converting a driver's license, TB testing, etc.

www.hollandexpatcenter.com

B. Incentives and grants/support programmes

1. Highly-Skilled Migrant Permit

Highly-skilled migrants do not require an employment permit to work in the Netherlands. The national scheme for highly-skilled migrants is available for employee transfers that do not fall under the scope of the EU's intra-corporate transfers (ICT) directive. This may be the case for employees who, for the duration of their assignment, are placed on the Dutch payroll of the recipient company. Japanese nationals and Turkish nationals do not require an ICT residence permit either; they can apply for a highly-skilled migrant residence permit.

WHAT IS A HIGHLY-SKILLED MIGRANT?

A highly-skilled migrant or knowledge migrant (in Dutch, a kenniswerker) is any foreign employee who:

- comes to the Netherlands to work as an employee;
- earns at least €4,612.00 (excluding holiday allowances and 13th cheques) gross per month;
- or earns at least €3,381.00 (excluding holiday allowances and 13th cheques) gross per month, if under the age of 30.

These salary amounts are applicable for 2020. The sums are index-linked annually.

Fixed allowances for housing and a company car may be added to the employee's base salary in order to comply with the above salary criteria, but only if these allowances are agreed to in writing and paid in monthly instalments.

An application for a permit can be declined if the salary is not a competitive one in the industry in question. This income requirement does not apply to scientific researchers and physicians training to become specialists, or to people working for educational or research institutions.

Employers that wish to employ highly-skilled migrants are no longer required to also apply for work permits for these employees, and they now only have to submit an application for admission and residence for the employee and his family to the Immigration and Naturalisation Department (IND). The application procedure takes two to three weeks. A residence permit for highly-skilled migrants will be granted for the duration of the intended employment, up to a maximum of five years.

Professional soccer players and ministers or teachers of religion are not eligible for residency as highly-skilled migrants. Directors and major shareholders cannot apply for the knowledge migrant scheme either if they hold a stake larger than 24% in the company, as they are then liable for any company risks and can influence their own incomes.

The income requirement for highly-skilled migrants will be reviewed on 1 January of every year on the basis of the most recent index figure for negotiated salaries, as published by Statistics Netherlands (CBS). The average yearly increase of the salary criteria has been 2.6% for the past three years. Whenever a highly-skilled migrant submits an application for the extension of his or her residence permit or switches employers, the IND will apply the most recently indexed salary criteria. Thus, if a highly- skilled migrant applies to extend his or her residence permit three years after being admitted for the first time, he or she must take into account that the applicable salary criteria has increased by almost 8%.

If a highly-skilled migrant under the age of 30 continues working for the same employer after turning 30, the lower salary requirement that was in force when he or she first applied for a residence permit remains applicable. If the highly-skilled migrant applies for an extension and continues to work for the same employer, the most recently indexed salary criteria for the under-30 age category is applicable. However, if this employee switches employers after turning 30, the most recently indexed salary for those over the age of 30 is applicable.

2. The 30% Ruling (Tax-free Allowance)

The Netherlands has a special tax regime for expatriates, known as the 30% ruling, which exempts them from a substantial portion of their income tax (up to 30%). This is viewed as a reimbursement of the extra costs involved in living abroad, the extraterritorial expenses. Rather than having to specify and prove the extraterritorial expenses incurred by an employee or an employer for its employees each year, the costs are set at a maximum of 30% of the taxable remuneration. In addition, the employer may reimburse certain costs tax-free. This includes international school fees, certain relocation expenses and a moving allowance up to a given limit.

THE PART OF THE INCOME TO WHICH THE ALLOWANCE APPLIES

Under the tax rules, the employer may grant the employee a tax-free allowance of up to a maximum of 30% of his or her taxable remuneration package. Incidental and flexible forms of income such as bonus payments and stock options that are paid out during the duration of the 30% ruling are also included. Severance and pension payments, however, are excluded.

METHOD OF CALCULATION

Under the regulation, the taxable and the non-taxable part of the income has to be split in the employment contract itself. In other words, the 30% tax-free allowance must be granted as a separate part of the employee's salary. Standard wording is used to state this in either the employment contract or in a separate addendum to the contract. For employees with net salary contracts and irregular payments, it can be difficult to precisely determine the non-taxable part of 30% on a monthly basis, and so in these cases they may determine and pay the exact tax-free reimbursement on an annual basis.

RULING AND PENSION

An employee cannot accrue a pension under a qualifying plan in the Netherlands (or social security benefits) on the tax-free allowance. This affects employees who have a pensionable base equal to their full gross salary. Employees who may apply the 30% ruling may only accrue pension on the taxable part of their salary. There is way to avoid this, although the employer must fulfil a number of legal formalities and draft special documents for this purpose.

EXTRATERRITORIAL COSTS

The 30% ruling is a practical solution for employers wishing to reimburse, tax-free, the additional costs incurred by the employee working in the Netherlands as opposed to their home country, the extraterritorial costs (instead of keeping all receipts of the actual costs claimed by the employee). The Dutch State Secretary passed a special decree that further detailed which costs, allowances and benefits in kind that are typically paid to expatriates qualify as extraterritorial costs. In the case an employee who was hired or assigned from abroad to work in the Netherlands and was not deemed eligible for the 30% ruling, it is still possible to reimburse the de facto extraterritorial costs to this employee tax-free. In this event, the employer must retain proof of the extraterritorial expenses incurred.

INTERNATIONAL SCHOOL FEES

Under the 30% ruling, the employee may receive an additional tax-free reimbursement of the fees paid for children to attend an international school. A school is regarded as an international school when a) the education is based on a foreign school system, and b) in principle the school only accepts the children of foreign employees.

RELOCATION EXPENSES/MOVING ALLOWANCE

The costs of moving as well as the costs for transporting household goods as part of the employment or secondment package are not considered extraterritorial costs, which means that these costs can - to a certain extent - be reimbursed tax-free. Actual relocation costs of up to €7,750 (2019) can be reimbursed.

PERIOD OF VALIDITY OF THE 30% TAX-FREE ALLOWANCE

The 30% ruling is available for a period of five years (60 months). The rules stipulate that the tax authorities can demand that the employer demonstrates at all times that the employee still meets the conditions. Where the employee no longer meets the conditions of the 30% ruling, it can no longer be applied. This will result in a retroactive adjustment (when required). If the employee's contract in the Netherlands has ended, the 30% ruling will also simultaneously cease to apply. As such, the 30% ruling cannot be applied to any payments made after that time.

The duration of any previous stay or period of employment in the Netherlands is subtracted from the maximum five-year period. However, this reduction will not occur if the expatriate has not stayed or worked in the Netherlands during the 25 years preceding his or her most recent arrival date in the Netherlands (or has only stayed in the country for very limited periods).

CONDITIONS FOR QUALIFYING

In order to qualify for the 30% ruling, the following conditions must be met:

- The employee (board members and supervisory board members also qualify for the 30% ruling) must be recruited (or assigned) from abroad;
- The employer must be a Dutch wage tax-withholding agent. If the employee has a Dutch resident employer (a Dutch corporation or branch of a foreign corporation) this condition is usually met. If the employee has a foreign based employer which has no taxable presence in the Netherlands, the employer must have one or more employees working in the Netherlands, perform payroll administration in the Netherlands, and be registered as a withholding tax agent with the tax authorities.
- The employee must have lived outside of a 150 km radius from the Dutch borders for at least two-thirds of the 24 months prior to the start of their employment in the Netherlands;
- The employee must have the specific expertise required to perform the function and which is not available or scarce on the Dutch labour market. This is based upon a salary standard that must be met; and
- The 30% ruling must be contractually agreed upon between the employer and employee. This also implies that the employee is aware that the 30% ruling reduces his or her gross salary.

3. Incentives for Research and Development Costs in the Netherlands (WBSO)

Companies established in the Netherlands performing research and development work (Speur- en Ontwikkelingswerk: S&O or R&D) may be eligible for tax relieve on wage costs and additional costs. The WBSO R&D scheme is intended to provide entrepreneurs with an incentive to invest in research by means of reducing the R&D wage costs. The WBSO scheme for R&D includes salary and other costs and expenses directly related to R&D activities.

The benefit amounts to 32% of the first EUR 350,000 of R&D costs (both salary and other costs and expenses) and 16% for R&D expenses above €350,000. For startups, the percentage for the first bracket is higher, at 40% instead of 32%. The WBSO does not have an upper limit, although the maximum benefit may not exceed the wage sum.

CONTRIBUTION

The R&D allowance takes the form of a reduction in wage taxes and social security contributions. The WBSO can be applied to costs and expenditure directly allocable to the company's R&D activities, whereby:
1) costs must be incurred exclusively (for 100%) for R&D;
2) expenditure must serve R&D (can also be partly allocable).

When applying for the WBSO one can choose between a lump-sum application (based on the number of R&D hours; no R&D expenditure will be subsidised) or an estimate of the actual amount of costs and expenditure incurred.

ACTUAL COSTS AND EXPENDITURES

Only costs and expenditure directly allocable to R&D and which serve R&D purposes can be taken into account. In this respect, note that not all activities related to R&D projects can be recognised as R&D work. For example, administrative and organisational costs are excluded.

As far as the costs are concerned, it is only those costs that are borne by the taxpaying company itself. When it comes to expenditure, the allowance only applies to newly manufactured business assets insofar as:

- these assets have not been previously used;
- they have not been included in previous R&D declarations (subsidy applications);
- these assets fall under own R&D activities;
- expenses are borne by the taxpaying company payer(or a group company of an affiliation, in tax terms, that the taxpaying company is a part of

CONDITIONS

The R&D project must meet the following conditions before one can apply for the R&D allowance:

- the proposed R&D activities take place within your own company
- the technological development is new to your company
- the development brings with it technical issues
- the R&D work has yet to be undertaken (which means you must always submit a WBSO application in advance).

R&D work is defined as a systematically organised activity, related directly and exclusively to:

- technical scientific research
- the development of:
  - (Parts of) physical products
  - (Parts of) physical production processes
  - Software (technically new (parts of) software)
  - Software components (technically new)

WBSO support is explicitly NOT intended to support feasibility studies, software upgrading, software modifications for different hardware or software platforms, developing services, routine activities, market research, organisational or administrative work, policy and strategy studies, the adaptation or deployment of purchased goods, quality control and assurance, the adaptation or implementation of existing technology, pilot plants and related products on a production scale with commercial value.

4. Innovation Box

Companies can benefit from an effective tax rate of just 7% for income from intangible assets created by their Dutch taxpaying entity. The effective tax rate of 7% will increase to 9% in 2021. Patented intangible assets as well as intangible assets that have been created by the Dutch taxpaying entity and for which an R&D declaration (an approved WBSO application) was obtained, may qualify for the Innovation Box. In practice, this means that technological innovations developed in-house qualify.

The lower tax rate of 7% is claimed in the corporate income tax return filed by the Dutch taxpaying company. The lower tax rate is actually an exemption for a substantial part (72%) of the profits that can be allocated to the Innovation Box. By applying the general Dutch corporate income tax rate of 25%, this results in an effective rate of approximately 7%.

The Innovation Box does apply:

- in situations where the period between an application for a patent and the granting of the patent is unusually long. Subject to certain conditions, profits that are attributable to the relevant patented asset may, during the period from the year in which the patent was applied for up to the year preceding the year in which the patent was granted, also be brought within the scope of the Innovation Box.

The Innovation Box does not apply:

- to marketing intangibles such as trademarks and logos
- to intangible assets for which a patent was obtained if the asset was already in existence before 1 January 2007
- to intangible assets for which an WBSO R&D declaration was obtained if the asset was already in existence before 1 January 2008

As a result of EU talks on favourable EU IP regimes and the introduction of minimum rules for preferential IP regimes (OECD BEPS project), as of 2017 the Netherlands has altered the Innovation Box regime in order to be compliant with the new requirements. The changes relate to the entry tickets to the Innovation Box (you now require a WBSO R&D declaration) and allocation of income that qualifies for the special tax rate.

Originally, there was no cap on the amount of profits that could be allocated to the Innovation Box, although a taxpayer had to be able to prove that the profit was related to the qualifying intangible assets. As of 2017, restrictions have been introduced (the modified nexus approach). It is recommended that an agreement be reached in advance with the Dutch tax authorities on which method to apply – they will do this on request. At present, the Innovation Box regime has the following relevant features:

R&D ACTIVITIES (ENTRY TICKET)

Originally, the Patent Box or Innovation Box incentive could only be applied to income generated from registered patents, but this has now been extended to include income from R&D projects for which a WBSO R&D declaration has been obtained. Henceforth, a distinction is drawn between small and other taxpaying companies.

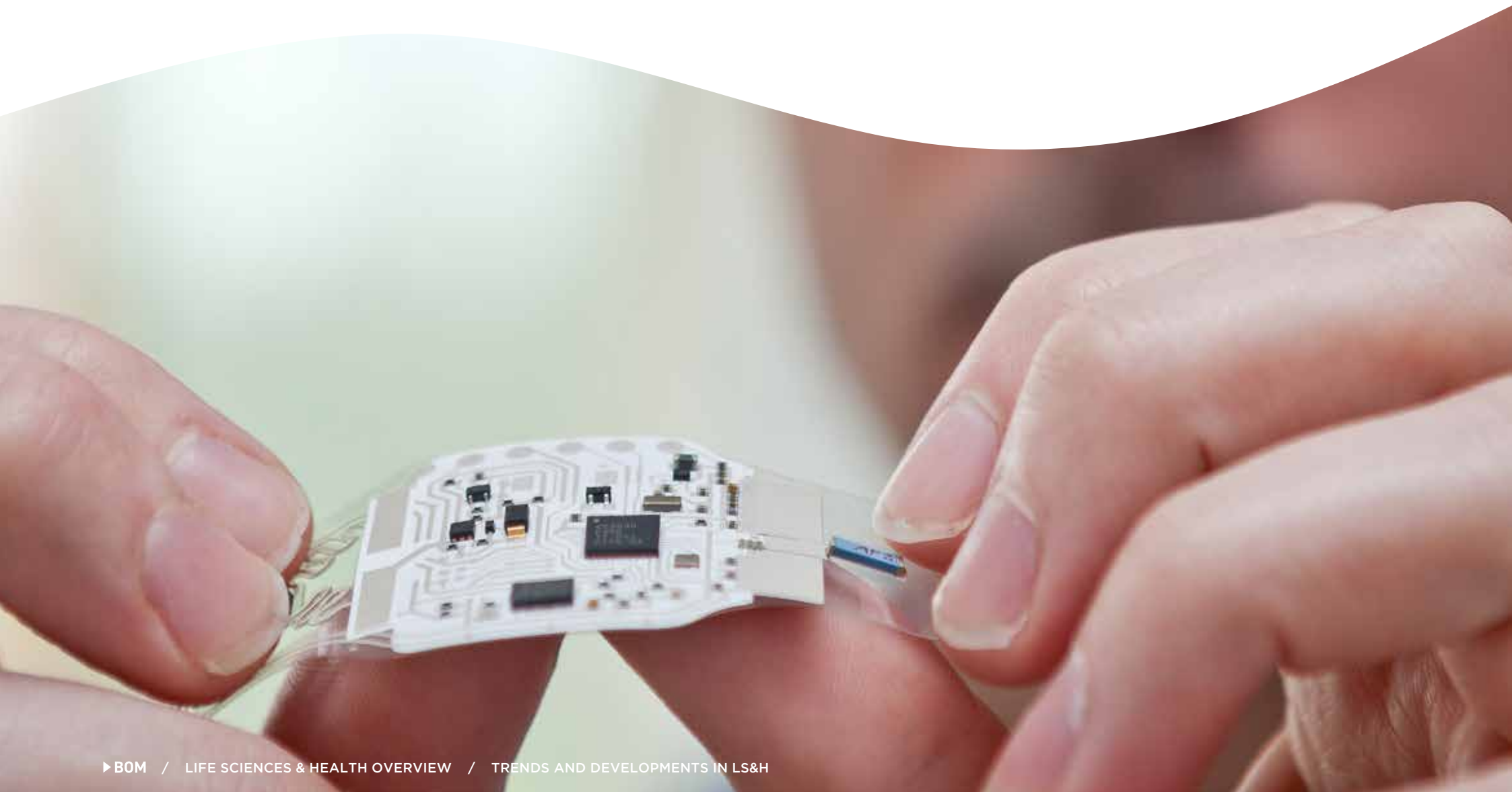
Small taxpayers are companies with worldwide net group sales of under €50 million per year and a gross benefit from IP not exceeding a total of €37.5 million in five consecutive years (an average of €7.5 million per year). For small taxpaying companies the WBSO R&D declaration suffices as an entry ticket to the Innovation Box.

Larger taxpaying companies not only need to obtain a WBSO R&D declaration but must also have a recognised legal access ticket. For larger taxpaying companies, only income from patents, utility models, software, plant breeders' rights and pharmaceutical certifications qualify for the Innovation Box. This category of taxpayers will thus be subject to a twofold test. A small taxpaying company can also include unprotected IP in the Innovation Box regime.

MAXIMUM REVENUES (ALLOCATION OF INCOME)

A restriction is in place with respect to the level of income that can be allocated to the Innovation Box (the modified nexus approach). It is now more important whether or not R&D will be performed in-house and how R&D costs are divided between the parties involved. This implies that the more R&D activities are outsourced to related parties, the lower the profits that can be allocated to the intangibles resulting from such R&D activities.

9. TRENDS AND DEVELOPMENTS IN LS&H

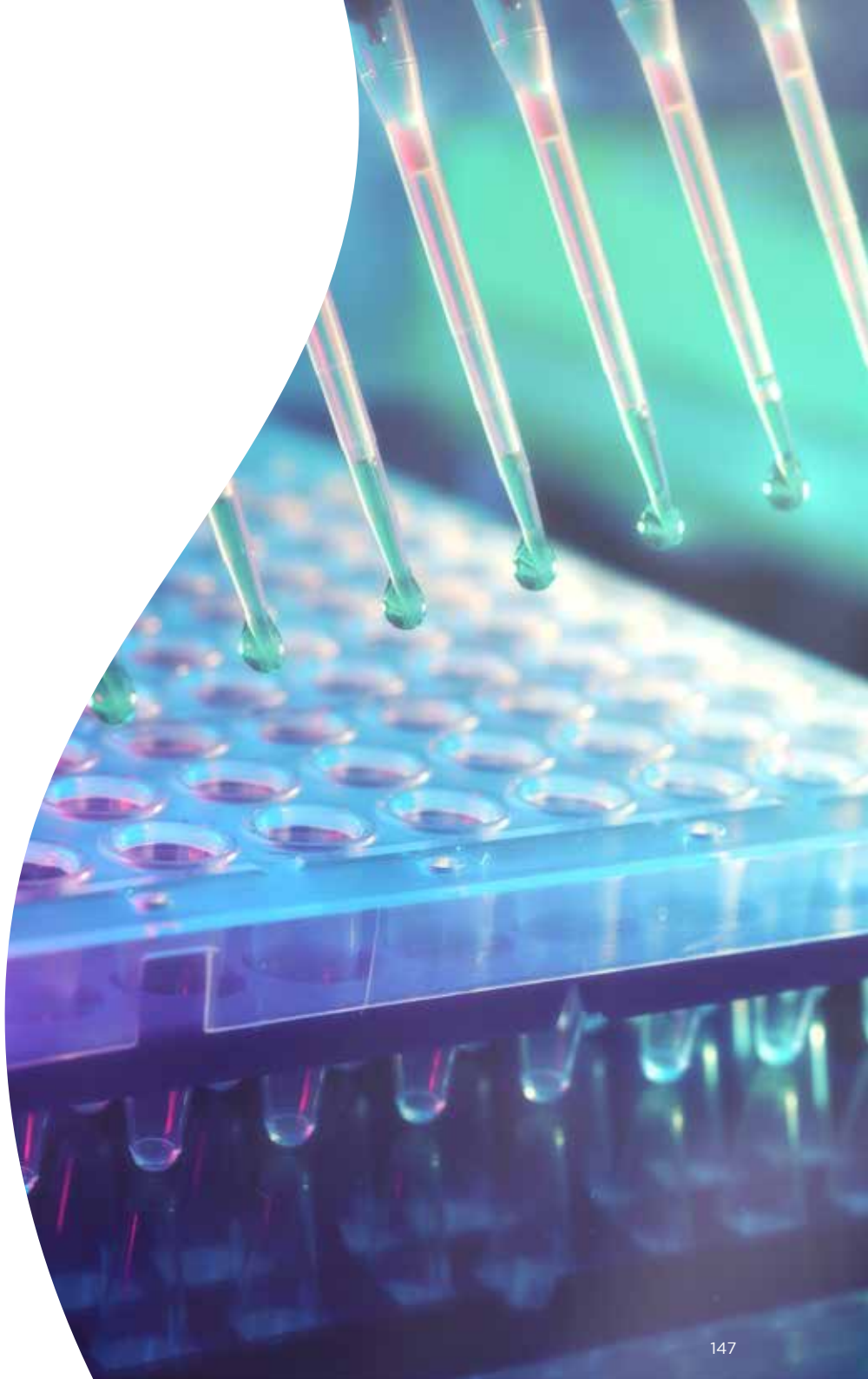


In this chapter we take a closer look at two perspectives of national and international trends and developments in Life Sciences & Health:

A.
We will first summarise the most important Dutch innovation policy in LS&H, the Health & Care Knowledge & Innovation Agenda for 2020-2023. This four-year plan has been jointly developed by government, industry, the healthcare sector, patients and citizens and outlines anticipated developments in the Netherlands in healthcare, the healthcare industry and healthcare science and education.

B.
Next, we take a bird's eye look at the most significant trends and developments in the global healthcare, breaking them down into three main areas:

1. Medical technology
2. (Bio)pharmaceuticals
3. The support sector



A. The Netherlands

Health & Care Knowledge & Innovation Agenda for 2020-2023

VITAL CITIZENS IN A HEALTHY ECONOMY

In the Netherlands, all healthcare partners – government, the healthcare industry, science and education and citizen and patient representative bodies – have come together to create a joint innovation policy for 2020–2023: the Health & Care Knowledge & Innovation Agenda for 2020-2023 – Vital Citizens in a Healthy Economy (KIA 2020-2023). The KIA 2020-2023 sets out the most important trends and developments the industry will be focusing on in the Netherlands in the period between 2020 and 2023.

THE PRIORITY INDUSTRY POLICY, 2011-2019

From 2011 to 2019 the principal Dutch policy for the Knowledge Economy was its Priority Industry Policy, the industrial policy created by the Ministry of Economic Affairs and Climate (EZK). The emphasis was on nine leading industries, or 'Priority Industries', that already occupied a strong position on the world stage and that were to be economically and scientifically further strengthened through incentivising public-private research and development (R&D). One of those nine industries that was identified as having global clout thanks to the knowledge it holds is the Dutch Life Sciences & Health (LS&H) Priority Industry.

PARTNERSHIPS BETWEEN INDUSTRY, SCIENCE AND EDUCATION AND GOVERNMENT

The ecosystem of this LS&H Priority Industry was further nourished through extensive partnerships between the business community, knowledge institutions and the government (a cooperative approach dubbed the triple helix), together with national health funds and other Priority Industries using ten specific roadmaps. The number of startups and science parks adjoining knowledge institutions grew, with the transfer and commercialisation of knowledge considered a priority. National and international companies and, increasingly, SMEs set up shop in these science parks, paving the way for new forms of local public-private partnerships (PPPs) in regional projects and large national public-private partnerships, in areas such as:

- Cardiovascular diseases (Dutch CardioVascular Alliance)
- Oncology (Oncode Institute)
- Medical technology (IMDI – Innovative Medical Devices Institute)
- Medicines (European Lead Factory)
- Infectious diseases (Netherlands Center for One Health)
- Regenerative medicine (RegMed XB)

THE NEW POLICY:
MISSION-DRIVEN INNOVATION BETWEEN 2020 AND 2023

Around 2018, citizens and patient organisations also became involved in the strategic partnership and a new approach towards the future development of the Life Sciences & Health industry started taking shape. This approach allocated a prominent role to sustainable development goals, key enabling technologies and methodologies and cooperation between leading industries, provinces, regions and citizens. This mission-driven approach was inspired by recommendations developed within the European Union, and has now replaced the earlier Priority Industry policy.

The missions that are part of the larger Netherlands' innovation policy concern the major global challenges, as set out in the United Nations Sustainable Development Goals, and are collected into four social themes:

1. Energy transition and sustainability
2. Agriculture, water and food
3. Health and care
4. Security

THE MISSIONS FOR HEALTH & CARE

The Ministry of Health, Welfare and Sport (VWS) and its industry, science, healthcare and society partners have formulated the overarching central mission and four support missions for the social theme of Health & Care. These five missions form the guidelines for public-private partnerships for technological and social innovation over the next few years.

CENTRAL MISSION

By 2040 all Dutch citizens will live at least five years longer in good health, and the health disparities between the lowest and the highest socioeconomic groups will be reduced by 30%.

THE FOUR SUPPORT MISSIONS

I. Lifestyle and Living Environment - By 2040, the burden of diseases brought by an unhealthy lifestyle and unhealthy environment will have decreased by 30%
II. Access to Healthcare Innovation - By 2030 home-based care (as opposed to care institutes) will have increased by 50% (or more), working together with a person's social network.
III. People with Chronic Illnesses - By 2030, the proportion of people with a chronic illness or lifelong disability that can participate in society, in accordance with their own desires and capacity, will have increased by 25%.
IV. People with Dementia - By 2030, the quality of life of people with dementia will have increased by 25%.

The time horizon for the central mission and the first mission is 2040 – while the deadline for missions II to IV is 2030 – because lifestyle and environmental change and the reduction of the burden of disease will take much longer to take effect and only result in the positive health developments envisaged by the central mission by 2040.

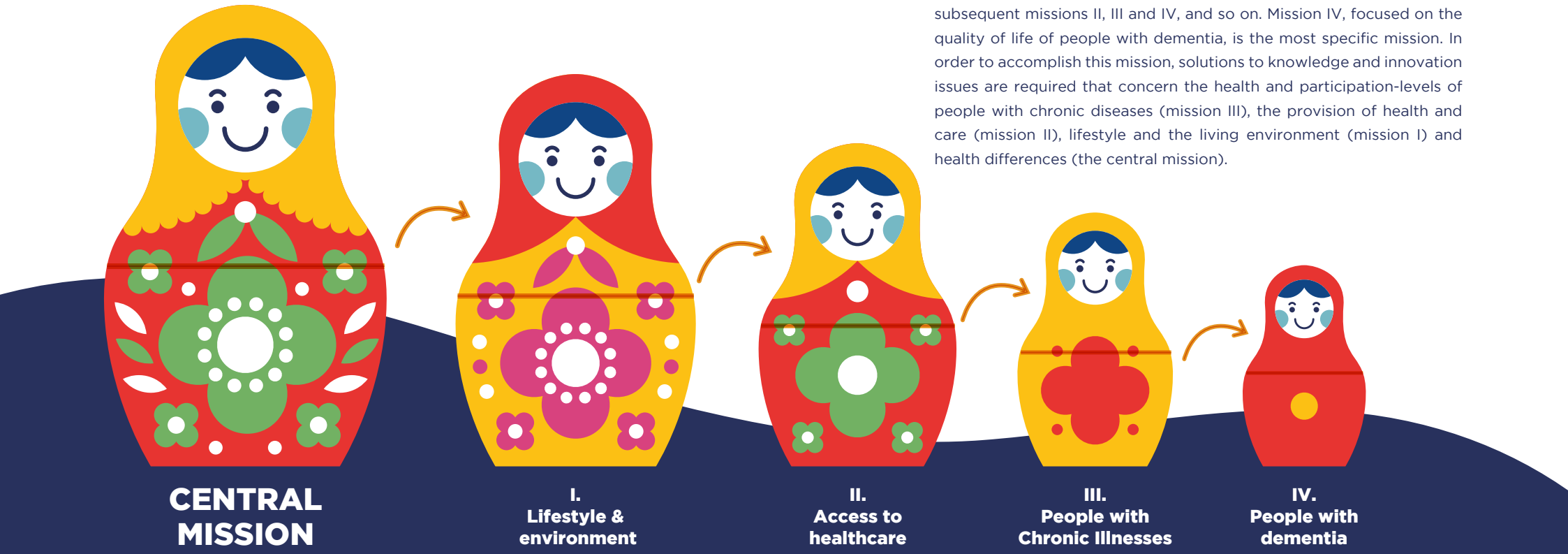


Figure: Consistency of the missions. Like a matryoshka doll, the central mission holds all the other missions. Mission I also includes the subsequent missions II, III and IV, and so on. Mission IV, focused on the quality of life of people with dementia, is the most specific mission. In order to accomplish this mission, solutions to knowledge and innovation issues are required that concern the health and participation-levels of people with chronic diseases (mission III), the provision of health and care (mission II), lifestyle and the living environment (mission I) and health differences (the central mission).

A RADICAL TRANSITION IN THE FIELD OF HEALTH AND CARE

These challenging objectives can only be achieved if society as a whole undergoes a radical transition in the way it thinks, acts and abstains when it comes to health and care-related issues. Many new concepts, products and services are required in innovative (early) diagnostics, prognostics and prevention as well as for healing diseases, reducing the burden of disease and maintaining and encouraging good health, particularly health preservation and promotion, particularly within the context of our physical environment.

The aim of the transition is to create better health for citizens and, above all, to contribute to their participation in society. The health and participation-levels of citizens are a goal in itself, but can also be seen as an important means to that end. Participation has a preventive effect and offers people a social and economic perspective. Moreover, at the end of the day citizens make up the largest contingent of health-workers and caregivers, both now and in the future, in the form of the informal care they provide.

The shift in emphasis to people continuing to function and participate in society means that new research methods are needed, due in part to the extensive digitisation. A fluid transition requires products and services to be delivered to the end users at an accelerated pace. This not only means enhanced accessibility, commercialisation and the creation of markets, it also means a new approach to implementation, and thus implementation strategies are required. Barriers must be removed and opportunities created by means of legislative and regulatory changes, funding, protocols, guidelines, care standards, prevention and care training and other matters.

VISION: THE ABILITY TO FUNCTION IN ONE'S ENVIRONMENT

The new vision on health is focused on the ability to function in one's own environment, which shall facilitate physical, mental and social wellbeing, provide a sense of meaning and quality of life and, in particular, encourage citizens to participate in society. Participation is an important health-promoting factor, including for people with chronic conditions. That is why the LS&H Priority Industry slogan 'The vital functioning of citizens in a healthy economy' is a part of the new LS&H innovation policy.

MORE PEOPLE, LESS PATIENTS

Preventive support

In the (near) future, the individual will receive prevention-oriented support in and from their own environment. The urban environment and green zones, the infrastructure and the indoor environment – at home, at school and at work – play a role in a person's vital functioning and participation-levels. Where prevention is insufficient, people shall learn to solve health problems themselves, based on their own talents (self-management) and with the help of those around them (joint management). If that fails, then appropriate technology must offer a solution: from walking frames and innovative variations through to artificial intelligence (AI) – technology that has been developed and validated with the person and his/her social circle and – in the environment in question – ecologically validated.

Continued participation

New technology such as eHealth applications, wearables, home automation, robotics and exoskeletons mean that citizens can continue to participate despite illnesses and handicaps. Technology can also help to make the informal and formal support system work together more closely and, if necessary, ensure that these systems are utilised in good time.

At the same time, social and technological innovations must relieve the burden on informal caregivers and care professionals, for example through respite care and the restructuring of care professions and training. Devices can be designed so that they are easier to use by citizens and professionals, such as by using new methodologies like data-enabled design.

Superior inpatient care but increased focus on cure instead of care
Anyone who requires acute or complex care will also attend an inpatient facility in the future. But, thanks to a higher degree of prevention, self-management and joint management, this is required much less frequently. In addition, diagnostics and therapy shall increasingly focus on actual healing (cure) instead of combating symptoms (care). In-depth fundamental research - from the building blocks of life through to regenerative medicine and personalised medicine – will provide a better understanding of disease mechanisms and targets for therapy.

Novel cures for currently untreatable diseases
It will also become possible to cure conditions such as cancer, cardiovascular disease, depression and anxiety disorders, diabetes, osteoarthritis and infectious diseases. Even the treatment of Alzheimer's disease, the causes of which are still unclear, will eventually be within reach.

TRANSITION

A major transition is required for the health and care missions to succeed under this vision... and time is short. This is why the LS&H Priority Industry will continue to bolster the public-private knowledge and innovation ecosystem with its many partners during this 2020-2023 period. In order to accelerate the transition, products and services that are demonstrably effective and safe and must be available to the end user at a more rapid pace.

New PPPs are being launched and there are new, relevant domains, such as the key enabling technologies and methodologies and the relevant routes adopted by the National Science Agenda (NWA). New players, such as citizens, trainers and employers, play an important role in the innovation process. But existing PPPs are also being further expanded and supported during the implementation and acceptance phase.

THE ESSENTIAL ROLE OF FIELD LABS

It is crucial that field labs be created, as they provide an environment in which experiments are conducted on integrated social and technological innovations. These experiments are performed in a range of real-life environments in cities and in the countryside. The field labs see citizens, government, knowledge institutions and companies from both within and outside the traditional health industry, health insurers and other professionals working together.

The end users in their own environment are of central importance in the field labs, whether because of the questions they ask, their conversion of knowledge into innovations or by means of validating those innovations. Customised solutions are being created – after all, an application designed for young and healthy working men cannot automatically be expected to be suitable for retired women living in a low-income neighbourhood.

TIMEFRAME

By 2023 the field labs will serve as an inspiring showcase for the health and care transition process, creating a greater understanding of the following core elements:

- Benefits (socially, improved health and greater participation in society, and economically, increased employment, turnover and exports for companies)
- Availability (of both outpatient and inpatient prevention and care)
- Usability (for all end users in their own environments)
- Affordability (essential for the sustainability of the system)

By 2023 it will also be evident how the innovations contribute to (international) economic returns and the intended 10% growth in exports by 2030.

B. Bird's eye view on global trends in Life Sciences & Health

OVERALL TRENDS

Three global trends influence every aspect of the full value chain in healthcare, from medical technology and biopharmaceuticals through to the support sector and services. These trends have been described as follows by KPMG's Global Strategy Group in 2019 in its report Unlocking the full potential of the Dutch Life Sciences sector.

1. Technology and Digitalisation

Advanced technologies are being adopted within life sciences at a rapidly increasing rate, especially within R&D. Examples include the use of machine learning to generate data about antibody usage or 3D printing for artificial organ materials. Furthermore, innovations in cellular, gene and tissue engineering are replacing existing methods in fields such as animal toxicity testing.

Data science and analysis have become a critical component, particularly when it comes to shortening the R&D process. Cloud-based platforms are becoming commonplace and ever more data is collected remotely via medical devices and being used in clinical trials.

As new technology and digitalisation transform the world of research, the life sciences industry must be proactive in creating data platforms and introducing appropriate legislation to enable new solutions. KPMG states in its report that this is particularly true in the Netherlands.

2. Rapidly-changing R&D environment

The speed of change in R&D is driven by an increased understanding of the molecular basis of diseases, including proteomics, genomics and metabolomics, along with advances in and the availability of relevant data. Such developments are accelerating the shift to personalised medicine aimed at smaller groups of patients.

Many of today's financial, business and operating models are not geared towards greater personalisation. To adapt, R&D teams must become fully patient and consumer-centric (as opposed to product-centric). Life sciences companies need to urgently foster cultures that embrace new technologies and new approaches to research.

EXAMPLES IN BRABANT

A selection of highly innovative biopharmaceutical companies at Pivot Park that specifically aim to develop personalised, precision drugs:

- **Noviocell** is a highly innovative biotech company. It is focusing on the development of the first ever synthetic solution for 3D cell culturing, ranging from organoid growth to personalised medicine. 'Our mission is to accelerate life science research by making 3D cell culture feasible for every cell biology researcher.'
- **NTRC** is a precision medicine company dedicated to the development of new anti-cancer drugs. NTRC facilitates the development of novel therapies by providing immunotherapy assay development and screening, cancer cell line profiling, pharmacogenomics analysis, combination studies, and target residence time measurements for protein kinases. Assay readouts for the cancer immunotherapy drug targets Arginase 1, IDO1, and TDO are supplied to clients globally. NTRC has internal drug discovery programmes for TTK, IDO1 and TDO.
- **Lead Pharma** has developed a pipeline of drug candidates for key targets in oncology and autoimmune diseases. The company has particular expertise in the development of novel chemotypes and can also address targets that evade conventional drug development strategies, either because expression, production and assay development have been too complicated to date or because the ligand-binding domains are inaccessible for conventional chemotypes. For example, Lead Pharma has developed a novel class of compounds against nuclear receptors and transcription factors.

3. The demand for returns on R&D spending

Globally, the cost of bringing a biopharmaceutical product to market increased between 2010 and 2018 from €1,005 million to €1,950 million; in the same time period peak sales per asset declined from €734 million to €366 million. As a consequence, overall returns on R&D plummeted from 10.1% in 2010 to just 1.9% – and some forecasts suggest they may fall further to 0% by 2020 [KPMG analysis, 2019].

Many life sciences companies' initial response was to reduce R&D through the shared usage of certain capabilities. Industry and research players are pooling their funds to rent specific technologies, talent and services from shared service providers. Crowdfunding has also emerged as a new method for distributing R&D risk.

As returns on R&D continue to fall, life sciences hubs with extensive shared research infrastructure and access to novel funding opportunities are likely to be better-prepared for the more austere investment climate. It is consequently crucial that any region aiming to remain competitive in the life sciences and health arena (including the Netherlands) positions itself as such a hub.

A BRABANT EXAMPLE

Pivot Park is the ultimate example when it comes to sharing facilities, knowledge, equipment and outsourcing in biopharmaceutical drug discovery and development. The 60 companies that are present and their 600 employees are highly interconnected in terms of discovering and manufacturing the latest immunology-based treatments in, for example, oncology. Startups can use laboratories and equipment virtually free of charge and research and manufacturing activities can be outsourced to companies such as:

- Pivot Park Screening Centre (a UHTS screening facility)
- BioConnection (contract services and manufacturing organisation for the development and manufacture of injectable (bio) pharmaceutical products)
- Ardena (cGMP manufacturing, quality control and stability studies)
- ImmunoPrecise Antibodies (full-service, therapeutic antibody discovery company)

Trends in individual areas of activity/subsectors

TRENDS IN MEDICAL TECHNOLOGY

- Medical technology is increasingly becoming a part of the full care and cure process. Building upon and evolving from imaging and monitoring technologies towards wearables, surgical robots, diagnostics, care support systems, etc, medical technology, IT systems and data processing are indispensable in today's healthcare processes.

A BRABANT EXAMPLE

PHILIPS SET TO TREAT LUNG CANCER (NOVEMBER 2019):

- New X-ray equipment can detect smaller cancer tumours in the lungs at an earlier stage.
- Tumours can be frozen or burned as they are diagnosed.
- Philips is developing new technology in 20 different hospitals.

Philips has designed a new way to treat lung cancer. Using advanced X-ray equipment, the Dutch company believes that doctors can detect smaller tumours in the lungs at a relatively early stage. Moreover, treatment can immediately take place during the diagnosis.

OTHER TRENDS AND DEVELOPMENTS IN MEDICAL TECHNOLOGY

(a selection from KPMG's 2017 Advisory Report to the Dutch Ministry of Health, Welfare and Sports)

- Hospitals are gradually shifting from invasive to less-invasive technologies, potentially reducing the duration of treatments and complexity of the resulting wounds
- There is a continual shift from therapy and treatment to prevention, driven by e-health solutions and smart apps in particular
- Healthcare is becoming increasingly personalised and medical technology is becoming more focused on the specific patient
- Patient care is gradually shifting from intramural care to care in the home environment, aided by advancements in medical technology. Patient-data-sharing technologies, such as wearables and the Internet of Things, are further evolving to enable the seamless remote delivery of care, as well as in clinical/hospital settings
- The increasing use of smart apps integrated with medical devices to provide real-time access to patient data and help to improve clinical decision-making.

A BRABANT EXAMPLE

EINDHOVEN'S E/MTIC AND MEDTECH, DATA EXCHANGE AND ANALYSIS IN HEALTHCARE

Carmen van Vilsteren, Director of Strategic Research Area Healthcare at the TU/e, Eindhoven University of Technology

'e/MTIC (the Eindhoven Medical Technology Innovation Center) is a combination of the strengths offered by TU/e, Philips Healthcare and three top clinical hospitals in Brainport Eindhoven, which aims to accelerate clinical innovation. The launch of e/MTIC is the end result of a fruitful project-based collaboration that has been operating for 15 years and makes it possible to continue it in a stronger, structural and strategic form.' […]

'Medical technology delivers an indispensable contribution to affordable care solutions that have a positive impact on the patient. In the past, medtech was frequently only concerned with the development of high tech medical devices for diagnostics and treatments; today it is a much broader field that also covers prevention, as well as big data analysis for purposes such as clinical applications.'

What is the added value of e/MTIC in respect of data exchange and data science?

'We hope to shed the burden that lies on researchers, each of whom have to find out individually how to deal with data exchange or have to seek permission for clinical research. In an e/MTIC context, we are building an infrastructure for data acquisition and data exchange and we manoeuvre through the jungle of regulations, medical committees and certification as a single body. In this way, we can move from idea to prototype to test phase to market-ready product faster and accelerate the pace of innovation, without rushing any essential steps.'

What makes e/MTIC fit in at Brainport Eindhoven?

'e/MTIC is a reflection of Brainport Eindhoven. Philips was a co-founder of TU/e and as such maintains a relationship with the university going back over 60 years. And the Máxima Medical Centre and TU/e are two institutions that can also boast of a 15-year partnership. Gynaecologist Guid Oei, for example, is a part-time professor at TU/e. It proves that being close together works: it makes it easier to enter into partnerships, easier to connect and the ball can start rolling quickly. That is also a true strength of e/MTIC – five parties that complement each other in terms of their activities and that are also within cycling distance of each other.

In addition, there is the valuable connection to the high-tech ecosystem in the region that actually allows innovations to find their way to the market. The partnership that evolved into e/MTIC has already generated at least ten successful medtech startups.' […]

Trends in the (bio)pharmaceutical industry

In reviewing the pharmaceutical sector, it becomes clear that the traditional biopharma business model of focusing on a limited number of molecules and then trying to develop them into billion-dollar blockbuster drugs is on the wane. Medical treatments and prescribed drugs are increasingly becoming more personalised and as such leading to reductions in target group size and a subsequent loss of financial turnover for the companies developing and producing them. As a result, the drug development and commercialisation process and structure are changing.

Some of the most significant developments leading to new business and cooperative models in the biopharmaceutical industry are:

1. Healthcare policymakers and funding organisations increasingly determine what doctors can prescribe
2. A growing number of organisations within the healthcare system monitor the health benefits of medicines. As they have access to electronic patient records, they have the data they need to guide and steer biopharmaceutical suppliers towards value-based pricing
3. The boundaries between the different forms of healthcare are fading as previously fatal illnesses become chronic thanks to advances in clinical care and as the self-medication industry grows
4. Governments and healthcare professionals are increasingly stressing the importance of prevention rather than cure
5. Certifying authorities are becoming more careful in approving genuinely innovative medicines.

PwC Advisory Netherlands identified some of these developments as the biggest threats and opportunities for the industry in 2020 and beyond.

A BRABANT EXAMPLE

In interviews with some of the most active biopharmaceutical companies in the Netherlands (AMGEN, MSD and Janssen Pharmaceuticals), the authors of this study heard very similar arguments every time: the innovation-based biopharmaceutical companies are confident that value-based healthcare is an excellent way to fund future healthcare and drug development in a realistic and honest manner and they are actively working together to make this possible.

ANOTHER EXAMPLE OF CHANGING COOPERATIVE/INVESTMENT MODELS

ONNO VAN DE STOLPE (CEO GALAPAGOS): 'THIS IS JUST THE BEGINNING'

Trends, 7 November 2019, Bert Lauwers

You made a historic deal with the US company Gilead this summer. What are your reflections on it?
'Everyone should be really satisfied,' says Onno van de Stolpe. 'The agreement means that billions of euros of private money are now available for innovative research. I also received very positive signals from our research department. Gilead is incredibly open-minded in this partnership. They want to share everything. What's good for Galapagos is good for Gilead – that is now our common understanding. That's easy for me to say, but we see it on the work floor too.

How do you think the partnership will proceed?
'This is only the beginning. I have been saying that for a long time, but seeing how far we got with the extremely limited resources at our disposal at the time, this means enormous new opportunities,' says Van de Stolpe. 'You can consider this as the start of Galapagos 2.0, and I am very optimistic that great things will emerge. We must make the most of the Galapagos-Gilead combination to make a real difference in the biotech sector. […]

What does Galapagos do?
The drug developer is a flagship of the biotech sector in Belgium and the Netherlands and is nearing the commercial launch of its first drug, Filgotinib, for the treatment of rheumatism. In the second half of next year, Filgotinib should be approved in the US, Japan and Europe. Analysts estimate that the drug could eventually earn Galapagos billions of euros annually, as it may also treat other diseases. Galapagos also has a full pipeline of potential blockbuster drugs, such as a candidate drug for the lung disease IPF, and the Toledo research programme, which aims to create a successor drug to Filgotinib.

Hence the choice
Onno Van de Stolpe is the founder of Galapagos and has been its driving force for two decades. Passion and perseverance, even after major setbacks, are his trademark. Van de Stolpe is also known as a very clever negotiator. In mid-July, he reached the pinnacle of his professional life with a historic billion-dollar deal with Galapagos' US pharmaceuticals partner, Gilead. Gilead has undertaken not to launch a takeover bid for ten years and is pumping over 4.5 billion euros into the Mechelen-based company.

The standout moment of the past year?
'Our deal with Gilead, because it will give us at least ten years of independence, plus an incredible cash injection. Incidentally, those billions are contractually committed to investing in innovative R&D. So with that money we will quickly ramp up our research efforts.' […]

Trends in the healthcare industry's support sector and services

Current developments in society, both from a financial perspective and from the perspective of healthcare, population growth and the ageing population, exhibit a single overarching change in the healthcare industry – the continued rise of outsourcing in medicine and medtech research, development, manufacturing, logistics and distribution.

An ever-increasing number of activities in the healthcare industry value chain are performed by academic research groups, CROs, CMOs and 3PL/4PLs. Many excellent examples of these third party specialists can be found in Brabant, including BioConnection and Lead Pharma on Pivot Park for drug discovery and development, Movianto (Owens & Minor), a logistics services provider in Oss servicing European biopharma and medtech companies in all activities except for R&D, and Philips Innovations Services. Philips Innovations Services, or PINS, is a company based at High Tech Campus Eindhoven that performs research for clients and/or advises them in all phases of the development of medical technology.

A BRABANT EXAMPLE

BioConnection offers young and innovative biopharmaceutical companies access to its state-of-the-art GMP manufacturing facility and a broad range of support services. It is a contract services and manufacturing company for the development and manufacture (filling and freeze drying) of injectable (bio) pharmaceutical products. The company's expertise ranges from small molecules up to advanced products, like proteins, vaccines, peptides, antibodies and complex formulations.

Source: BioConnection

Deloitte identified two major outsourcing developments in the near future:

1. A shift from transactional outsourcing relationships to more strategic, relationship-based models for biologics, data-driven clinical innovation and manufacturing capacity
2. Outsourcing expertise in AI, robotic and cognitive automation and cloud computing

The consequences are:

- That the outsourcing wave by large biopharmaceutical companies will likely stimulate biologics and data-driven clinical innovation and bolster manufacturing capacity (note that it is estimated that today only a third of manufacturing – in all stages – is conducted inhouse)
- That outsourcing of expertise, especially in cognitive automation, AI and cloud computing has already seen a significant increase
- That increasing levels of biopharmaceutical outsourcing is leading to growth in the industry: strategic partnerships by large biopharmaceutical companies with academia and contract research organisations (CROs) indicate that these companies feel the need to focus on strengthening their R&D capabilities

KEY TAKEAWAY

Strategic, long-term partnerships are a requisite for pharmaceutical companies to streamline supply chains, better manage the capacity gap arising from the shift to biologics and personalised medicine, and thereby improve time-to-market. Sustaining close relationships with vendors is critical for maintaining compliant operations, because any oversight may cost a pharmaceutical company its reputation. Knowledge management is moving to the next level in the pharma space, with advanced technologies like AI, machine learning and the IoT.

A BRABANT EXAMPLE

The Eindhoven Artificial Intelligence Systems Institute (EAISI, pronounced 'easy') is the new institute of the Eindhoven University of Technology devoted to artificial intelligence. The launch of EAISI reflects the university's intention to play a role in the growing importance of AI in society, business and science and to cater to the rapidly increasing demand for education, engineers and expertise in the field of AI. TU/e has been active in the field of artificial intelligence for decades, which gives the new institute an excellent starting position to build upon.

Over the period extending to 2025, TU/e will invest €100 million in EAISI's education and research facilities, and a total of up to 150 people will be directly or indirectly involved in EAISI. This money comes primarily from the university's own resources. EAISI also intends to attract an additional €30 million a year from so-called third-tier grants (NWO, EU and other funders) and from industry directly. There are already about a hundred AI scientists working at TU/e, while the university intends to also recruit some 50 new researchers. In total, up to 150 people will be directly or indirectly involved in EAISI.

Unlike other AI institutes, EAISI will focus on the use of data and algorithms in machines, such as robots and autonomous cars, which has always been a strong point of TU/e and the Eindhoven Brainport region. The new institute will also prioritise research into AI applications for healthcare, the interaction between man and machine, and the moral and ethical aspects of AI.

The institute will focus on the following health care applications topics:

- Improved diagnostics
- Personalised and wearable healthcare
- A better understanding of personal health
- Preventive health management

TU/e has been active in the field of AI for years, with innovative research in the fields of intelligent machines, smart mobility and healthcare. The Data Science Center Eindhoven and High Tech Systems Center mean that the university also has two leading institutes that are actively involved in research into and the applications of AI.

Building on the traditionally close ties of TU/e with industry players, EAISI has partnered with a number of relevant companies and organisations at a regional, national and European level. These include:

- ASML
- Philips
- NXP
- Brainport Eindhoven
- AI NL Coalition
- 4TU.Federation
- EuroTech

TU/e
EAISI

10. SUMMARY OF BRABANT'S STRENGTHS AND OPPORTUNITIES IN LS&H

A. Summary of Brabant's strengths in LS&H

Notwithstanding the fact that there are many additional initiatives and organisations in Brabant that perform top-class work and distinguish themselves from others, the main strengths of Brabant in the world of Life Sciences & Health can be summarised as follows:

1. A complete and well-developed LS&H value chain

Every activity in the biopharmaceutical and medtech value chain can be found in Brabant. And, generally speaking, they are all receptive to partnerships and further business relationships.

See figure on page 164.

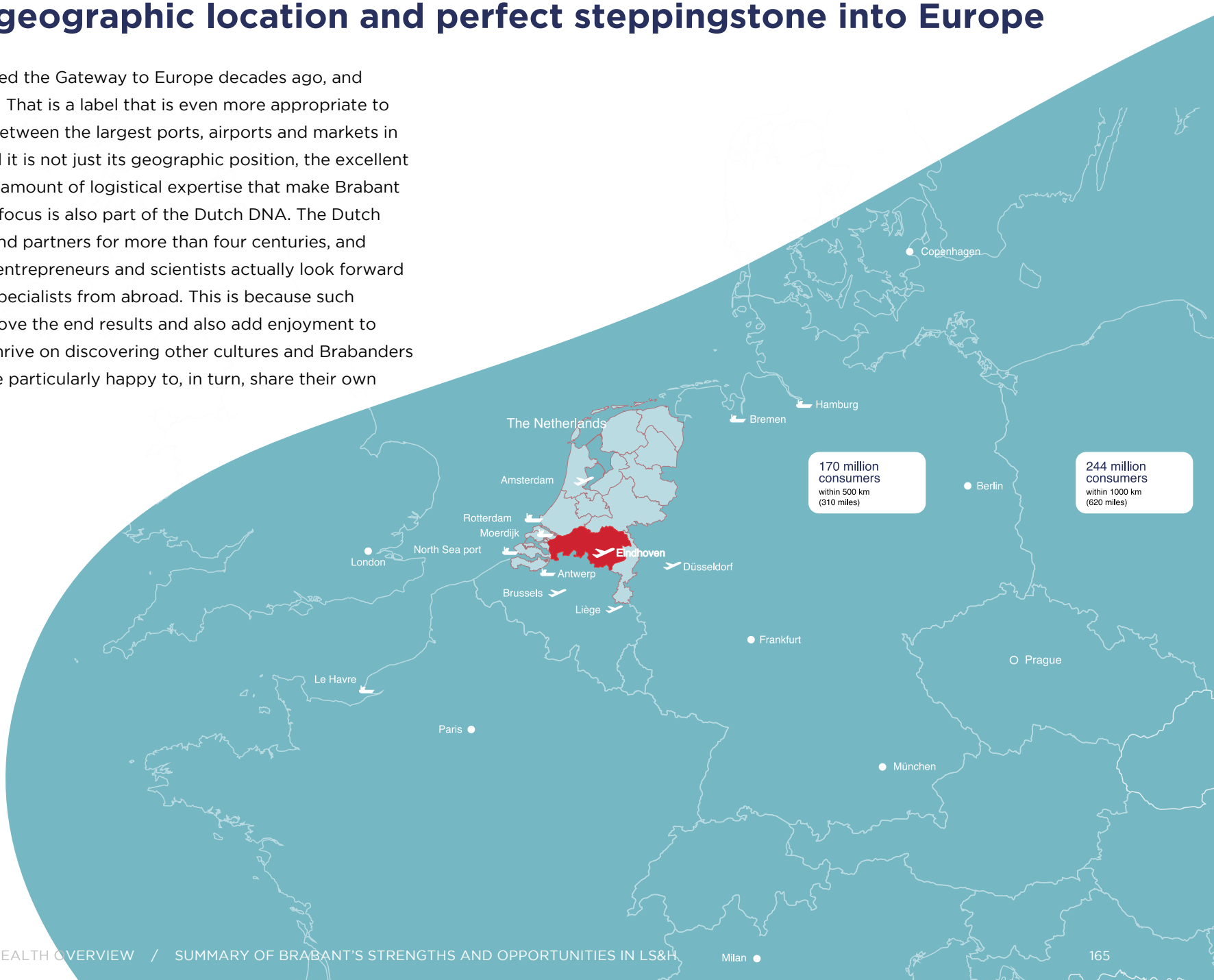
2. The distinctive and constructive Brabant cooperative model

Brabant has a distinctly strong culture, history and tradition in informal and constructive partnerships based on trust and open innovation. The advantage of this culture is that partnerships, whether informal and/or highly professional and intensive, come naturally in the region. Business, science and government thought leaders in the region publicly invite interested parties to contact them and explore mutual interests.

In short: building partnerships in the region is a quick and fluid process – and faster than anywhere else in the Netherlands. Outsiders who wish to join the club and make an actual contribution will quickly and easily reap the rewards.

3. The ideal geographic location and perfect steppingstone into Europe

The Netherlands was dubbed the Gateway to Europe decades ago, and nothing has changed since. That is a label that is even more appropriate to Brabant, located midway between the largest ports, airports and markets in north-western Europe. And it is not just its geographic position, the excellent infrastructure and the vast amount of logistical expertise that make Brabant stand out; an international focus is also part of the Dutch DNA. The Dutch have been global traders and partners for more than four centuries, and Dutch and Brabant-based entrepreneurs and scientists actually look forward to working together with specialists from abroad. This is because such partnerships can only improve the end results and also add enjoyment to (working) life. The Dutch thrive on discovering other cultures and Brabanders (the people of Brabant) are particularly happy to, in turn, share their own culture with others!



4. Unique manufacturing cluster in biopharmaceuticals and medical technology

The largest and most advanced Dutch manufacturing facilities in (bio) pharmaceuticals and medical technology are all located in Brabant. And most of the suppliers – especially for medical technology – are located there too. The largest plants for human biopharmaceuticals are to be found in Oss (MSD and Aspen), and in Boxmeer for animal vaccines (MSD). Meanwhile, Amgen also has a significant biopharmaceuticals factory in Breda. All these cities are home to many more production facilities that may be just as advanced, but they are smaller and more specialised or operating as CMOs.

The same holds when it comes to medtech production. The largest, the most advanced (big and small) and the most diverse medtech operations are located in and around Eindhoven. Philips Healthcare, VDL ETG (Enabling Technology Group), GE Healthcare Life Sciences Core Imaging and Medtronic are just a few of the dozens of companies active in this domain.

5. Highly developed biopharmaceutical and medical technology campuses with unique expertise and resources

- **Pivot Park, Oss**
- **High Tech Campus, Eindhoven**

Both these campuses are superbly equipped for cooperative ventures and joint innovation in their own specialties. Everything at Pivot Park revolves around biopharmaceutical drug discovery, development and manufacturing, while at the High Tech Campus medical technology development is one of the priority areas. And, with 60 companies and 600 dedicated specialists at Pivot Park and 200 companies and 12,000 researchers at the High Tech Campus, plenty of expertise and skilled partners and suppliers can be found nearby.

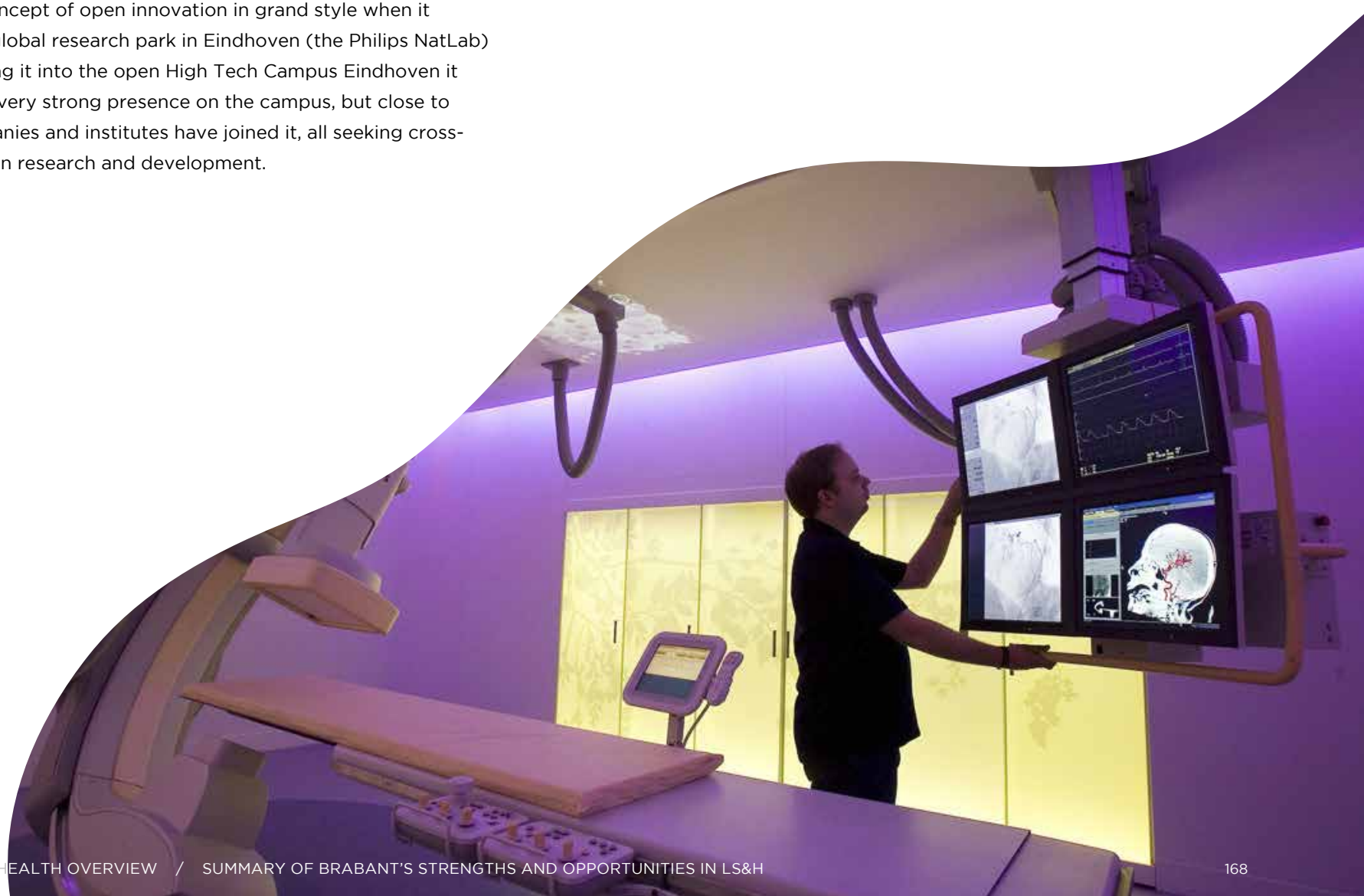
6. Top-class knowledge institutes active in LS&H

- **TU/e, Eindhoven University of Technology (Eindhoven)**
- **Radboud University Medical Center (Nijmegen)**
- **Holst Centre (Eindhoven)**
- **JADS - Jheronimus Academy of Data Science (Den Bosch, Tilburg and Eindhoven)**

Four knowledge institutions within a 50-kilometre radius, all of them receptive to joint research projects and aiming to raise healthcare to an even higher level. They are easily accessible and easy to connect with, where necessary with free support provided by regional public agencies such as BOM and Brainport Development.

7. Royal Philips medtech cluster and its full LS&H supply chain

Eindhoven is the home of Philips Healthcare and, over the space of 125 years, a perfectly woven network of knowledge institutes (TU/e, Holst Centre), suppliers and partners has evolved in the region. Every strand of medical technology and advanced healthcare expertise can be found in the region. It was Philips itself that launched the concept of open innovation in grand style when it opened up its top secret global research park in Eindhoven (the Philips NatLab) and moved towards turning it into the open High Tech Campus Eindhoven it is today. Philips still has a very strong presence on the campus, but close to 200 other research companies and institutes have joined it, all seeking cross-fertilisation opportunities in research and development.



B. Brabant's complete and fully-developed LS&H value chain

A graphic outline is the best way to illustrate why professionals in the LS&H industry should keep the region in mind and/or set up business operations in the region. Throw in the fact that there are excellent universities and highly innovative campuses in the region and nearby, and then the picture is truly a complete one.

THE INTEGRATED VALUE CHAIN LIFE SCIENCES & HEALTH BRABANT – A SELECTION OF COMPANIES

INBOUND LOGISTICS

- AMGEN
- Abbot Logistics
- Thermo Fisher Scientific
- Medtronic
- Zimmer Biomet Global SSC
- Hollister

FUNDAMENTAL RESEARCH

- Cytura Therpeutics
- ImmunoPrecise
- Citryll
- Certara
- Acerta Pharma (AstraZeneca)
- Philips Healthcare
- Thermo Fisher Scientific Electron Microscopy Solutions
- DEMCON
- GE Healthcare Life Sciences Core Imaging
- VanBerlo Agency
- Hendrix Genetics
- MicroSure
- Preceyes

PRODUCT DEVELOPMENT

- Glycostem
- Lead Pharma
- Synnafix
- NTRC
- Acerta Pharma (AstraZeneca)
- Philips Healthcare
- VDL ETG, Enabling Technologies Group
- Thermo Fisher Scientific Electron Microscopy Solutions
- DEMCON
- GE Healthcare Life Sciences Core Imaging
- Össur
- MicroSure
- Preceyes

HEALTH, SAFETY & EFFICACY RESEARCH

- Charles Rivers Laboratories
- BioFacilities, Landerd Campus
- Janssen-Cilag
- Venn Life Sciences
- Edwards Life Sciences
- Ardena
- Philips Healthcare
- GE Healthcare Life Sciences Core Imaging
- Bambi Medical

PRODUCT APPROVAL

- InnSense
- Janssen-Cilag
- Zwiers Regulatory Consultancy
- MSD (Merck) Biologicals & Pharmaceutical Operations
- MSD (Merck) Animal Health
- Philips Healthcare
- Thermo Fisher Scientific Electron Microscopy Solutions
- GE Healthcare Life Sciences Core Imaging

MANUFACTURING

- Aspen
- MSD (Merck) Biologicals & Pharmaceutical Operations
- MSD (Merck) Animal Health
- AMGEN
- Agglomix
- Dechra Pharmaceuticals
- Philips Healthcare
- Thermo Fisher Scientific Electron Microscopy Solutions
- GE Healthcare Life Sciences Core Imaging
- Össur
- DEMCON

MARKETING & SALES

- AMGEN
- Janssen-Cilag
- Covetrus Animal Health
- MSD (Merck) Animal Health
- Brocacef
- Centrafarm/STADA
- Philips Healthcare
- Medtronic
- Össur
- Illumina
- Adimec
- Ventinova Medical
- Blue Medical Devices/ Wellinq
- MedEye

OUTBOUND LOGISTICS

- AMGEN
- Abbot Logistics
- Thermo Fisher Scientific / Pantheon Softgels
- Alliance Healthcare
- Brocacef
- Zimmer Biomet Global SSC
- Hollister
- B. Braun Medical
- Boeren Medical
- Illumina
- Malvern Panalytical
- GCX Corporation

SUPPORT INDUSTRY & SERVICES: HR, FINANCE, IP, IT, CERTIFICATION, PACKAGING, INFRASTRUCTURE ETC.

Systemair – Tjaopack – Sioux Embedded Systems – Omron – Neways Technology – Thales Cryogenics – IT&Care – STERIS / Synergy – Arnold & Siedsma – PerkinElmer / One Source

OUTSOURCED SERVICES: LOGISTICS (3PL, 4PL); RESEARCH (CRO); MANUFACTURING (CMO); SALES (AGENTS & DISTRIBUTORS)

BioConnection – Rhenus – Ardena – O&M Movianto – Pivot Park Screening Centre – DB Schenker Healthcare Hub – ImmunoPrecise – HealthLink – Eurofins / Spinnovation Analytical

UNIVERSITIES & KNOWLEDGE INSTITUTES

Radboud University Medical Center (Nijmegen) – TU/e. Eindhoven University of Technology – JADS, Jheronimus Academy of Data Science (a.o. Den Bosch)
Avans University of Applied Sciences (a.o. Breda) – Fontys University of Applied Sciences (a.o. Eindhoven, Den Bosch) – Holst Centre (Eindhoven)

Source: Engel – Een Heldere Blik helder@benengel.nl – +31 (0)652612671

■ (Bio)Pharma
■ MedTech or MedTech and (Bio)Pharma

C. Opportunities in LS&H – Brabant's leading niches

On the occasion of this in-depth review of Brabant's Life Science's & Health industry, the authors have performed a SWOT analysis of the industry. The interviews with the many operational and academic representatives of the industry were of invaluable help in this work.

This analysis has led to the conclusion that the following eight therapy and technology areas distinguish themselves as fields where Brabant companies and institutes, both large and small, increasingly play a leading role. These fields can be regarded as Brabant's priority niches in Life Sciences & Health:

1. **Immunology**
2. **Drug Discovery and Development**
3. **Regenerative Medicine/Regenerative Engineering and Biomaterials**
4. **Animal Health**
5. **Imaging, Diagnostics and Monitoring**
6. **Robotics in Healthcare**
7. **Highly Complex Machines**
8. **Data Science and Big Data in Healthcare**

1. Immunology

Area of application/Therapeutic Area	a.o. Oncology
(University) Hospitals/Universities/Research institutes involved	Radboud UMC; Utrecht UMC; Maastricht UMC; et al.
Leading companies/disruptors/best practices	MSD (Keytruda); Glycostem; ImmunoPrecise Antibodies Europe; Acerta Pharma; Citryll; Lead Pharma; NTRC; Enpicom
Leading cooperative programme	European Lead Factory (Pivot Park Screening Center)
Industry/Academic Leaders	Charlotte Kluit (Director of Oncology, Netherlands MSD); Hans van Eenennaam (EVP Antibody Research Aduro Biotech); Andrea van Elsas (CSO Aduro Biotech); Troels Jordansen (CEO Glycostem); Allard Kaptein and Tjeerd Barf (founders of Acerta Pharma); Helmuth van Es (CEO Citryll)
Facilities/Locations/Campuses	Pivot Park Oss

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF IMMUNOLOGY (A.O. ONCOLOGY)?

The city of Oss in Brabant used to be home to the pharmaceutical company Organon (founded in 1923), which became a part of the chemicals company AkzoNobel. Having been the target of an acquisition twice in a very short period (Schering Plough in 2007 and Merck & Co/MSD in 2009), things looked bleak when Merck decided to transfer all R&D activities out of Oss to the United States. The extensive site in Oss was set to remain a large-scale MSD manufacturing operation, both for pharmaceuticals and biopharmaceuticals.

The state-of-the-art research facilities and equipment were sold to a government-led consortium at a good price, and national, regional and local authorities proceeded to create Pivot Park in 2012 with the objective of transforming it into a high-quality ecosystem of companies and knowledge institutes focused on innovation in life sciences in general and drug development in particular. Pivot Park is located right next to the MSD and Aspen manufacturing plants.

Pivot Park helps innovative entrepreneurs to accelerate and innovate in the field of drug development and diagnostics. The campus can be considered an incubator that connects the knowledge and experience available within the community to the university and company startups and spinouts that are based on campus. Many of the R&D specialists (often long-term Organon researchers) that were laid off by MSD started their own spinoffs and startups at Pivot Park.

Since 2012, there have been many very positive developments onsite, with two cases providing what may be the best examples of how much biopharmaceutical expertise, talent, creativity and entrepreneurship is available in Oss and in Pivot Park.

CASE 1: KEYTRUDA (PEMBROLIZUMAB) – HOW A DUTCH CANCER DRUG CONQUERED THE WORLD

Extract from an article in published in the FD newspaper, the Netherlands, 15 November 2018, author: Thieu Vaessen

Organon researchers in Oss have discovered an antibody that is now making waves as an immunotherapy against an increasing number of types of cancer.

Ms Patricia Dobbe was in a dire situation in 2015. Tumours had been found in the abdomen of the 55-year-old from The Hague, metastases from a melanoma that had been removed much earlier. And although it was commonly held that no further treatments would help, Dobbe got lucky. At the time when the metastases were discovered, pembrolizumab had re-entered the Dutch market. The new medicine was immediately administered to Dobbe in the form of 12 doses using an IV. And after two or three months, almost all the tumours were gone. 'That was incredible.' Much earlier than expected, in September 2016, the doctor stopped administering pembrolizumab. 'It was no longer necessary. I was clean,' says Dobbe.

Thousands of other men and women receive similar diagnoses: patients with metastatic cancer who can no longer benefit from surgery, radiation or chemotherapy. Some of these patients appear to respond very well to immunotherapies, a new class of medicines that enable the human immune system to detect and destroy cancer cells.

The most successful new agent, at least commercially, is pembrolizumab, an antibody often referred to by its brand name Keytruda in international publications. It has quickly become one of the best-selling medicines in the world [Keytruda had a turnover in 2019 of €10.1 billion]. The large American pharmaceutical group Merck & Co – known in Europe as MSD – has experienced a dramatic resurgence thanks to Keytruda.

What is less well-known is that Keytruda was invented in the Netherlands at Organon in Oss. Two of the Keytruda research pioneers at Organon (now Merck/MSD) were Hans van Eenennaam and Andrea van Elsas, both of whom still work in Oss. Pembrolizumab was developed in an attempt to slow down the human immune system in order to help battle autoimmune diseases such as rheumatism. To their surprise, the MSD researchers noticed that the substances did not slow down the immune system but instead actually boosted it. In retrospect, that was the key to their success. 'We could also have said: let's start over,' Van Eenennaam recounts. 'But we saw that the surprising results offered an opportunity in a completely different field: oncology.' The idea was that an enhanced immune system might be able to eliminate the smart cancer cells.

Merck realised that the group had a potential blockbuster drug in pembrolizumab, and the Americans did everything possible to demonstrate that remarkable results could also be achieved through 'Dutch' immunotherapy for various forms of cancer and at various stages of treatment. And they succeeded wonderfully. 'It really was a daring feat,' says Van Elsas.

The MSD branch in Oss played an important role in the process, and the factory began to produce the new drug in large quantities in order to deal with as many patient studies as possible. 'Our former colleagues really worked 24/7 there,' says Van Eenennaam. Merck installed a 27,000 litre bioreactor vessel, an exceptionally large size. The underlying motive was that initially Merck was well behind its rival BMS, which had introduced a second immunotherapy called Opdivo, or nivolumab. But Merck played catch-up and quickly gathered more evidence on the effectivity of Keytruda in fighting various tumours at different stages of development.

Keytruda now outsells Opdivo, mainly as a result of the different research strategy employed, targeting various patient subgroups and achieving better results. One of the outcomes is that Keytruda, in combination with chemotherapy, is now the standard treatment for many forms of lung cancer.

KEYTRUDA EXPECTED TO BE TOP DRUG IN ANNUAL REVENUES BY 2023

02 October 2019, GlobalData Healthcare

Merck & Co (Kenilworth, NJ, US) and Otsuka Holdings' (Chiyoda, Japan) Keytruda (pembrolizumab) is projected to top the list of top drugs in annual revenue terms in 2023, according to a consensus of financial analyst sales forecasts from GlobalData. The monoclonal antibody is forecast to bring annual revenue of $22.2 bn by 2025, figures from the GlobalData Pharma Intelligence Center Drug Sales and Consensus Forecast database show.

CASE 2: ACERTA PHARMA, ASTRAZENECA AND ACALABRUTINIB

Acerta Pharma was founded in 2012 by Allard Kaptein and Tjeerd Barf, two senior researchers previously associated with Organon. They started their own company after Merck decided to withdraw all its R&D activities from Oss, and they saw this as the opportunity to achieve their dream of creating a ground-breaking new medicine in hematology/oncology. In 2015, the company acquired licenses for a 'covalent bonding technology' developed at Organon and now owned by the US company Merck and its Dutch subsidiary MSD. The new technology formed the basis for the medicines that Acerta Pharma is developing to treat lymphocytic leukaemia and lymph node cancer.

In 2015 the company reported successful tests on leukaemia patients using the principal drug it was developing, acalabrutinib. It may also be suitable for combating other cancers and for treating autoimmune diseases.

In February 2016, AstraZeneca acquired a 55% majority share of Acerta Pharma via a USD $4 billion investment, motivated by the lead investigational Bruton tyrosine kinase (BTK) inhibitor, acalabrutinib and the opportunity to expand its hematology/oncology pipeline. AstraZeneca is a committed partner to the development of these innovative drug candidates.

CALQUENCE'S MARKET POTENTIAL

Fierce Pharma, 17 June 2019, Kyle Blankenship

When AstraZeneca ended a late-stage trial for Calquence early after seeing promising results, the news boded well for the drug's chances for previously treated chronic lymphocytic leukaemia (CLL). Now, the drug maker has unveiled the detailed data it plans to take before regulators later this year. [...]. ***The raft of positive results could help the drug make a run at Johnson & Johnson and AbbVie's oncology blockbuster Imbruvica.*** But Calquence's nemesis has a major head start, thanks to three separate indications in CLL. [...] In the first quarter, Calquence cleared just $29 million in global sales after a full year on the market, a pittance compared with Imbruvica's $784 million in the same time span. [...]

DUTCH CANCER DRUG TESTED AS A CORONA PILL

FD, 15 April 2020, Maarten van Dun, Thieu Vaessen

[...] A cancer drug developed in the Netherlands may play a role in combating the coronavirus pandemic. There is initial evidence that the drug called Calquence is also effective against Covid-19. The pharmacy group AstraZeneca will now test the drug on 400 patients in a study that has been rapidly set up. The Tuesday morning announcement is one of the most surprising developments to date in the global search for a drug that could stop the pandemic. [...]

AstraZeneca's cancer medicine Calquence was originally developed by the Dutch Oss-based biotech company Acerta. The British-Swedish pharmaceutical group bought a majority stake in Acerta for $4 billion in 2015, thereby acquiring the rights to Calquence. Depending on the success of the drug, that amount can add up to $7 billion. [...]. Calquence (substance name: acalabrutinib) is a so-called BTK inhibitor that has been developed for the fight against blood cancers. The agent acts on the immune system. It may dampen an excessive immune response – the so-called cytokine storm – that many patients with severe Covid-19 experience. [...]

Acalabrutinib is Acerta Pharma's lead asset and is being studied in over 20 clinical trials for both monotherapy and in combination with other targeted molecules and is under investigation in multiple phase 3 clinical trials. Acalabrutinib (brand name Calquence) received accelerated approval by the FDA for previously treated mantle cell lymphoma patients.

Today, Acerta Pharma serves as AstraZeneca's Hematologic Oncology Center of Excellence. As such, it has the responsibility of developing both internally discovered compounds as well as AstraZeneca-sourced compounds for hematological malignancies. Over 200 employees are engaged in the development of acalabrutinib and other pipeline compounds for hematologic malignancies.

2. Drug Discovery and Development

Area of application/Therapeutic Area	(Bio)Pharmaceuticals
(University) Hospitals/Universities/Research institutes involved	Pivot Park Screening Center; Radboud UMC; Utrecht UMC; Erasmus UMC; Amsterdam UMC; Centre for Drug Design and Discovery (CD3) of the KU Leuven; et al.
Leading companies/disruptors/best practices	MSD (Merck & Co.); Aspen; Acerta Pharma (AstraZeneca); Glycostem; Citryll, Lead Pharma; BioConnection; Synaffix; Ardena; ADC Therapeutics; Cytura Therapeutics; ImmunoPrecise Antibodies – Europe; NTRC;
Leading cooperative projects/programs	European Lead Factory (ELF)
Industry/Academic Leaders	Charlotte Kluit (Director of Oncology, Netherlands MSD); Troels Jordansen (CEO Glycostem); Allard Kaptein and Tjeerd Barf (founders of Acerta Pharma); Helmuth van Es (CEO Citryll)
Facilities/Locations/Campuses	Pivot Park, Oss; High Tech Campus Eindhoven; NovioTech Campus, Nijmegen

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF DRUG DISCOVERY AND DEVELOPMENT?

The pharmaceutical company Organon was founded in Oss in 1923 and has had a very strong presence in the region ever since. The company was active in all pharmaceutical fields, from fundamental R&D all the way through to manufacturing, distribution and marketing and sales. The company saw significant growth over its history but also underwent restructurings as a result of takeovers by Schering-Plough and Merck & Co (MSD in the Netherlands). These have left their mark on the city's biopharmaceutical community, but the industry remains strong and very much alive with – depending on the definition used – between 3,000 and 5,000 people directly employed by (bio) pharmaceutical companies.

MSD and Aspen, for instance, still have multiple major manufacturing operations in place and MSD's most important blockbuster drug (pembrolizumab or Keytruda) was discovered in Oss and is also manufactured there. Additional investments worth tens of millions of euros in manufacturing have been announced and hundreds of new jobs are expected to be created. In addition, there is the biopharmaceutical campus Pivot Park, which was spun out of Organon/MSD in 2012 as a home for innovative biopharmaceutical startups, scaleups and experimental manufacturers. Pivot Park alone is home to 60 companies and institutes, employing close to 600 highly educated pharmacologists and microbiologists.

As a result, the city of Oss, with Pivot Park at its heart, has built up a strong network of biopharmaceutical companies (both large and small), CROs, CMOs and service providers, an ultra-high-throughput screening centre, research institutes and partnerships with university medical centres dedicated to drug discovery and development.

KEY EXAMPLES OF CROS, CMOS AND SERVICE PROVIDERS AT PIVOT PARK

- **BioConnection** is one of the first European CMOs to provide sterile production facilities as well as expertise for small/medium sized (bio)pharmaceutical companies. Services include the aseptic production of small-scale clinical batches, filling and freeze-drying as well as 250 L scaled production of commercial batches. All processes are EMA and FDA certified. As such, BioConnection helps startups, scaleups or larger experimental companies with development and manufacturing capabilities to bring products from the concept-phase to the clinics and the market.

- **Ardena Oss** supports pharmaceutical companies through the development of active pharmaceutical ingredients and nanomedicines. Ardena Oss develops and validates the manufacturing process and the analytical methods, and also performs the cGMP manufacture, quality control and stability studies.

- **Certara (Quantitative Solutions)** provides pharmacometric services in support of drug discovery and development – developing mathematical-statistical models that enable the analysis and interpretation of data from (pre-)clinical studies.

- **Eurofins Spinnovation Analytical** is a CRO specialised in delivering high-end analytical services in process and drug development, product characterisation, manufacturing process optimisation and troubleshooting, QC/QA Testing and batch release of APIs and biologics.

- **Zwiers Regulatory Consultancy** provides full regulatory and pharmacovigilance support for medicinal products and medical devices, throughout the entire drug/product lifecycle.

- **The Pivot Park Screening Centre** is equipped with advanced robotic systems and offers ultra-high-throughput screening (uHTS) and lab automation services to accelerate drug discovery programmes. The uHTS lab hosts a state-of-the-art, fully automated robotic system in an industrial set-up that can efficiently run the major HTS assay technologies (absorbance, luminescence, fluorescence-based) in 384- or 1536-well formats and can produce over 300,000 data points per day.

TYPICAL EXAMPLES OF HIGHLY INNOVATIVE (BIO)PHARMACEUTICAL COMPANIES AT PIVOT PARK

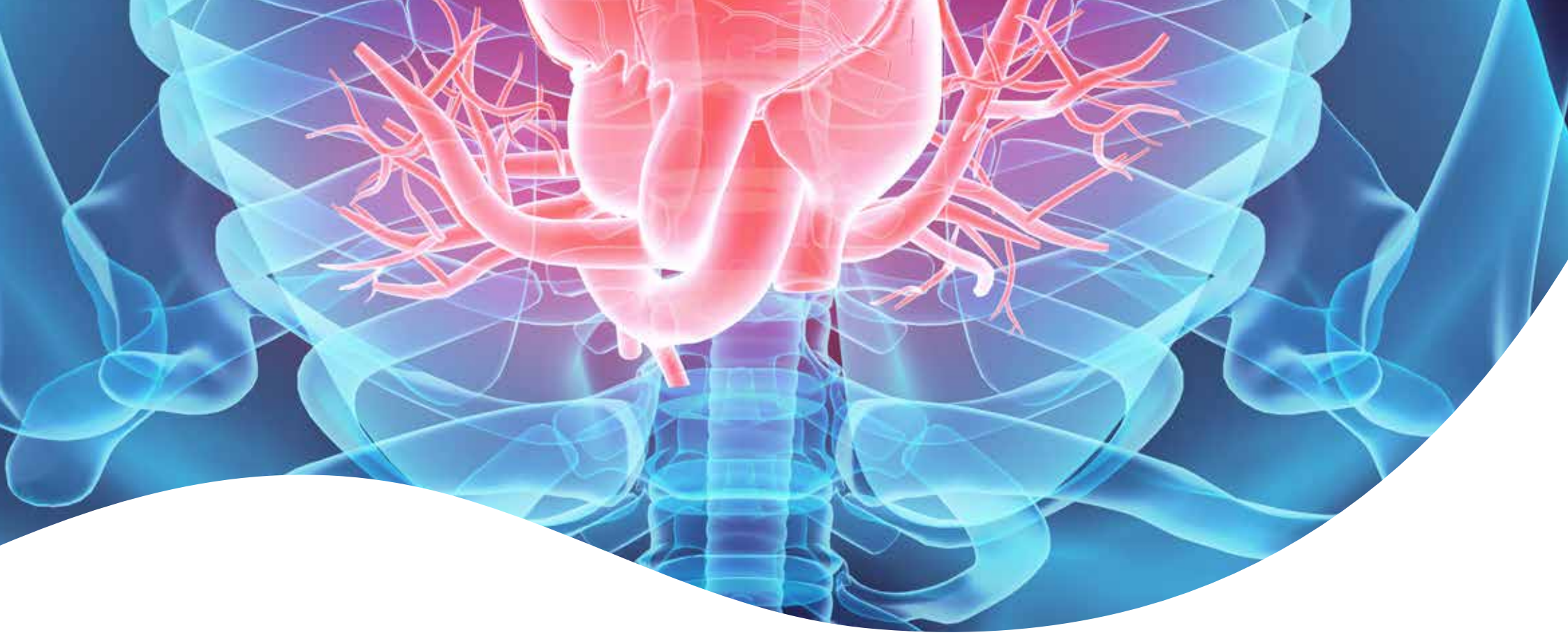
- **Citryll** (therapeutics targeting the autoimmune disease, lupus)
- **Acerta Pharma (AstraZeneca Group)** (therapeutics targeting hematological cancers, including the successful leukaemia drug Acalabrutinib)
- **Glycostem** (allogeneic cellular immunotherapy using natural killer (NK) cells for treating leukaemia, lymphoma and solid tumours)
- **Synaffix** (antibody-drug conjugate (ADC) technologies)
- **ImmunoPrecise Antibodies** (therapeutic antibody discovery services)
- **Cytura Therapeutics** (therapies targeting genomic instability in cancer)

CITRYLL

Citryll is a private pharmaceutical company that is dedicated to the development and commercialisation of therapeutics that target NETosis and NETs. Citryll was founded by ModiQuest, originator of the tACPA patents, Helmuth van Es, CEO of Citryll (co-founder of Audion Therapeutics, Galapagos, Antabio and Effecta Pharma) and Renato Chirivi, CSO of Citryll and co-inventor of tACPA antibodies.

The company was founded in 2015 and is developing a medicine with a new working mechanism, as director Helmuth van Es describes it. ‘The drug was first developed for the autoimmune disease lupus, and clinical research begins in just under two years. Later the drug may be investigated for lung fibrosis, organ damage due to sepsis and wound healing in diabetes. It is really very innovative.’

Citryll is attracting international interest and recently acquired a large Chinese biotech company as an investor. Yet Van Es refuses to consider moving operations abroad. ‘Oss is not the most obvious place to establish your business, but it is very practical. You have an entire ecosystem of companies here, and Pivot Park has a strong name and reputation: that makes it easier to hire new people. By the way, we still have an opening.’



3. Regenerative Medicine/Regenerative Engineering and Biomaterials

Area of application/Therapeutic Area	Orthopedic; cardiovascular
(University) Hospitals/Universities/Research institutes involved	TU/e Eindhoven; Radboud UMC and other UMCs in the Netherlands and Belgium
Leading companies/disruptors/best practices	Xeltis; LifeTec Group; Osteo-Pharma; Fujifilm; SupraPolix, IME Medical Electrospinning; SyMOChem
Leading cooperative projects/programs	RegMed XB; ICMS
Industry/Academic Leaders	Bert Meijer (Distinguished Professor of Molecular Sciences, TU/e); Carlijn Bouten (Professor of Cell-Matrix Interactions in Cardiovascular Regeneration, dept. of Biomedical Engineering, TU/e)
Facilities/Locations/Campuses	High Tech Campus Eindhoven; TU/e Campus

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF REGENERATIVE MEDICINE AND REGENERATIVE ENGINEERING?

REGENERATIVE MEDICINE – INTRODUCTION AND EDUCATION

Regenerative medicine is an area where biomedical research, technology development and tissue culturing join forces. It aims to develop novel therapies to help human bodies restore or regenerate organs and tissues that have been damaged by injury, ageing, cancer and disease. This rapidly-growing multidisciplinary field has had a significant impact on current and future healthcare. It combines the expertise of researchers in healthcare, new materials, pharmacy, medical technology and many other fields.

That is why the Eindhoven University of Technology (TU/e) and the Faculty of Medicine at Utrecht University have developed a special master's programme called Regenerative Medicine and Technology. This specialist course, which first saw the light of day in September 2012, aims at training a new generation of scientists and engineers in regenerative medicine and technology. TU/e offers the courses on molecular cell biology, biomaterials, image processing techniques, computer models, bioreactor technology and translational research.

RESEARCH IN REGENERATIVE MEDICINE

TU/e Eindhoven, its research institute ICMS and a number of spinoff companies are leading the way in the development and application of biomaterials in tissue and organ regeneration. Professors Bert Meijer and Carlijn Bouten play a pivotal role in this field of research, heading and directing several national and international research institutes and cooperative consortiums, such as ImaValve (Intelligent materials for in-situ heart valve tissue engineering) and ICMS (Institute for Complex Molecular Systems).

Both also play strategic roles in the European RegMed XB project, Meijer as a member of the Scientific Board and Bouten as a member of the Strategic Advisory Board.

RegMed XB stands for Regenerative Medicine Crossing Borders. It is a virtual institute comprising Dutch and Belgian public (universities and governments) and private (health foundations and companies) partners that are working together to develop regenerative medicine solutions for health challenges. A more detailed profile of the RegMed XB initiative can be found in Chapter 7. Partnerships and Networks in Brabant.

ICMS is the TU/e's Institute for Complex Molecular Systems. TU/e research in this domain is dedicated to a fundamental understanding of complexity in molecular systems by unifying basic principles of chemistry, biomedical sciences, engineering, physics and mathematics. The knowledge obtained provides the basis for the development of future technologies in materials science, health, energy and mobility.

PRINCIPAL OBJECTIVES

1. The design and synthesis of smart materials for the creation of molecular devices
2. Unravelling the molecular complexity of living systems and transforming biology into an engineering science

THE RESEARCH ON COMPLEX MOLECULAR SYSTEMS HIGHLIGHTS THE RESEARCH OF TU/E SCIENTISTS IN SEVEN FOCUS AREAS

1. Polymer Science and Technology
2. Chemical Biology
3. A grip on Complexity
4. Advanced Analysis of Complex Molecular Systems
5. Molecular Devices
6. Materials for Regenerative Medicine
7. Functional Supramolecular Systems

A more detailed profile of the ICMS institute can be found in Chapter 7. Partnerships and Networks in Brabant.

HEART VALVE REGENERATION

One of the research groups at TU/e led by Professor Bouten focuses on cell-matrix interactions in cardiovascular regeneration in the Department of Biomedical Engineering (Soft Tissue Engineering & Mechanobiology research group). The group investigates the interplay between living cells and the mechanobiological cues originating from the extracellular matrix under conditions of tissue growth, adaptation, and regeneration and degeneration.

The group uses 'living' model systems at different scales of length (cell, cell-matrix, engineered tissue, native tissue) to quantify these aspects, preferably in real-time. This knowledge is applied using engineering approaches to regenerate living tissues, in particular for the human heart. The most prominent success story is that the group has succeeded in developing a synthetic, biodegradable heart valve prosthesis that helps the human body to regenerate a new living heart valve at the site of implantation.

SUCCESS BREEDS SUCCESS

As a result of the excellent results that were being achieved in developing biomaterials for new heart valves, in 2017 the Dutch government decided to invest €18.8 million in R&D for new biomaterials. In the future, these materials could be used by the body itself in the event of heart failure, kidney failure and worn out intervertebral discs to heal. The research is being conducted by a multi-disciplinary cluster of scientists from the universities of Eindhoven, Utrecht and Maastricht, led by TU/e Professor Carlijn Bouten. Professor Bouten is one of the academic leaders in the successful development of endogenous new heart valves with the aid of biodegradable biomaterials.

The follow-up ten-year research project is based on the same principle of the cell and tissue regeneration and repair process, but this time focused on healing (other) human organs. The three universities together added €6 million to the overall €25 million research budget. The added funding has significantly accelerated the research process, thanks to the expanded laboratories and increased interest of researchers and students.

THE DISTINGUISHING CHARACTERISTIC IN THIS PROGRAM REMAINS THE COOPERATION BETWEEN ENGINEERS, BIOLOGISTS AND MEDICAL SPECIALISTS. "THIS CROSS-POLLINATION IS UNIQUE", SAYS BOUTEN.

'DUTCH RESEARCH IN THIS AREA HAS TAKEN THE LEAD GLOBALLY AND WE MUST MAINTAIN THAT POSITION.'

ACADEMIC AND INDUSTRY PARTNERSHIPS IN RESEARCH AND DEVELOPMENT

Research and industry are cooperating intensively in the area of regenerative medicine and regenerative engineering. This is highly evident in a partnership such as the ICMS Industrial Consortium, comprising the companies DSM, Fujifilm, SupraPolix, Clariant, SyMOChem, Zhejiang Tianhe Resin and Stahl.

It is exemplified maybe even more by the birth and growth of a number of ground-breaking spinoffs and scaleups in the past decade, including Xeltis, Osteo-Pharma, SupraPolix, IME Medical Electrospinning and SyMOChem

TU/E SPINOFF'S IN REGENERATIVE MEDICINE/REGENERATIVE ENGINEERING

- **Xeltis** developed a synthetic supramolecular, biodegradable heart valve implant that 'coaxes' the body to create a new living heart valve at the site of the implantation by recruiting cells from its environment. Clinical trials started in 2016. The company was founded in 2006 as a spinoff from the University of Zurich and in 2012, QTIS/e, a TU/e spinoff, merged with Xeltis and both companies continued under that name. It has a workforce of 50, five based in its Zurich headquarters and the remainder on the TU/e campus. R&D is performed in Eindhoven.
- **IME Medical Electrospinning** produces the medical sponges that are used to make Xeltis' heart valves. The plastic material used for these sponges was developed at TU/e, and IME is itself a child of the university too. IME supplies machines to Xeltis and dozens of other laboratories and medical companies around the world.
- **Osteo-Pharma** focuses on developing local treatments to improve the healing of bone fracture and defects. Its proprietary OsteoActivator platform is used to develop biodegradable membranes, microspheres and coatings for implants with the sustained release of small molecule drugs that enhance bone formation while simultaneously inhibiting bone resorption. A number of the company's projects are currently in late stage preclinical development and it anticipates launching its first human clinical trials in the course of 2020. The company is based at Pivot Park in Oss.

EINDHOVEN-BASED XELTIS HEALS EIGHTEEN HEART PATIENTS WITH A SOLUBLE HEART VALVE

Source: 12 March 2020, Eindhovens Dagblad by Harrie Verrijt (extract)

EINDHOVEN - What could possibly be better than curing sick children? Thanks to its regenerative heart valve, Xeltis in Eindhoven has already given 18 children a new lease on life.

[...] It is a solution that appeared impossible, but it is possible now thanks to an invention that was born in Eindhoven. Martijn Cox obtained his doctorate in 2007 for work on a body-soluble synthetic material that he co-developed for this specific purpose at the Eindhoven University of Technology (TU/e). At a later stage he established the company QTIS/e, which merged with Xeltis and now creates these bio-synthetic heart valves.

70 million euros already invested in the company

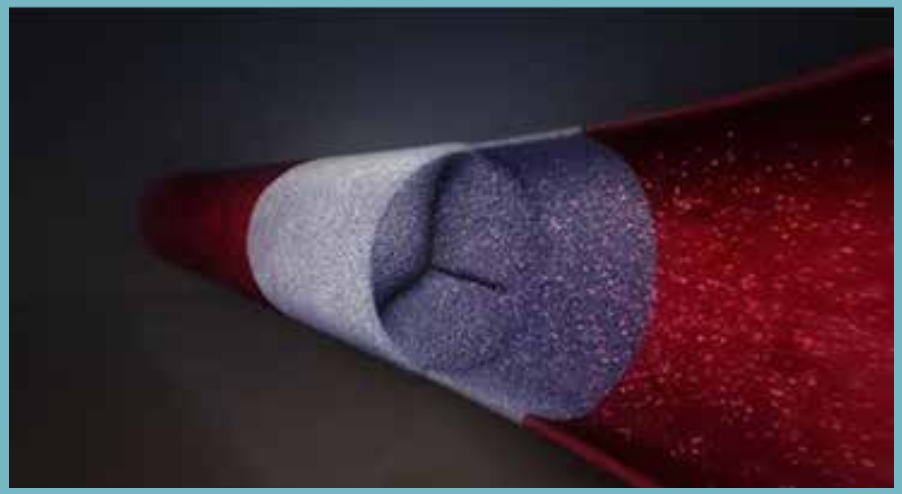
Now that these heart valves are functioning properly in 18 children, the thirty or so staff members of Xeltis in the Catalyst building on TU/e grounds are in a celebratory mood. 'In the past ten years, about 70 million euros has been invested in our company,' says General Manager Eliane Schutte. 'The fact that these children can now lead a normal life thanks to our heart valve is a wonderful outcome. After 2023, tens of thousands will follow suit after approval is received in Europe and America.' [...]

SMALL FACTORY OF HEART VALVES

The Xeltis laboratory is a small factory for heart valves. Using an electrospinning process, a perfect thread is spun at a voltage of 1,000 volts from the synthetic material developed at TU/e. That very thin thread is then wound in a zigzag pattern on a bobbin in the exact shape of the required heart valve. Under the microscope it looks like spaghetti, with the open space between the wires making up 60 percent of the device. Once in the body, this porous material absorbs blood and the patient's own body tissue grows between the threads. The plastic slowly dissolves and, during that time, the patient has grown his or her own heart valve which develops at a matching pace as the child grows to adulthood.

It almost seems like a miracle and Schutte wants this miracle to be made available to the tens of thousands of children who are born every year with faulty heart valves. 'We are starting a new clinical study with 50 patients in Europe and the US – the next step is receiving approval from the authorities.'

In addition, Schutte also sees opportunities for other products. She brandishes a flexible tube made of the same material. 'A bypass, an operation for heart patients that is done a million times a year, usually still involves a vein being removed from the leg. With this tube there is no longer a need to remove that vein, and the solution is also more durable.'



An artist's impression of the plastic heart valve developed in the Xeltis laboratory.

FUTURE GROWTH

[...] At the end of this year, Xeltis will again turn to its backers for an additional financing round of 12 million euros. The funds will be used to develop the process and gear the company towards the production and sale of the heart valve from 2023 onwards. At that point in time, required investments will spike at an even higher level than before, Schutte expects. 'We cannot rule out joining a large pharmaceutical company. The advantage of this is that we can use existing sales channels. But if no attractive propositions arrive, we must scale up ourselves. That could then possibly be financed with an IPO.'

THE NANO-SPAGHETTI CAN ALSO BE USED FOR OTHER ORGANS

Magnification of the spaghetti-like material

The medical sponges used to make the Xeltis heart valves are wholly an Eindhoven product and can also be used for many other purposes. The plastic was developed at TU/e and the manufacturing company, IME Medical Electrospinning in Waalre, also originated from the university. IME supplies machines to Xeltis as well as to dozens of other laboratories and medical companies around the world.

IME machines produce a wire that is a factor of 5 to 500 times thinner than a human hair and that is used to make the "nano-spaghetti". It is a porous material in which blood circulates and in which new body cells feel so at home that they multiply into new human tissue. It is the body's own tissue, so rejection does not occur.

According to experts, the material can replace tissue in many places in the body. In addition to the heart, it can also be used in the eyes, skin, veins, windpipe and oesophagus. For some tissues, the plastic can dissolve completely in the blood after a period of time, while in others a degree of support is required.

4. Animal Health

Technical niche	Healthcare & Nutrition for animals
Area of application/Therapeutic Area	Healthcare and nutraceuticals for animals, both companion and farm animals
(University) Hospitals/Universities/Research institutes involved	Utrecht University Hospital and University; Wageningen University & Research; Eindhoven University of Technology
Leading companies/disruptors/best practices (selection)	MSD (Merck) Animal Health; Hendrix Genetics; Nutreco; Marel Poultry; Covetrus; Dechra Veterinary products; Dopharma; Floris Pharma; Perstorp; Produlab Pharma; Charles River Laboratories; Royal Canin (MARS); MS Schippers; AgriFirm; Nijsen/Granico (Limburg)
Leading cooperative projects/programs	IMAGEN (An**IMA**l **G**roup **SEN**sor)
Industry/Academic Leaders	Leo den Hartog (Professor at Wageningen University (WUR), Director R&D and Quality Affairs Nutreco); Johan van Arendonk (Chief Innovation and Technology Officer Hendrix Genetics); Luc Grisez (MSD Animal Health, Global Director R&D Aquatic Animal Health and R&D Operations Boxmeer); Ruud Segers (MSD Animal Health, Head of Global R&D Swine Biologicals); Roger Claessens (Managing Director (EVP) Marel Poultry)
Facilities/Locations/Campuses	Boxmeer Health Campus

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF ANIMAL HEALTH?

Three remarkable individuals laid the foundations for this extraordinary animal health cluster in Brabant a hundred years ago:

- Mr Wim Hendrix, who started selling chickens in Boxmeer in 1916;
- Mr Saal van Zwanenberg, who founded a slaughterhouse for export in 1887 in Oss;
- Mr Frederik Philips, who built a modest light bulb factory in 1891 in Eindhoven.

Their small businesses flourished, grew, diversified and developed into hugely successful corporations with many well-known subsidiaries and spinoff companies, such as:

- Hendrix Genetics, MSD (Merck & Co.) Animal Health, Nutreco and Marel Poultry
- Chefaro and Organon (AkzoNobel), today part of MSD (Merck & Co.), focusing on human health – developer of Keytruda, one of most successful recent cancer drugs on the planet
- Royal Philips in Eindhoven, a global 18 billion euro-company with 74,000 employees that also gave birth to other icons, such as ASML, FEI Company, Thales and NXP, all of them still headquartered in the region or with their global research centres based in the province

In Brabant, in and around the city of Boxmeer, forming a triangle with Oss (biopharma) and Eindhoven (high tech and medtech), the AgriFood & Animal Health cluster alone comprises:

- 3,600 companies
- 40,000 jobs
- 455 million euro spent on R&D
- €4.3 billion in AgriFood exports

THE FLAGSHIP COMPANIES IN ANIMAL HEALTH ARE MSD (MERCK) ANIMAL HEALTH, HENDRIX GENETICS, NUTRECO AND MAREL POULTRY:

- MSD Animal Health has approximately 1,500 employees in Boxmeer. The operation is the European headquarters and the single largest animal health vaccine manufacturing and R&D site in the world. MSD, as a whole, employs 68,000 people and generates an annual turnover of roughly €35 billion.

- Hendrix Genetics has over 3,000 employees, has locations in more than 25 countries worldwide and is a global leader in turkey, layer hen and trout breeding. The company also has a growing international share in swine, salmon and guinea fowl breeding. Its global head office and core R&D operations are based in Boxmeer and the company's annual turnover of €500 million is increasing at a rapid pace.

- Nutreco has its roots in Boxmeer. It was initially named Hendrix' Voeders, after its founder Wim Hendrix. Decades later and after several takeovers, Nutreco today has some 12,000 employees worldwide and 100 manufacturing sites in 35 countries and generates an annual turnover of over €5 billion. While nine out of ten employees work outside the Netherlands, the Boxmeer site still plays a key role, with 250 staff members engaged in research, communication and marketing.

- With 1,500 employees, Boxmeer is also home to Marel's principal site (6,000 employees worldwide and a turnover of around €1.2 billion). In 2008, Marel Poultry (called Stork PMT at the time) was acquired by the Icelandic company Marel. Boxmeer is the global head office and R&D centre for all of Marel's poultry processing activities. Marel has a presence in some 150 countries.

5. Imaging, Diagnostics and Monitoring

Technical niche	Imaging, Diagnostics and Monitoring
Area of application/Therapeutic Area	Diagnosis; treatment determination; facilitation of treatment; health monitoring; aftercare monitoring; recovery monitoring
(University) Hospitals / Universities / Research institutes involved	TU/e, Eindhoven University of Technology; Holst Centre; Radboud UMC; Catharina Hospital; Jeroen Bosch Hospital; Maxima Medical Center; Kempenhaeghe epilepsy and sleep centre; other UMCs; etc
Leading companies/disruptors/best practices	Philips Healthcare; GE Healthcare Life Sciences Core Imaging; Teledyne Dalsa; Thermo Fisher Scientific; Bambi Belt; LifeSense; Phenom; NTS Group; Sioux Technologies; Adimec
Leading cooperative project/programme	e/MTIC, Eindhoven Medtech Innovation Center
Industry/Academic Leaders	Professor Josien Pluim (TU/e, Eindhoven University of Technology, Medical Image Analysis (IMAG/e) research group); Professor Lukas Dekker (Cardiologist, Catharina Hospital Eindhoven); Professor Frans van de Vosse (TU/e, Cardiovascular Biomechanics); Professor Guid Oei (TU/e, Signal Processing Systems group and gynaecologist at the Máxima Medical Center) – further information below
Facilities/Locations/Campuses	High Tech Campus Eindhoven; TU/e University Campus; Healthcare Campus Philips (Best); Catharina Hospital and Maxima Medical Center (Eindhoven), Kempenhaeghe epilepsy and sleep centre (Heeze), TU/e, Eindhoven University of Technology and Royal Philips (Eindhoven/Best)

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF IMAGING, DIAGNOSTICS AND MONITORING?

The creation and growth of Royal Philips (also known as Philips Healthcare) lies at the heart of the vast industrial and knowledge cluster in imaging, diagnostics and monitoring that has been gathered together in Brabant, in particular at Brainport Eindhoven in the Eindhoven metropolitan area. OEMs Philips, ASML, NXP, FEI (Thermo Fisher), GE Healthcare Life Sciences Core Imaging and most of their tier-1, 2 and 3 suppliers can be found in or within a radius of 50 kms of Eindhoven.

Royal Philips is a global health technology company, leading in market segments such as diagnostic imaging, image-guided therapy, patient monitoring and health informatics, as well as in consumer health and home care. Philips' business groups are clustered around three themes:

1. **Personal Health** - Enabling people to take care of their health by delivering connected products and services

2. **Diagnosis & Treatment** - Enabling efficient, first-time-right diagnosis and precision therapies through digital imaging and clinical informatics solutions:
   - Diagnostic Imaging
   - Image-Guided Therapy
   - Ultrasound

3. **Connected Care and Health Informatics** - Empowering consumers and care professionals with predictive patient analytics and clinical informatics solutions with a high degree of informatics and software-related competencies:
   - Patient Care and Monitoring Solutions
   - Healthcare Informatics, Solutions and Services
   - Population Health Management

In the past 25 years, Philips has laid the foundations for the Brainport Eindhoven region as we know it today. A top technology region that is renowned for its open innovation, co-creation and unique collaborative ventures between companies, knowledge institutes and government.

Today healthcare is Philips' core business. In Brabant, Philips has a large Imaging Campus in Best and multiple labs and research departments on the High Tech Campus in Eindhoven (HTCE), the centre for technology-enabled innovation in the Netherlands. Philips employs some 3,500 people in Best, and in Eindhoven close to 2,000 Philips specialists work on healthcare technologies and treatments.

The High Tech Campus Eindhoven half-jokingly calls itself 'the smartest square kilometre in Europe', as it is home to more than 200 research companies, startups and institutes. Some 12,000 researchers, developers and entrepreneurs from companies all over the world work there on developing future technologies and products that will affect the lives of billions of people. As such, the High Tech Campus Eindhoven has become an incubator for innovation in its priority areas of health, energy and smart environments.

PARTNERSHIPS BETWEEN ACADEMIA, HEALTHCARE AND INDUSTRY – E/MTIC

The Eindhoven Medtech Innovation Center (e/MTIC) is a large-scale research partnership between Royal Philips Eindhoven, the Eindhoven University of Technology (TU/e), the Catharina Hospital, the Maxima Medical Centre and the Kempenhaeghe Epilepsy and Sleep Center in the fields of cardiovascular medicine, perinatal medicine and sleep medications. This partnership has evolved over several decades, has a strong scientific and commercialisation track record and currently involves around a hundred PhD students, supervised by a similar number of experts from the various partners.

The goal of e/MTIC is to create and develop an ecosystem that dramatically increases the speed of high tech health innovation, maximising value for patients, taking technical innovations all the way from initial research

- **MedSim** - the world's most lifelike childbirth simulator called Victoria. She has accurate anatomic proportions and state-of-the-art pregnancy monitoring technology;
- **The Smart Baby Bottle** - a sensor-equipped sleeve that tracks bottle feeding routines and provides parents with personalised advice regarding their baby;
- **Smart Monitoring** - patient self-monitoring solutions for hypertension, obstructive sleep apnoea and atrial fibrillation using unobtrusive wearable sensing techniques integrated in watches or patches for timely detection;
- **3D Needle** - using a 3D Ultrasound probe to visualise and guide needle and catheter interventions by automatically detecting and visualising the entire instrument.

e/MTIC
Eindhoven MedTech Innovation Center

ACADEMIC LEADERS IN E/MTIC

Prof. Josien Pluim
TU/e, Eindhoven University of Technology, full professor of Medical Imaging, Dept. of Biomedical Engineering, Medical Image Analysis p(IMAG/e) research group and part-time professor of Medical Image Analysis at Utrecht University.

Prof. Lukas Dekker
Cardiologist at the Catharina Hospital Eindhoven, specialist in diagnosis and treatment of patients with cardiac arrhythmias. Closely involved in collaborative international research. Part-time professor at TU/e, Departments of Electrical Engineering and Biomedical Engineering.

Prof. Frans van de Vosse
TU/e, leads the Cardiovascular Biomechanics research group at the Department of Biomedical Engineering. Research topics: computational and experimental biomechanical analysis of the cardiovascular system and its application to clinical diagnosis and intervention, cardiovascular prostheses, extracorporeal systems and medical devices.

Prof. Guid Oei
Part-time professor at TU/e in the Signal Processing Systems group, where he is chair of Fundamental Perinatology. Oei initiated several methods for pregnancy monitoring. He leads the fundamental perinatal care research group, which studies the care mother and child receive right after birth. He initiated and heads the Perinatology Technological Research Group (TOP) that studies the analysis and processing of maternal, foetal and neonatal signals under physiological and pathophysiological circumstances. Oei has worked as gynaecologist at the Máxima Medical Center since 1996, where he is cofounder of the Woman Mother Child Centre, the Obstetrics High Care Unit and the NICU.

PHILIPS SET TO TREAT LUNG CANCER

Source: FD, Financieel Dagblad, Thieu Vaessen, 27 November 2019

- New X-ray equipment can detect smaller cancer tumours in the lungs at an earlier stage.
- Tumours can be frozen or burned as they are diagnosed.
- Philips is experimenting with new technology in 20 different hospitals.

Philips has designed a new way to treat lung cancer. Using advanced X-ray equipment, the Dutch company believes that doctors can detect smaller tumours in the lungs at a relatively early stage. Moreover, treatment can immediately take place during the diagnosis

The Philips approach to lung cancer is the latest form of "new surgery". In these procedures, doctors usually insert a catheter into the bloodstream through the groin, and then perform procedures in the blood vessels, heart or even brain. Philips supplies the imaging equipment, the scanners that enable doctors to lead a catheter to the right place. [...]

Pulmonologist Erik van der Heijden of the Radboud University Medical Center (UMC) hopes that the new technology will make the early detection and early treatment of lung cancer possible. Van der Heijden is working closely with Philips in the development of the technology. [...]

Van der Heijden expects that the first treatment – "heating by a kind of microwave effect" – can already be performed using catheters next year. Two other companies are developing suitable catheters and have already treated about 20 patients with them. [...]

According to Philips, the new technology can detect much smaller tumours than has been possible to date with the help of a bronchoscope, a tube with a miniature camera attached to it. Philips is currently experimenting with new technology in 20 different hospitals, one of which is Radboud UMC in Nijmegen. [...]

It is anticipated that not only a better picture of the lungs can be generated but that doctors can also immediately burn or freeze tumours with the help of the catheters. According to Van Meurs, this is a significant benefit, because at present three to four months often pass by before a diagnosed patient can be treated. [...]

The improved techniques have blurred the line between diagnosing and treating a disease. It also means that Philips' activities in healthcare are increasingly moving towards treating diseases.

6. Robotics in Healthcare

Area of application/Therapeutic Area	Surgery; Care
(University) Hospitals/Universities/Research institutes involved	TU/e Eindhoven; Maxima Medical Center; Catharina Hospital; Jeroen Bosch Hospital; Maastricht University Medical Center; Rotterdam Eye Hospital
Leading companies/disruptors/best practices	EMR, Eindhoven Medical Robotics; Microsure; Preceyes
Industry/Academic Leaders	Maarten Steinbuch (full professor at TU/e and entrepreneur); Carmen van Vilsteren (Chair of the Netherlands' LS&H Priority Industry and Director of the Health Strategic Area at TU/e); Gerrit Naus (founder and CEO of Preceyes); Anupam Nayak (founder and CEO of Eindhoven Medical Robotics); Lars Schiemanck (COO of Microsure)
Facilities/Locations/Campuses	TU/e Campus; High Tech Campus Eindhoven

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF ROBOTICS IN HEALTHCARE?

The (Brainport) Eindhoven region has a century-old tradition of high technology, from the initial automation introduced in the factories of Philips and the arrival of the technical university through to the current activities in the fields of mechanical engineering, electrical engineering, physics, optical engineering, software and design. In the field of high tech machine-building the region is fairly unique, and the most complex machines in the world are built in the region by OEM companies such as ASML, FEI (Thermo Fisher), Philips and their tier-1, 2 and 3 suppliers. ASML, for example, is global market leader (with an 85% share) in lithography machines (IC manufacturing) and Philips is one of the three largest medical equipment manufacturers in the world.

MEDICAL ROBOTICS

Because of the presence and the intersection in Eindhoven of both medical knowledge and high tech machine-building, new technological and business opportunities have arisen, and one of these is medical robotics.

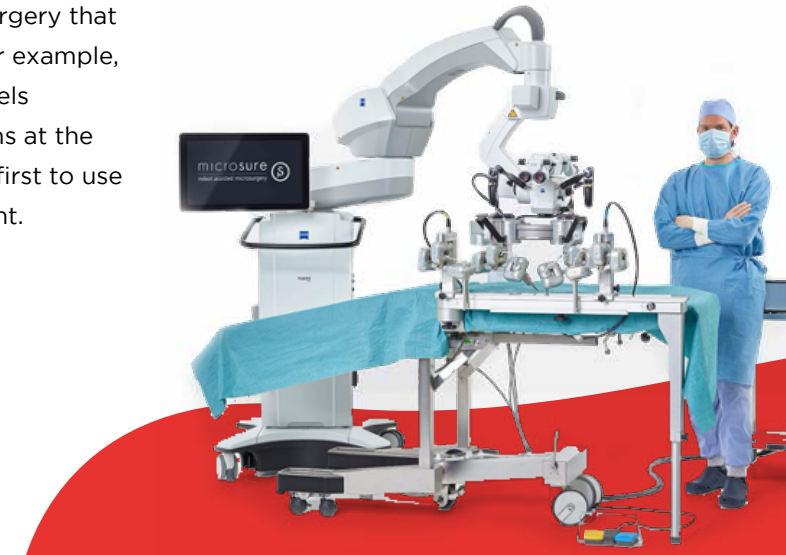
Spinning out of the university – out of, for instance, the system and control engineering group – a number of students have founded robotic surgery companies. Professor Steinbuch is convinced that surgical robots have a bright future. 'Medical robots can be used for very precise eye operations, for joining vessels together or for carefully milling away bone when removing brain tumours. We are also working on the development of a remote-controlled catheter for cardiac catheterisation and of a robot that can assist in complex brain surgery.'

The resulting knowledge has led to the establishment of several high tech companies in medical robotics:

1. **Preceyes** - Preceyes is a medical robotics company with a CE-marked product for the treatment of patients requiring vitreoretinal surgery. The Preceyes Surgical System is a robotic assistant for eye surgery, providing surgeons with a precision greater than 20 Qm to position and hold instruments. This high surgical precision aims to improve treatment outcomes and empowers surgeons to establish new innovative surgical techniques, including the delivery of advanced therapeutics.

2. **EMR, Eindhoven Medical Robotics** – EMR is developing the first autonomous surgery robot. Going one step beyond the development process, the surgeon will be directing the surgical procedure but no longer directly performing it. EMR has high ambitions: 'We develop image-guided high precision surgical robotic systems. We aim to be a world leader in this industry with a team of over a thousand people in the next decade,' says Anupam Nayak, founder and CEO of EMR.

3. **MicroSure** – Microsure is a medical device company founded by the Eindhoven University of Technology and the Maastricht University Medical Centre in 2016. The company develops robot systems for microsurgery. MUSA, designed in close cooperation with microsurgeons and engineers, is the world's first surgical robot for open microsurgery. MUSA allows microsurgeons to work with superhuman precision, enabling new types of surgery that are currently impossible to perform by hand. For example, MUSA enables lymphatic surgery on lymph vessels smaller than 0.3 mm in diameter. Plastic surgeons at the Maastricht University Medical Centre+ were the first to use MUSA to surgically treat lymphedema in a patient.



Source: Microsure

7. Highly Complex Machines

Area of application/Therapeutic Area	Complex machinery used in biopharmaceutical R&D and manufacturing; also used in the development and manufacturing of robotic systems in healthcare
(University) Hospitals/Universities/Research institutes involved	TU/e Eindhoven; Holst Centre; Catharina Hospital; Maxima Medical Centre; JADS
Leading companies/disruptors/best practices	ASML; KMWE Group; NTS Group; Demcon Group; Sioux Technologies; Thermo Fisher Scientific (FEI); VDL-ETG; Royal Philips; GE Healthcare Life Sciences Core Imaging; OMRON; Neways Technologies; Frencken Mechatronics; Applied Micro Electronics (AME); Thales Cryogenics; Adimec; Luminex; VanBerlo Group; AAE, The Art of Mechatronics
Leading cooperative projects/programme/initiatives	Brainport Industries; BIC – Brainport Industries Campus
Industry/Academic Leaders	Maarten Steinbuch (full professor at TU/e and entrepreneur); Marc Hendrikse (CEO NTS Group); Ben Gorissen (Global Director R&D Product and Process Improvement/R&D Site Leader MRI, Philips); Raymond Schrijver (Sr. Director Pharma, Thermo Fisher Scientific – FEI); Dennis Schipper (CEO Demcon Group)
Facilities/Locations/Campuses	High Tech Campus Eindhoven; TU/e Campus Eindhoven; BIC – Brainport Industries Campus

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF HIGHLY COMPLEX MACHINES?

Building on the ever-growing technological strengths of Royal Philips, founded 125 years ago in Eindhoven, the region has become the smartest high tech region in the Netherlands, aptly named ‘Brainport Eindhoven’.

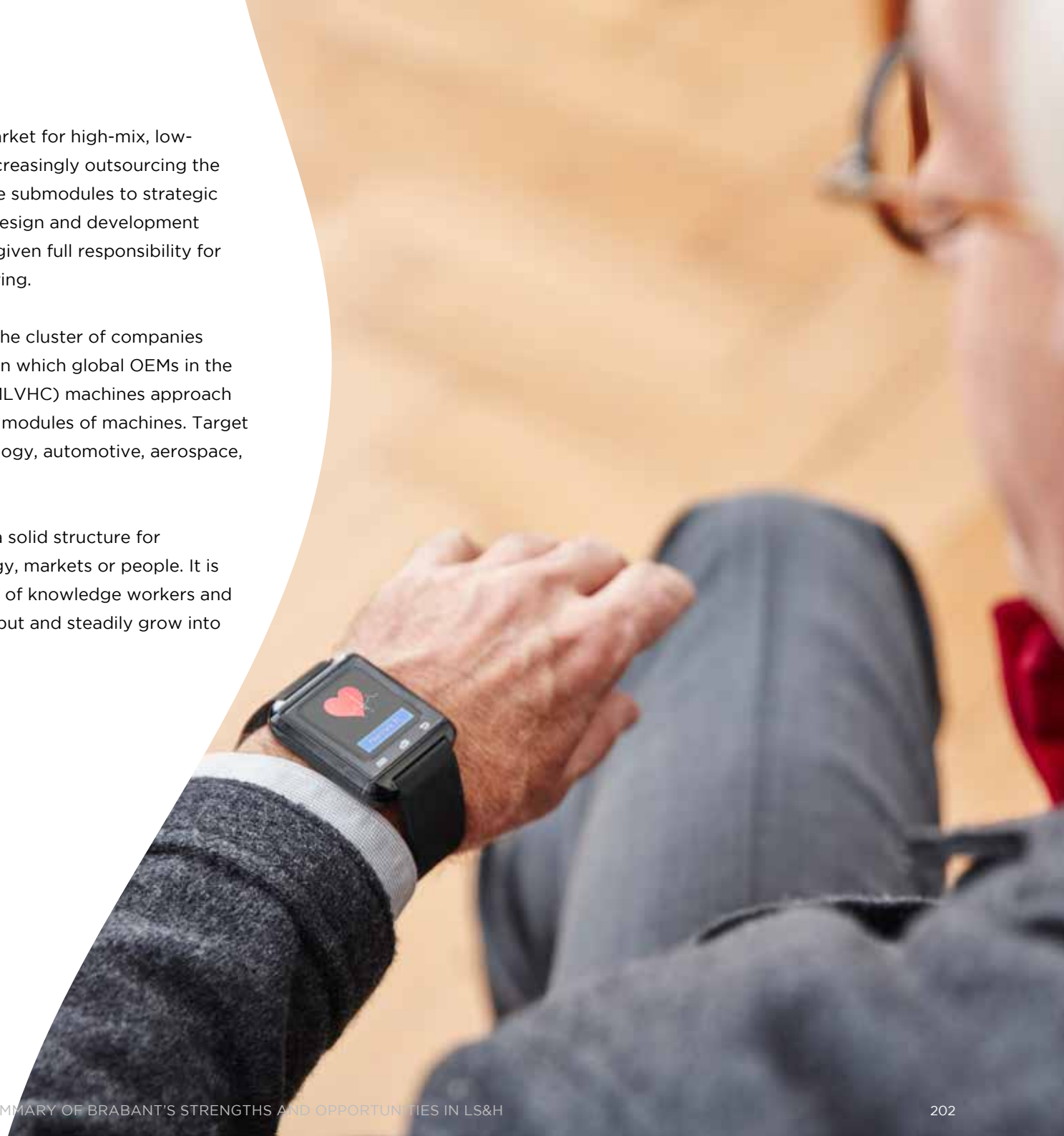
Today, Brabant is arguably one of the smartest high tech regions in all of Europe. World-beating OEM companies such as Philips, ASML and FEI (now part of Thermo Fisher Scientific) have gathered their suppliers and knowledge institutes (such as TU/e, Eindhoven University of Technology and the Holst Centre) around them to create a tightknit and highly flexible industry cluster.

The more than 100 tier-1, 2 and 3 suppliers in the open high tech supply chain in the region have created their own association, called ‘Brainport Industries’. The companies affiliated in Brainport Industries design, develop and manufacture leading, advanced, precise and intelligent high tech equipment and components, individually and jointly.

Their clients are global OEMs competing on the market for high-mix, low-volume, high-complexity machines and who are increasingly outsourcing the manufacture of sub-assemblies and larger non-core submodules to strategic suppliers. They are also starting to outsource the design and development of the equipment they manufacture. Suppliers are given full responsibility for these modules, from design through to manufacturing.

Brainport Industries' aim is a straightforward one: the cluster of companies strives to be the number-one high tech supply chain which global OEMs in the field of high-mix, low-volume, high-complexity (HMLVHC) machines approach to have their concepts converted into machines or modules of machines. Target industries include semiconductors, medical technology, automotive, aerospace, analytical, print and photovoltaics.

Brainport Industries provides a fertile ground and a solid structure for collaborative projects, whether involving technology, markets or people. It is an environment that provides for a continuing flow of knowledge workers and experts and enables suppliers to increase their output and steadily grow into market leaders.

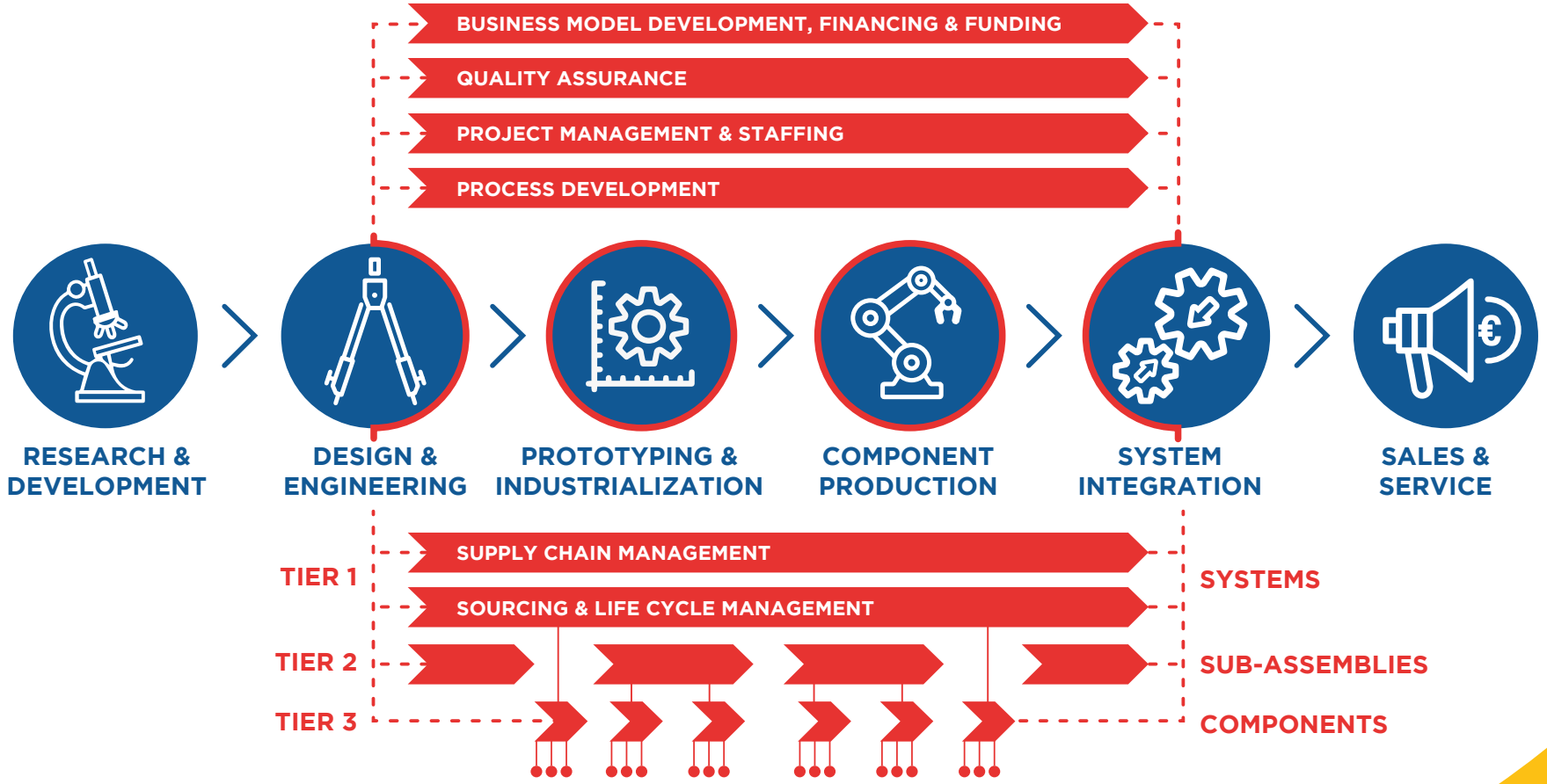


BRAINPORT INDUSTRIES: THE GLOBAL OPEN SUPPLY NETWORK FOR HIGH TECH COMPANIES

Together, the members of Brainport Industries create a unique ecosystem that can manage the entire supply chain for high-mix, low-volume and high-complexity systems, sub-assemblies and components.

SERIES PRODUCTION OF CUTTING-EDGE TECHNOLOGY

The members of Brainport Industries design and manufacture highly complex systems, sub-assemblies and components in series. They have a proven track record and long-standing B2B relationships with companies such as Philips, ASML and FEI.



Source: Brainport Industries

8. Data Science and Big Data in Healthcare

Area of application/Therapeutic Area	Support of care, diagnosis and cure in healthcare
(University) Hospitals/Universities/Research institutes involved	TU/e Eindhoven; JADS (Jheronimus Bosch Academy of Data Science); Tilburg University; Holst Centre; Catharina Hospital; Maxima Medical Center; Kempenhaeghe epilepsy and sleep centre
Leading companies/disruptors/best practices	Philips Healthcare; Sioux Technologies; Salvia BioElectronics; Enpicom; GE Healthcare Life Sciences Core Imaging; The SleepCompany; Additive Industries; InProcess-LSP; Eindhoven Medical Robotics; Preceyes
Leading cooperative projects/programs	e/MTIC – Eindhoven Medtech Innovation Center
Industry/Academic Leaders	Jeroen Tas (Chief Innovation and Strategy Officer, Philips); Leon Giesen (CEO Sioux Technologies); Maarten Steinbuch (Distinguished Professor in Systems and Control and Chair of Control Systems Technology TU/e)
Facilities/Locations/Campuses	High Tech Campus Eindhoven; TU/e Campus Eindhoven, Mariënburg Campus Den Bosch, BIC - Brainport Industries Campus

HOW DID BRABANT BECOME SO STRONG IN THE WORLD OF DATA SCIENCE?

DATA SCIENCE IN HEALTHCARE

Over the centuries, global healthcare has become far more advanced, far more complicated and far more expensive, while the challenges resulting from population growth, the global increase in lifespans and the and rise of 'new' age- and/or lifestyle-related diseases have likewise become greater.

One of the developments that may help face these challenges is the increased use of data, data science and data communication in healthcare. The goal of using data is to make the healthcare structure and healthcare professionals smarter, resulting in improved healthcare, better cost-efficiency and, preferably, a combination of the two.

A number of examples of typical data applications in healthcare:

CARE AND CURE

- Intelligent planning and scheduling of personnel and resources
- Medical decision-support in diagnosis, treatment and follow-up and monitoring
- Real-time health warning by predictive analyses using patient monitoring data

MEDTECH

- Preventive maintenance of very expensive healthcare equipment using sensor data
- Personalisation of devices for better quality of healthcare, using data concerning treatment outcomes, results and patient characteristics
- Adding smart functionalities to medical equipment and devices, such as pattern recognition based on sensor data

PHARMA

- Acquiring real-world data about the efficacy of medication using digital biomarkers
- Preventing over- and undertreatment of patients by personalising treatment using data analysis of the treatment/dosage, treatment outcome and individual patient characteristics

DATA SCIENCE AND BIG DATA IN BRABANT

Becoming strong in the world of data science was a natural development for Brabant, where high tech and life sciences and health have gone hand-in-hand for many decades. Brabant is of course home to Philips (healthcare), one of the world's largest medical technology providers, as well as FEI (now Thermo Fisher Scientific) and GE Healthcare Life Sciences Core Imaging and their suppliers on the life sciences and health side, and ASML, NXP, Philips (Research and Innovation) and their full supplier network on the 'traditional' high tech side.

These communities met, mingled and matched and data communication became an integral part of their business models. The High Tech Campus Eindhoven in particular is one of those hotspots of open innovation where research companies – large and small – have been combining their various fields of expertise for ages. The challenge in healthcare today has been formulated very clearly by Sioux Technologies, one of those Eindhoven high tech companies and heavily involved in healthcare technology development:

'Because of the rising number of elderly people, we are seeing an increase in chronic diseases and staff shortages. This has profound consequences for the care-lifecycle. Because of increasingly complex technology and digitisation, the need for reliability and the security of devices and data is also growing. Technological innovation therefore determines the success of OEMs in the medical industry. In addition, the technology must find its way to the market in a fast and cost effective manner in the shape of sensible user-friendly products.'

EXAMPLES OF BRABANT'S HIGH TECH HEALTHCARE INDUSTRY WITH A SIGNIFICANT DATA SCIENCE COMPONENT

- **Additive Industries** - Metal Additive Manufacturing for Medical Applications. In the medical arena, metal additive manufacturing is used in many applications, such as dental (unique cobalt chrome crowns and bridges) and orthopaedics (complicated life-altering procedures have been made safer using 3D printing). Advances are causing surgeons, dental laboratories, hospitals, implant manufacturers and health systems to turn to 3D printing for all medical applications. Additive Industries' MetalFAB1 is designed for industrial manufacturing in markets that require compliance with regulatory standards like ISO 13485 for medical devices.

- **InProcess-LSP** – NanoFlowSizer. The NanoFlowSizer is a new innovative system for continuous, real-time nanoparticle size characterisation of colloidal systems, nanosuspensions, nano-emulsions and other dispersed nanoproducts directly in manufacturing processes (inline) or in a laboratory setting (offline).

- **Salvia BioElectronics** – Bioelectronic solutions for battling chronic migraines. The human body is controlled by patterns of electrical impulses transmitted through nerve fibres. In the event of a chronic neurological disease, these electrical patterns are different. Bioelectronics are smart devices that use mild electrical impulses to influence nerve activity. Electrical stimulation is nothing new (cardiac pacemakers have been in use for decades), but scientists are just beginning to realize the possibilities of regulating nerve signals to actually treat disease. Salvia's objective is to deliver bioelectronic solutions that restore people suffering from chronic migraines to good health.

- **Sioux Technologies** – Reliable healthcare hardware and software. Sioux is a multidisciplinary service provider in intelligent software and mechatronics. The company designs and builds medical systems and applications for the prevention and early diagnosis of medical problems and post-treatment monitoring (ISO 9001 and ISO 13485 certified):
  - Life Sciences: rapid microbial detection systems, fluorescence microscopy, antidepressants and family planning production equipment
  - Medical Diagnostics: pulmonary testing, digital pathology scanner, MRI/CV/X-ray scanner systems, radiotherapy systems, mobile health monitoring
  - Medical Treatment: respiratory devices, washer disinfectors and dryers for flexible endoscopes, radiotherapy simulation software, blood and fluid warming systems

- **The SleepCompany** – SleepAssist. SleepAssist is a new treatment option for positional sleep apnoea. SleepAssist uses a completely new sensor technology that is unique in the world. The innovative sensor network is placed under the fitted sheet beneath the upper body. On the basis of the algorithm – based on artificial intelligence – the position of the user is measured during sleep. If the user turns on his or her back, the mat emits small vibrations to make the user turn in a position other than the supine position. The vibrations are not perceived as disturbing during sleep, but they do have the desired effect. SleepAssist was developed through a partnership with TNO/Holst Centre and Vention, which originated on the High Tech Campus in Eindhoven.

DATA SCIENCE EDUCATION:

JADS – JHERONIMUS BOSCH ACADEMY OF DATA SCIENCE

Because of that heritage, it is not surprising that the two Brabant universities, TU/e, Eindhoven University of Technology and Tilburg University (including economics, business and entrepreneurship, law, digital sciences) have joined forces and established JADS, the Jheronimus Academy of Data Science. Data Science can be studied, researched and applied through bachelor and graduate programmes, PDEng course and data science centres and incorporated into existing ecosystems at three different locations (TU Eindhoven, Tilburg University and Mariënburg Campus in Den Bosch). Some 1,500 to 2,000 students are studying a JADS course at any given time.

THE EINDHOVEN ARTIFICIAL INTELLIGENCE SYSTEMS INSTITUTE (EAISI)

The Eindhoven Artificial Intelligence Systems Institute (EAISI, pronounced 'easy') is the new institute of Eindhoven University of Technology in the field of artificial intelligence (AI). With the establishment of EAISI, the university wants to contribute to the growing importance of AI in society, business and science, and to meet the rapidly increasing demand for education, engineers and expertise in the field of AI. TU/e has been active in the field of Artificial Intelligence for decades, which gives the new institute an excellent starting position to build on. TU/e will invest 100 million euros in EAISI's education and research until 2025. In total, up to 150 people will be directly or indirectly involved in EAISI.

This money comes primarily from the university's own resources. EAISI also wants to attract an extra 30 million euros each year from so-called third tier grants (NWO, EU and other grants) and from industry directly. There are already about a hundred AI-scientists working at TU/e. On top of that, the university wants to recruit about 50 new researchers. In total, up to 150 people will be directly or indirectly involved in EAISI.

Unlike other AI institutes, EAISI will focus on the use of data and algorithms in machines, such as robots and autonomous cars, which has always been a strong point of TU/e and the Eindhoven Brainport region. The new institute will prioritize research into applications of AI in healthcare, the interaction between man and machine, and the moral and ethical aspects of AI.

In Health Applications, the institute will focus on the following topics:

a. Improved and explainable diagnostics capabilities
b Personalized and wearable health systems with monitoring, health risk detection and adaptation capabilities
c. Causal and systemic understanding of individual states of health
d. Preventive health management
e. Process optimization in health care systems

BRABANT DEVELOPMENT AGENCY (BOM): READY TO CONNECT YOU!

Based in Tilburg, BOM Foreign Investments & International Trade is part of the Brabant Development Agency (BOM). Our BOM Foreign Investments team assists new and existing foreign companies to make optimal use of the opportunities offered by Brabant as a business location. We can offer you our support when it comes to finding sites or real estate, building and environmental permits, labor market analysis, talent acquisition, matchmaking for logistics, employment regulations, fact-finding missions, incentives, and relevant networks in the regional private and public sector.

Our BOM International Trade specialists provide hands-on support to companies in Brabant in growing their business abroad. We offer valuable contacts in foreign countries and provide targeted information on markets and available funding. Our international trade specialists also promote the successful economy of Brabant and its thriving ecosystems to foreign companies around the world.

We offer a range of free services and support designed to provide you with the information and network you need to explore new (business) opportunities.

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