Report to Society 2021

pharma.be

ASSOCIATION GÉNÉRALE DE L'INDUSTRIE DU MÉDICAMENT
ALGEMENE VERENIGING VAN DE GENEESMIDDELENINDUSTRIE

Contents

Foreword

Caroline Ven
CEO

At the end of October 2021, pharma.be signed a joint charter with the federal government and many other stakeholders, pledging to strengthen Belgium's position in biopharmaceutical research and development (R&D), production, and access to innovative medicines for patients. The ambition is to ensure that Belgium takes its place as an international biopharmaceutical valley.

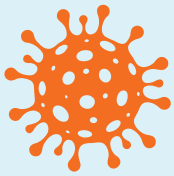
The biopharmaceutical sector's positive contribution to our country's healthcare system and economy cannot be underestimated. The medicines developed and produced in our country help patients all over the world. In 2020, the Belgian biopharmaceutical industry exported products to a total value of more than €56 billion. This makes us one of the top contributors in Europe. The sector employs 130,000 people, directly or indirectly.

This success is not the result of mere chance, but the result of ongoing investment in R&D and a dynamic ecosystem, connecting industry leaders, small- and medium-sized enterprises (SMEs), academia, and the public authorities. The biopharmaceutical sector is by its very nature deeply interwoven with many aspects of society.

As the umbrella organisation representing the innovative biopharmaceutical companies, pharma.be strategically helps build this ecosystem. Thus, co-signing the charter is a logical next step on the way to an even stronger commitment to health and innovation. First and foremost, we aim to ensure patients have access to innovative treatments as early as possible, while also strengthening our economy.

This first Report to Society demonstrates how we managed to achieve our goals in 2020, the year of the pandemic. It was a challenging year, one balancing the need for speed and the concern for safety and quality, and between coping with COVID-19 and continuing to find solutions for other diseases. It was a hopeful year that confirmed our sector's commitment and the will to collaborate. Above all, it was the year in which our mission of 'science serving life' became more tangible than ever.

COVID-19
#togetheragainstcovid19



After the first Belgian patient was diagnosed with COVID-19, no one could have imagined that our country would soon go into lockdown, and that our healthcare system would be put under such immense pressure.

Speed of action was required to ensure an adequate supply of medication to guarantee availability of critical pharmaceuticals. That is why the Belgian government launched a task force, led by Minister Philip De Backer, and a special workstream within the Federal Agency for Medicines and Health Products (FAMHP) to identify the impact of potential shortages of critical medicines.

Naturally, pharma.be was engaged in both initiatives. Our number one priority in the crisis was to find and deliver medicines where they were needed. To achieve this, we focused on:

- → helping **identify essential medicines at risk of shortage**, based on production forecasting
- → **gathering information on production and capacity** in response to questions from the FAMHP and the government
- → responding to the demand to increase **production capacity for COVID-19 medicines**
- → **flagging potential system issues**, such as the need for regulatory flexibility **to speed up deliveries**
- → finding proactive, **outside-the-box solutions**, for example: brainstorming alternatives for standard products and searching for active pharmaceutical ingredients (APIs) at the request of the FAMHP

Such a huge task cannot be achieved alone. All partners in the biopharmaceutical industry put in a collective effort, led by the Belgian authorities, resulting in an uninterrupted supply of essential COVID-19 medical products.

Throughout this Report to Society is more information about the concrete impact of COVID-19 on our industry and how we stepped up to meet the challenges. On our website is a summary of all the COVID-19 actions we took.

#togetheragainstcovid19

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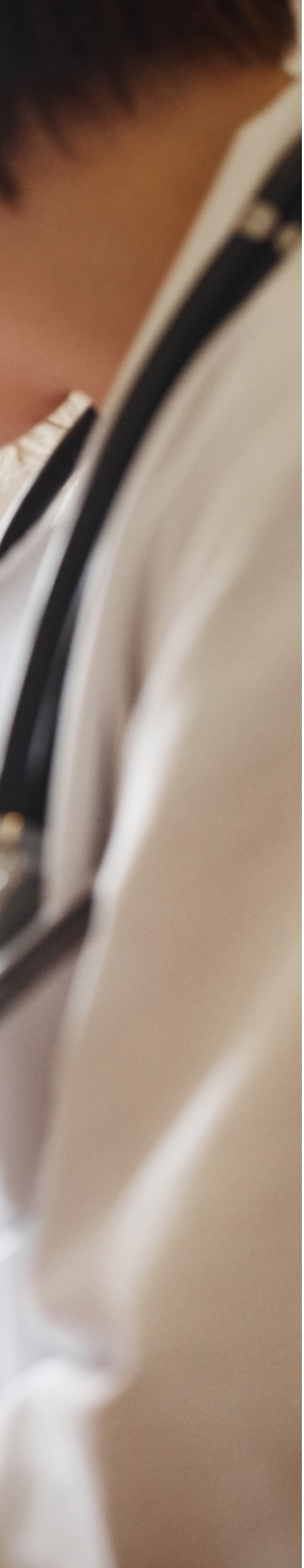
more information!

1 Who we are

1.1. For the patient's benefit

pharma.be is the ambassador of the innovative biopharmaceutical companies in Belgium and fosters a favourable business environment in a responsible manner. The aim is to make sure that patients have optimal access to therapeutic innovation. In this way, we also contribute to improving the Belgian healthcare system.



The manifesto of the biopharmaceutical industry in Belgium

Living life to the fullest. Spending quality time with family and friends. Enjoying good health. We all have the same needs. They define the way we live our lives. They drive us in everything we do, every single day.

We directly employ **40,500** people at 125 companies focused on the research and development of innovative biopharmaceutical medicines and vaccines.

For us, **health is key**. We want the best possible life for everyone in Belgium. That is why it is our mission is to develop health solutions to ensure Belgium is the healthiest place too grow up in, to live in, to work in and to enjoy old age in.

We are deeply rooted in science. History shows that the most crucial breakthroughs in healthcare happen in laboratories. Breakthroughs that have improved the treatment of breast cancer and turned HIV into a manageable chronic condition.

Science is a tool, not an end in itself. We are passionate about science but only because science allows us to make a positive impact on lives. **We are people who take care of others**.

The world is changing at a rapid pace, including new diseases and viruses, an ageing population, and ever- growing digitalisation. And there are numerous new questions emerging. Scientific progress rarely follows a straight line. In our industry, we fail far more often than succeed. There is nothing we can do about that. But being scientists at heart, we cannot just accept that. **We never give up**. It is our responsibility to continue to strive for the best health for all.

We are not alone. Together with patients, doctors, hospitals, mutual societies, pharmacists, universities, research groups, public authorities, and the government, we are united by a common goal: the best possible healthcare for all people in Belgium.

Together we make sure that everyone can live a healthy life.

1.2 125 members

pharma.be brings together **125 biopharmaceutical** companies operating across Belgium. They are present in every key aspect of the biopharmaceutical value chain: **from R&D and clinical trials to production, from market introduction to distribution of medicines**.

Group.10: driving innovation and health

Within pharma.be, Group.10 unites more than 70 small- and medium sized enterprises, start-ups and biotechnology companies. They are active in the research and development, production and distribution of medicines.

Together they represent:

- → **10 %** of the contribution of the innovative biopharmaceutical industry in Belgium
- → **3,710** jobs in 2020
- → **1,072** medicines on the market in 2020
- → **€251,593** added value per employee in 2020

Source: pharma.be, based on IQVIA and Bel-first

These smaller biopharmaceutical companies may be more affected by shifts in policy and market conditions, but they are a driving force for innovation and health.

Animal Health Group

The Animal Health Group is another important division within pharma.be. This group represents the biopharmaceutical companies in Belgium that are specialised in veterinary medicines.

In consultation with the government and with its partners, the Animal Health Group strives for easy access to innovative and high-quality veterinary medicines in Belgium, in a sustainable way.

The group is a full member of HealthforAnimals and AnimalhealthEurope.

The Animal Health Group accounts for:

- → **14** members
- → **more than 1,300** different veterinary medicines
- → **237** vaccines available in Belgium by 2021

Discover our members here:

COVID-19
Our members in action

The battle against COVID-19 took place on multiple fronts. Building on their knowledge and expertise, our members launched various initiatives to help fight the pandemic.

Some companies, for example, set out to develop a vaccine. Other companies started financial campaigns or supported employees helping in hospitals or residential care centres. They supplied equipment such as oxygen cylinders for patients in intensive care units and donated personal protective equipment such as face shields or gowns to ensure the best possible protection for front-line healthcare workers. Or they adapted manufacturing lines to make hand sanitisers. After all, in the first phase, it was particularly important that the basic equipment to control the pandemic, such as face masks, sanitiser and protective clothing, were in stock.

The companies that set out to develop a vaccine joined forces. Various partnerships were created between companies, and between companies and universities. Working side by side and in the shortest possible time, they managed to develop vaccines that exceeded expectations.

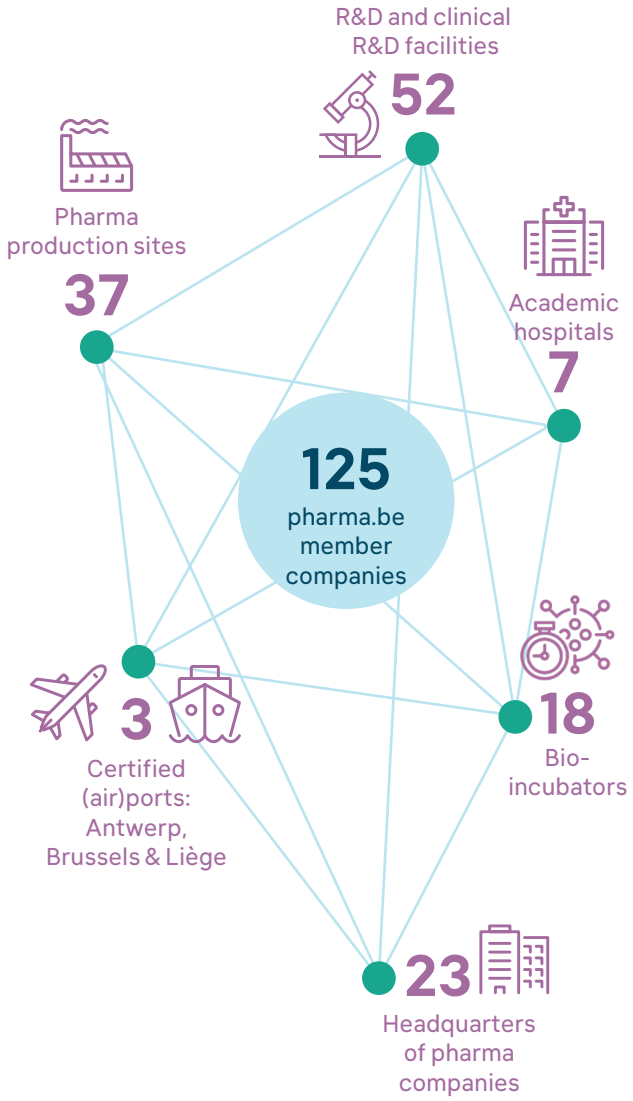
All the initiatives our companies have taken so far in the fight against COVID-19 can be found here.

#togetheragainstcovid19

Scan me for more information!

1.3 Part of a large ecosystem

The members of pharma.be are part of a Belgian biopharmaceutical ecosystem, together with universities and research centres, teaching hospitals, biotechnology and pharmaceutical incubators, and also logistics players such as airports and the port of Antwerp.



Source: pharma.be

1.4 A team of experts

The pharma.be team is composed of 27 highly motivated employees with a variety of skills and experience. They provide services to our member companies, represent them in relevant councils, committees and advisory bodies, and promote their interests at various levels.

Meet the pharma.be team

1.5 Committed directors

The Board of Directors is responsible for the strategic management of pharma.be and consists of 15 directors. The current Chair of the Board of Directors is Karel Van De Sompel (Pfizer). Vice Chair is Frédéric Clais (Eli Lilly Benelux). The members of the Board of Directors are elected at the General Meeting and hold office for a term of three years.

1 Karel Van De Sompel Pfizer, Chair pharma.be **2 Frédéric Clais** Eli Lilly Benelux, Vice Chair pharma.be **3 Renaux Decroix** AbbVie **4 Sztanislav Gabor** Amgen **5 Anne-Laure Dreno** AstraZeneca **6 Gilles Poncé** Bristol-Myers Squibb Belgium **7 Geert Van Hoof** Chiesi **8 Sabena Solomon** GlaxoSmithKline Pharmaceuticals **9 Sonja Willems** Janssen-Cilag **10 Brecht Vanneste** MSD Belgium **11 Guy Oliver** Novartis Pharma **12 Brigitte Nolet** Roche **13 Johan Heylen** Sanofi Belgium **14 Laurent Henaux** Takeda **15 Willy Cnops** UCB Pharma

1.6 Specialised partners

Biopharmaceutical knowledge and the regulatory framework are evolving at a rapid pace, leading to growing complexity. That is why, more and more, our members are looking for external expertise to keep up with the latest developments.

To promote interaction between our members and service providers, we have developed modular partner services. In this way we help create an active community, stimulate exchange and networking between our members and partners, and strengthen the Belgian biopharmaceutical ecosystem.

At the end of 2020, 48 organisations had partnered with pharma.be. These organisations are active in various fields of expertise such as pricing and reimbursement, drug registration, pharmacovigilance, clinical trials, legislation, therapy compliance and proper use of medicine, and logistics.

Discover our partners here:

1.7 Internationally embedded

As an association, pharma.be is also embedded internationally, first and foremost as a member of the European **Federation of Pharmaceutical Industries and Associations** (EFPIA). EFPIA represents the biopharmaceutical industry operating in Europe. Through its direct membership of 36 national associations, 39 leading biopharmaceutical companies and a growing number of small- and medium-sized enterprises (SMEs), EFPIA's mission is to create a collaborative environment that enables its members to discover, develop and deliver new therapies and vaccines for people across Europe, as well as contribute to the European economy.

pharma.be is also a member of the **International Federation of Pharmaceutical Manufacturers and Associations** (IFPMA), representing research-based biopharmaceutical companies, and regional and national associations across the world.

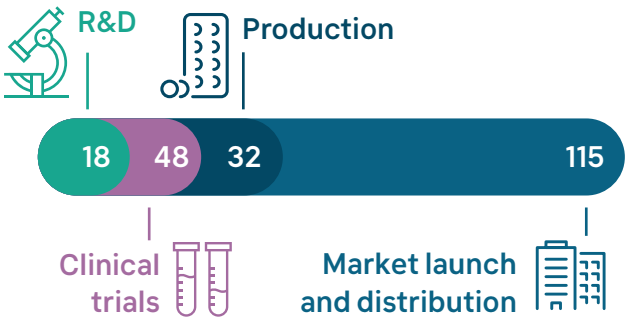
2

What we do

2.1 Operating throughout the entire value chain

As a whole, the pharma.be member companies **significantly contribute to every key aspect of the biopharmaceutical value chain** (i.e. R&D, clinical trials, production, market launch and distribution of medicines) in Europe. This is thanks to a unique combination of a well-developed ecosystem, a highly-skilled workforce, and support from public authorities and research centres.

Number of companies in Belgium



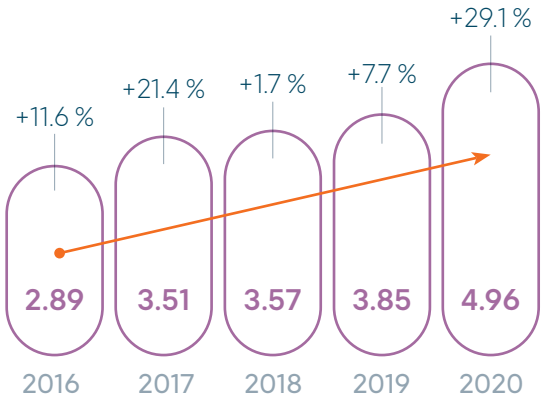
Source: pharma.be

An integrated value chain approach comes with substantial benefits, for patients and their carers, the healthcare system, and the economy. This became particularly evident during the COVID-19 pandemic. The Belgian biopharmaceutical sector was able to fully address the challenge, from research and production to the introduction of innovative solutions.

In this chapter, we will focus on our member companies' innovation activities in Belgium in support of better patient solutions, including: the amount and type of investments in R&D, the clinical studies they conduct, and the new therapies for which they have submitted reimbursement applications and that are now reimbursable and available to patients in Belgium. In chapter three we will look at the added value of these activities for patients, the healthcare system and society, and their economic return.

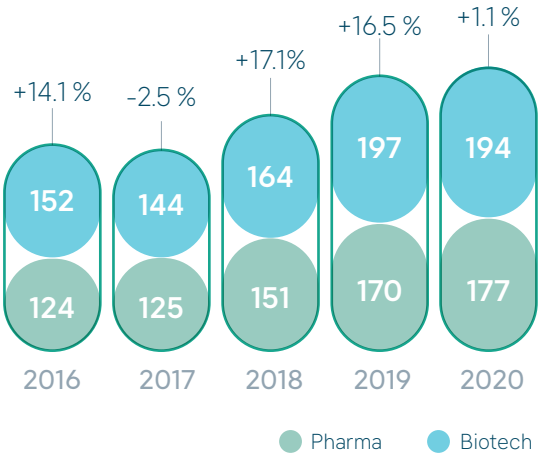
2.2 Research & Development: drivers of innovation

Evolution of R&D investments in Belgium (billions of euros)



Source: pharma.be, Survey amongst members

Evolution of number of patent applications in Belgium



Source: European Patent Office, European patent applications 2011-2020 per field of technology

2.2.1 R&D investments in Belgium

The large number of clinical trials conducted in our country provide participating patients with free and early access to the latest treatments (see 2.3). This leading position is not a given, however. To maintain this position, our companies are increasingly investing in R&D:

- In 2020, the sector invested **€13 million** in R&D every day, amounting to a total of **€4.96 billion**.
- Over the past five years, R&D investments have grown by **71 %.** In 2020, there was a **29 %** increase in R&D investments compared to the year before.
- In 2020, on average **one patent application** was filed per day in Belgium in the field of biotechnology and pharmaceuticals.
- Over the past five years, the number of patent applications from the biopharmaceutical industry has increased by **34 %.**

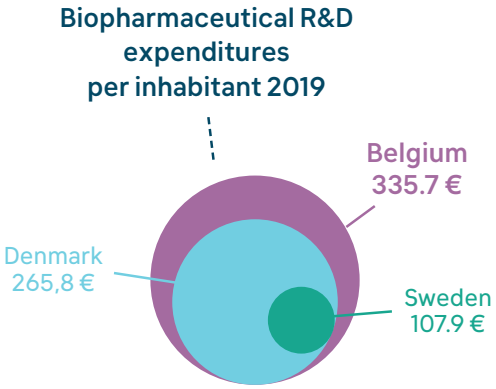
We should not forget, though, that because of the pandemic, in 2020 many companies put research into other therapeutic areas on hold to fully focus on the fight against COVID-19.

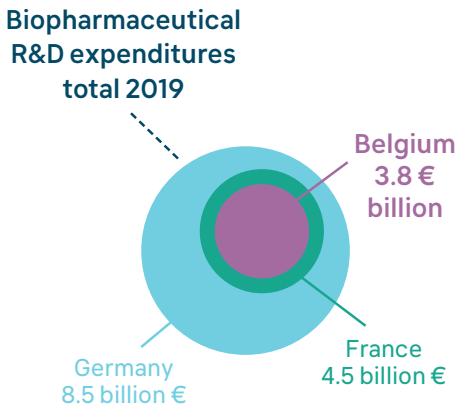
2.2.2
R&D investments compared to Europe

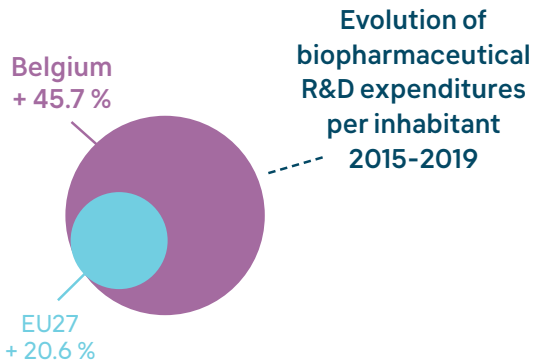
Although Belgium is a relavitely small country, the people and the healthcare system can count on a proportionately high investment in biopharmaceutical innovation. **The total biopharmaceutical R&D investment is comparable with of much larger European countries**. The 2019 figures (the most recent data available) show that Belgium holds the 3rd place, after Germany and France, while in terms of population ranks only 8th.

If we look at investment per inhabitant, Belgium has the highest biopharmaceutical R&D expenditures in Europe. Belgian investments in 2019 were 26 % higher than those in Denmark, second in the ranking, and three times higher than those in Sweden, number three in the ranking.

Over the period 2015-2019, R&D investments per inhabitant increased by more than 45 %, two times more compared to the growth of the total EU27 R&D expenditures per inhabitant. The other top three countries registered almost no growth (Denmark) or even a negative growth (Sweden).







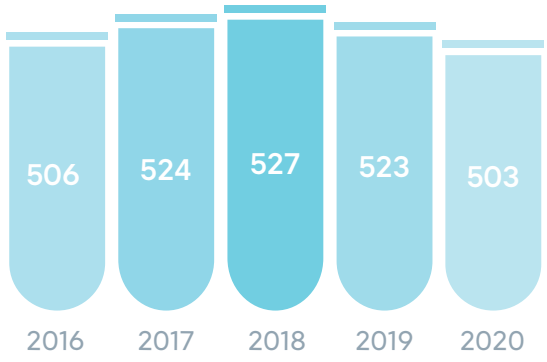
Sources: pharma.be, survey amongst members & EFPIA, The Pharmaceutical Industry in Figures, Key Data 2021

2.3 Clinical trials for new therapies

Clinical trials are a key phase in the development of new vaccines or biopharmaceuticals. Through clinical trials **medicines are tested for safety and efficacy** in humans. They also provide valuable new insights into the treatment or prevention of diseases. Clinical trials are therefore an important source of inspiration for new basic scientific research. At the same time, **through clinical trials patients get free and early access to the newest treatments**, even before they are commercially available on the market.

In **2020**, Belgium also confirmed its position as a European leader in clinical trials, with **503 authorised clinical trials, 80 % of which were sponsored by biopharmaceutical companies**. This leading position is the result of a combination of various elements: the large number and accumulated expertise of the biopharmaceutical companies, a high-level scientific community, state-of-the-art research and hospital infrastructure, and the level of expertise of researchers and the authorities involved, particularly the FAMHP.

Number of authorised clinical trials

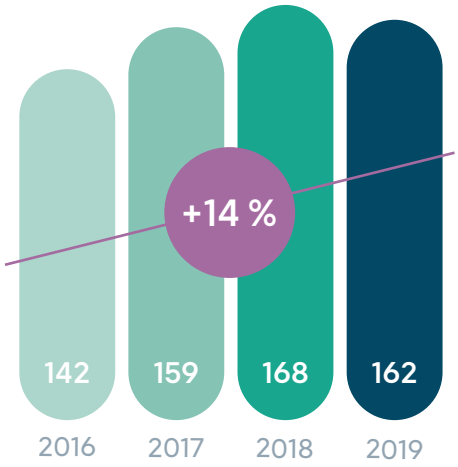


Source: FAMHP data

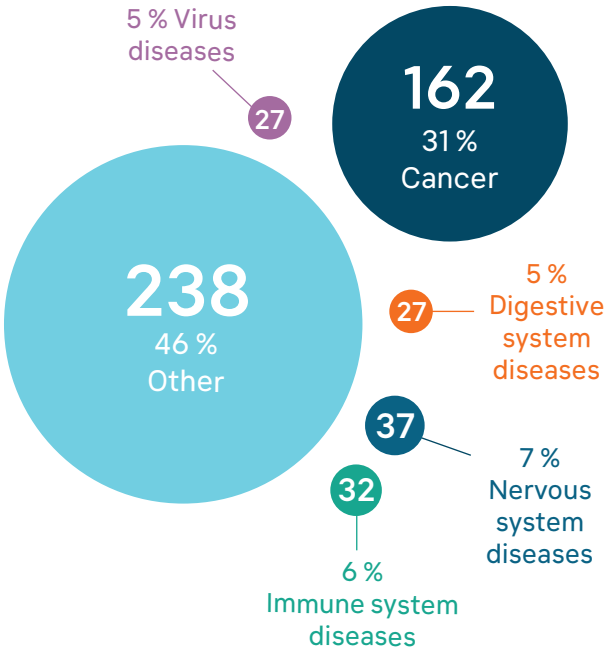
The large number of clinical trials shows that biopharmaceutical companies continue investing in our country to find new solutions for a wide range of therapeutic areas.

Testing new cancer treatments tops the list of clinical trials in Belgium, followed by trials addressing the central nervous system and immune system diseases.

Evolution of CTAs for cancer in Belgium

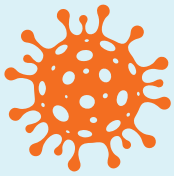


Proportion of cta's for selected disease areas in Belgium (2019)



Source : Deloitte report "Belgium as a clinical trials location in Europe – key results 2019"

COVID-19
Accelerated clinical trials



Naturally, clinical trials in 2020 were largely dominated by the fight against COVID-19. **Belgium and its biopharmaceutical industry played a leading role in the development of vaccines and treatments for COVID-19**. To provide optimal support for clinical trials during a crisis, where the speed of response was crucial, the federal government under the leadership of Minister Sophie Wilmès undertook several measures at the R&D Bioplatform in the spring of 2020.[1]

Thus, the FAMHP, in collaboration with the Clinical Trial College and the ethics committees, **reduced the period for evaluating clinical trial applications in the context of COVID-19 to four days**. Procedures for national scientific-technical advice on the development of medicines were likewise optimised and accelerated.

By the end of 2020, 32 clinical trials had been launched in Belgium in the context of COVID-19, including six for a vaccine, and the FAMHP had already issued 20 scientific-technical recommendations. This was only possible thanks to the cooperation of all those involved (regulatory authorities, biopharmaceutical industry, researchers) and the shared goal to find practical solutions in the fight against the pandemic.

Solutions were also developed to ensure the continuity of clinical trials in all therapeutic areas throughout the pandemic. Together with the Clinical Trial College and the ethics committees, the FAMHP developed a guideline for the management of clinical trials during the coronavirus pandemic, addressing the questions and needs of clinical trial sponsors (biopharmaceutical industry, academic research centres, etc.) in the field.[2]

The FAMHP and the biopharmaceutical industry also joined forces to establish compassionate use programmes (see 4.1.2) in the context of the COVID-19 pandemic, in response to a request from a biopharmaceutical company wanting to make a scientifically proven treatment available, free of charge, to patients who could not be adequately treated. By the end of 2020, three such programmes were up and running.

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2.4 Newly reimbursed medicines

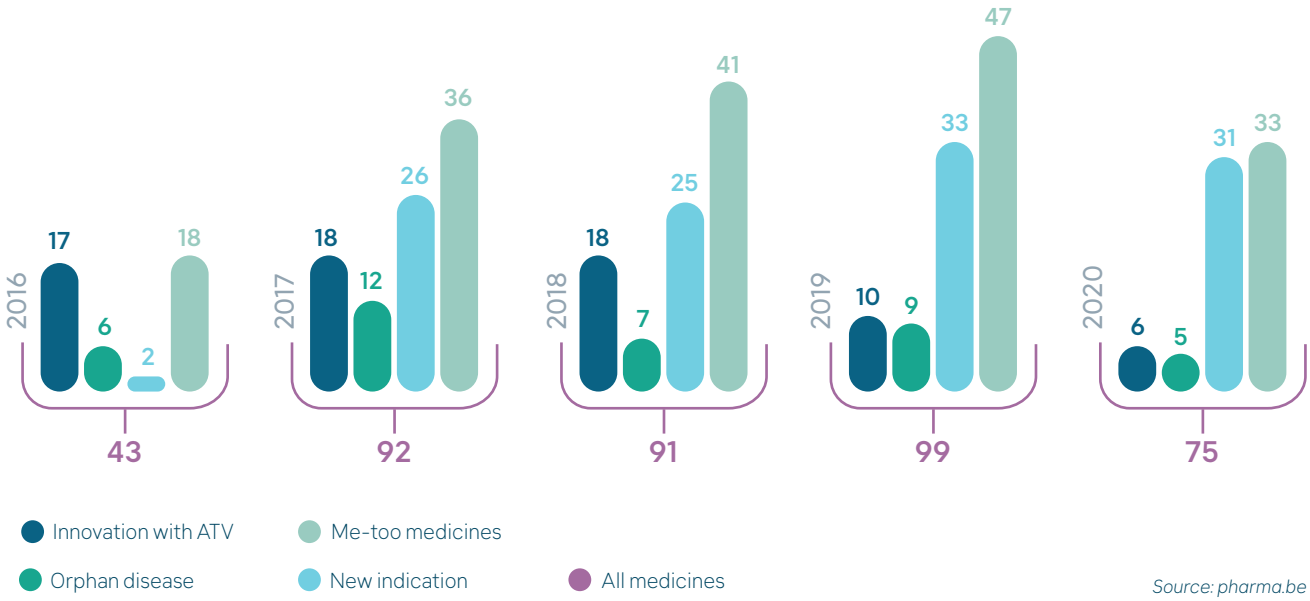
Our member companies' R&D activities and clinical trials in Belgium and abroad result in the development of new medicines. To make these available to patients in Belgium, companies apply for reimbursement with the NIHDI so that patients do not have to pay the full cost.

Below is more information on the evolution of the number of newly reimbursed medicines in Belgium. In chapter 3, we will focus on their added value. .

2.4 .1 According to type

The total number of newly reimbursed medicines increased from 2016 to 2019. In 2020, however, the number dropped due to COVID-19, as the committee that evaluates drug reimbursement requests had to temporarily suspend its operations.

Number of medicines per year



Source: pharma.be

Legend:

- → According to the biopharmaceutical companies involved, medicinal products **with added therapeutic value** (ATV) offer a higher therapeutic value than standard therapies. In other words, they are more effective in treating the disease.
- → Orphan drugs **treat rare diseases**, thus often addressing unmet medical needs.
- → **New indications for medicines** that are already reimbursed for a certain indication/condition and for which the company is requesting additional reimbursement for another indication/condition. For example, a drug that is already reimbursed for the treatment of lung cancer but that is now also reimbursed for the treatment of colorectal cancer.
- → **Me-too medicines** do not provide a higher therapeutic value compared to existing medicines for the same indication/condition, but they can offer added value to the patient because of an improvement in dosage, dosing times, convenience, or ease of use. Moreover, me-too medicines may guarantee continuity of treatment in case existing medicines are not available.

2.4.2
According to therapeutic area

The table below provides an overview of the therapeutic areas (Anatomical Therapeutic Chemical, ATC) for which new medicines were reimbursed in 2020. About half of these were new cancer medicines (ATC L). In addition, more new medicines became available for diseases related to the alimentary tract and metabolism (ATC A), and for blood disorders (ATC B).

ATC code	Number of medicines reimbursed in 2020	ATC main group	Examples of pathology
A	7	alimentary tract and metabolism	diabetes, nephropathic cystinosis
B	9	blood and blood forming organs	haemophilia A, venous thrombosis
C	1	cardiovascular system	heart failure
D	1	dermatologicals	atopic dermatitis
G	0	genito urinary system and sex hormones	uterine fibroids
H	3	systemic hormonal preparations (excluding sex hormones and insulins)	growth retardation
J	5	anti-infectives for systemic use	HIV infections, respiratory/ urinary tract infections etc.
L	38	antineoplastic and immunomodulating agents	solid and haematological tumours, RA, haemorrhagic colitis, psoriasis, etc.
M	1	musculo-skeletal system	osteoporosis
N	4	nervous system	severe pain, epilepsy, severe depression, etc.
P	1	antiparasitic products, insecticides and repellents	anthelmintics
R	3	respiratory system	asthma, obstructive airways disease
S	1	sensory organs	ocular cystinosis
V	1	various	contrast agent

Source: pharma.be

3 Our added value

First and foremost, our innovations lead to better health outcomes for patients.

This is evident from the significant increase in life expectancy in many disease area, such as HIV and certain types of cancer. At the same time, biopharmaceutical innovations also improve the quality of life of patients with chronic diseases. **They feel less pain, the progression of their disease slows down, they better tolerate the new treatments, and they have fewer side effects**.

This not only provides significant added value for the patients, but also for their families and friends and, ultimately, for society as a whole. Thus, getting the right medicines early on, can lead to total cost savings. Just think of shorter hospital stays or fewer surgical procedures. Thanks to new treatments, patients may no longer need to stay at home or can go back to work sooner, which also has a positive impact on their informal carers.

In 2020, pharma.be commissioned a study of the added value of medicines in Belgium (wherever country-specific data were available) in the past 20 years. Some remarkable results can be found below.

And it does not stop there. Our biopharmaceutical industry is also an important pillar of the Belgian knowledge economy. Employment and export rates, which were already impressive, are still growing, even in the challenging year that was 2020. Finally, it is also reflected in the positive cost-benefit analysis of our sector for the Belgian government.

The complete results are available here:

3.1 A positive impact for patients, the healthcare system and society

3.1.1 Contribution to life expectancy in Belgium

Between 1990 and 2016, life expectancy in Belgium at birth increased by 4.1 years for women and by 5.8 years for men. Today, the overall average lifespan is 81.3 years.[3] Between 2001 and 2015, premature mortality rates decreased by 22 %.[4]

The following table presents a qualitative assessment of the role of biopharmaceuticals per major disease between the years 1999 and 2019, zooming in on the overall reduction of Disability Adjusted Life Years (DALYs) and/or increase in survival rate. A colour code indicates the relative role of medicines in these outcomes: dark green when biopharmaceuticals are the primary treatment and light green when biopharmaceuticals are the secondary treatment in combination with another intervention, e.g. surgery.

	Stroke	Heart faillure	Diabetes Type 1	COPD	HIV	Hep C	Breast Cancer	Prostate Cancer	Colon Cancer	Leukemia (ALL)	Multiple Myeloma	Mela-noma
Decrease in % of DALY	- 17 %	- 40 %	- 30 %	- 8 %	- 65 %	- 60 %						
Overall survival (5 year)					99 %	99 %	91 % + 6 %	94 % + 5 %	67 % + 6 %	95 % + 24,5 %	58 % + 9 %	94 % + 8 %
Pharmaceuticals	■	■	■	□	■	■	■	■	■	■	■	■

■ Primary treatment ■ Secondary treatment

□ Primary treatment and improving external conditions

Orange % are percentage points evolution since 1999

Source: Seboio, "20 years of high societal impact: the value of medicines in Belgium", 2020

For diseases such as Chronic Obstructive Pulmonary Disease (COPD), stroke, heart failure and type I diabetes, the DALYs have decreased by 8-40 %. In these disease areas, pharmaceuticals are the primary treatment. In the case of COPD, improvements in air quality, lifestyle and working conditions also contribute to the decrease.

The strongest progress has been made in HIV and hepatitis C. For HIV, there is no curative treatment to date. However, out of 17,000 people diagnosed with HIV in Belgium, only 59 died in 2018, which is comparable to the general mortality rate.

In the case of hepatitis C, the new pharmaceuticals are, for the first time in history, leading to a cure, with patients being virus-free after 8 to 12 weeks of treatment.

In the case of cancer, we see a significant improvement in the five-year-survival rate for various types of cancer. Pharmaceuticals–chemotherapy and hormonal therapy–are often used in combination with surgery as primary treatment for breast cancer, prostate cancer and lung cancer. In the case of haematologic cancers such as leukaemia and myeloma, pharmaceuticals are the primary treatment, and bone marrow transplant is the secondary treatment.[5]

3.1.2
A broad scope of added value

The above results focus on clinical outcomes and post-treatment survival.

But innovative medicines also create added value in many other areas: fewer surgeries and hospital admissions, for example, or a shorter period of sick leave. In some cases, taking time off work can be avoided altogether, in other cases the patient can return to work more quickly after his/her treatment. Indirectly, family and friends can also return to work full-time more quickly, as the patient needs less care.

All this has a positive effect on the labour market, while at the same time limiting government expenditures and creating added value for the economy and society.

The value of pharmaceutical treatment for rheumatoid arthritis (RA)

RA is a progressive, debilitating disease that affects the joints and, if left untreated, can lead to severe disability. Patients are in constant pain and mobility becomes limited. Compared to the general population, the health-related quality of life (HRQoL) in rheumatoid arthritis patients is still very low.[6]

There are approximately 57,000 diagnosed cases of RA in Belgium. The number of patients has increased by 16 % since 2000.[7] Approximately 65 % of the patients are under 65 years of age.[8] They are treated with various pharmaceuticals, including biologics. The introduction of these highly innovative biologics around 2000 proved to be a game-changer, especially for moderate to severe cases.

Previously, the focus was on relieving symptoms through painkillers, anti-inflammatory medicines and joint replacement surgery, in the final stage. Biologics treat the problem rather than the symptom. They have a significant effect on the immune system and change the body's inflammatory response.

The new biologics have been proven highly effective. They not only reduce symptoms but also stop or slow the underlying joint destruction. They even improve cardiovascular side effects and mortality. The quality of life also increases substantially. Patients no longer suffer, or considerably less so, from joint inflammation, which also lowers hospitalisation and work incapacity rates.

Source: Seboio, "20 years of high societal impact: the value of medicines in Belgium", 2020

3.1.3
Added value of the newly reimbursed medicines

Despite COVID-19, numerous new medicines received reimbursement in 2020 (see 2.4), providing, once again, significant added value for the patients. Below, are some concrete examples from orphan drugs and from the group of medicines offering therapeutic added value according to the companies concerned. We will also look into the added value in general of cancer treatments that have been reimbursed in recent years.

Coronary heart disease

Patients suffering from coronary heart disease (CHD, coronary artery disease) and/or peripheral arterial vascular disease (PAD, reducing blood flow to the arms or legs) have a high risk of myocardial infarction, stroke, amputations and even death. This risk still remains, however, despite treatment with blood- pressure, lipid-lowering, diabetes and anti-platelet medicines, and despite lifestyle changes.

These cardiovascular diseases not only negatively impact a patients' quality of life, but they also impose a high economic burden on the healthcare system (treatment costs, hospitalisations, productivity loss and disability). As coronary artery disease, together with cancer, is expected to remain the leading cause of death worldwide in the next 20 years, there is a clear medical need for new treatment options.[9,10,11]

Clinical trials and Real World Data (RWD, see also 4.2.1) show that complementing the existing treatment of CHD and/or PAD with a low dose of a newly reimbursed anticoagulant that inhibits the blood clotting cascade via another, complementary route, will better protect patients from myocardial infarction, strokes and amputations, resulting in fewer hospitalisations and deaths.

Ovarian cancer

Ovarian cancer is a life-threatening disease which affects over 800 women in Belgium each year.[12] In case of advanced ovarian cancer (stage III or IV), fewer than four women in ten survive the disease five years after diagnosis. Women with a genetic predisposition, so-called BRCA mutation carriers, have an increased risk of developing ovarian cancer of up to 50 %. [13]

In 2020, a medicine was reimbursed that has a significant added value for women with the genetic predisposition since the drug inhibits the growth of BRCA tumour cells.[14] After standard treatment with surgery and chemotherapy, this drug significantly reduces the risk of relapse or death. In the longest study to date (a five-year follow-up), the time to relapse or death was lengthened by more than 4.5 years for patients with advanced ovarian cancer who were treated with this drug for a maximum of 2 years, compared with 1.2 years for placebo-treated patients.

This means that treatment with this drug can prolong the disease-free period by 3.5 years, an advantage that continues after the end of treatment, without increasing toxicity and while maintaining quality of life, which is highly important for these patients.[15] In addition, unlike other treatments this drug is administered as a pill instead of intravenously.[16] Given these significant clinical benefits, this drug is now part of the standard care for patients with newly diagnosed ovarian cancer, and even has the potential of a complete cure.

Haemophilia A

Haemophilia is a rare, genetic bleeding disorder. Due to a lack of the clotting factor VIII (FVIII), the blood fails to clot normally.[17,18] Haemophilia A is the most common form, affecting approximately 1,000 people in Belgium.[19] Because of its hereditary nature, about 90 % of the diagnosed patients are male.[20]

Haemophilia A is characterised by prolonged or excessive bleeding, particularly in the joints or muscles. Depending on the severity of the disease, joint and muscle bleeding can occur regularly, leading to chronic swelling, deformity, reduced mobility, and long-term damage. If left untreated, haemophilia A can lead to life-threatening bleeding.[21,22]

For the past 50 years, the standard treatment was prophylactic FVIII replacement therapy.[23] This is a lifelong preventive treatment of two to three infusions per week. Despite this intensive treatment, patients may still experience breakthrough bleeding.[24,25,26] A challenging complication of FVIII therapy is the development of FVIII inhibitors, which can cause the treatment to fail. Nearly one in three patients with severe haemophilia A develop FVIII inhibitors.[27]

Today, new treatments offer new standards of care. Among them is a new class of treatment that can replace the function of activated FVIII to help restore the blood clotting process. A new medicine in this class obtained reimbursement in 2020 and offers a preventive treatment that can be administered subcutaneously, thus avoiding complications.[28,29] It also limits the inconvenience to the patient as it needs to be administered less frequently, only once every four weeks. Moreover, this class will not normally cause, or be affected by, FVIII inhibitors.[30,31]

The treatment represents a substantial improvement in the management of this disease and provides a solution for the unmet needs of haemophilia A patients with and without FVIII inhibitors across all age groups in Belgium. [24, 28, 29, 32]

Hepatocellular carcinoma

Liver cancer is ranked number four in cancer mortality worldwide.[33] Of all types of liver cancer, hepatocellular carcinoma (HCC)has the highest mortality rate of all solid tumour cancers. It is also the cancer with the worst prognosis. In Belgium, liver cancer was responsible for 1,004 deaths in 2018, making it the 8th deadliest cancer in Belgium.[34]

HCC occurs most often in people with chronic liver disease, such as cirrhosis caused by hepatitis B or hepatitis C infections.[35,36] Patients with HCC thus suffer from two concurrent diseases: the underlying liver disease and HCC. Both cause considerable inconvenience to the patient (general debilitation and fatigue, pain, loss of appetite, diarrhoea, vomiting) and to the broader healthcare system. Because symptoms appear late, HCC is advanced or metastatic in most patients at the time of diagnosis.[36] This makes treatment particularly hard as there are no curative treatments at this stage.

Over the past 20 years, and thanks to considerable efforts by academia and the biopharmaceutical industry, significant progress has been made in the treatment of HCC, from an empirical approach of removing visible tumours, to a range of biopharmaceutical treatment options based on robust clinical evidence. Several large clinical trials show that today HCC patients not only live longer but also better.[37,38] The majority of patients see their quality of life improve and some even have a complete response, meaning that the tumour completely disappears for a longer period of time.

Atopic dermatitis

Since June 2020, Belgian patients suffering from severe atopic dermatitis (AD) can benefit from a new treatment option, a monoclonal antibody that targets a key source of inflammation deep beneath the skin, thus preventing flare-ups at the surface.

AD, also known as atopic eczema, is a chronic immunological disorder that can begin in childhood and increase in severity into adulthood.[39] Approximately 8.4 % to 18.6 % of children/adolescents younger than 18, and 4.4% of people aged 18 and older in Europe have AD.[40]

The condition disrupts the skin barrier, leading to inflammation and dryness. This causes extreme itching and sensitivity to touch.[41] In some cases, the skin may secrete fluid and bleed when scratched, leaving the surface vulnerable to inflammation.[42] Repeated scratching can cause thickening and hardening, making the symptoms even worse.[43] The chronic itch-scratch cycle is a typical feature of AD and recurs persistently, with flare-ups lasting six weeks or longer.[44]

Because of the debilitating nature of the condition, AD places a significant burden on patients in all aspects of their lives, from emotional well-being and relationships, to performance at work or school and daily routines.[45]

Moderate to severe AD often occurs in families with a history of AD, bronchial asthma, allergic rhinitis/rhino-conjunctivitis and food allergies.[46] The condition impacts multiple organ systems and more than half of patients with severe AD also have other atopic conditions such as asthma or allergic rhinitis.[47]

Cystinosis

Cystinosis is an orphan disease affecting 0.5 to 1 per 100,000 newborns. Cystinosis mainly causes damage in the kidneys and eye due to the accumulation of cystine in the organs. If left untreated, almost half of the patients die between the ages of 21 and 30.

The disease can be treated today. With optimal compliance, the average age for kidney transplantation increases, the occurrence of extrarenal complications is delayed and thus the survival of patients with cystinosis is improved. Medical advances now make it possible to survive into adulthood (up to 50 years and possibly longer).

Delaying kidney failure

In 2020, a new orphan drug obtained reimbursement for the treatment of proven nephropathic cystinosis. This new drug reduces cystine accumulation in some cells (e.g. leukocytes, muscle and liver cells) of patients suffering from nephropathic cystinosis. When treatment is started early, it will delay the development of kidney failure.[48]

Thanks to this new medicine, the intensive treatment plan can be reduced from administration four times a day to twice a day. This improves compliance, quality of life and treatment management for the patient and, in the long term, also has a positive impact on organ protection.

Specifically for (young) adults, the 12-hour dosing schedule improves social life and school/work life as the night-time dose is no longer required and the afternoon dose no longer has to be taken at school or work.[49,50] Patients and their informal carers see this as a great improvement in their quality of life because they are no longer bound to a strict time schedule. As one patient testifies: 'I have much more freedom. I take my medication in the morning and in the evening. It is so much easier for my parents now. Now my life is far less dominated by my medication and disease.' [51]

Reducing eye complications

As patients with cystinosis live longer, the accumulation of corneal crystal deposits may lead to serious long-term eye complications and hence to vision impairment, with blindness as the worst possible outcome. Early symptoms include photophobia (intolerance of bright light), which can have a major impact on patients' daily lives.

In 2020, a viscous eye drop was reimbursed for Belgian patients suffering from corneal cystine crystal deposits, particularly in adults and children older than 2 years.[52] This eye drop offers an effective solution to reduce cystine crystal deposits in the cornea, leading to a reduction or even total disappearance of associated symptoms, such as photophobia. Long-term data show that the treatment can help maintain normal vision, thus also contributing to maintaining quality of life of cystinosis patients.[53,54]

Added value of cancer medicines

As mentioned before, most of the new medicines that were reimbursed in 2020 are cancer medicines (see 2.4.2). Cancer is the second leading cause of death in Belgium; almost all of us will be confronted with cancer at one point or another, either directly or indirectly. The speed of innovation in this area is unprecedented, leading to promising results:

→ Between 1980 and 2017, the risk of **death from cancer** in Belgium **dropped** by 18 %, while the incidence continued to rise.[55]

→ Since 2010, the **relative mortality rate** in Europe has **improved** significantly, with only a **20 % increase** in the number of deaths compared to a 50 % increase in the number of cancer cases. [56]

→ EFPIA figures also show that this evolution is quite spectacular for certain types of cancer in Europe. The one-year **survival rate** for lung cancer is **10 times higher** than in 1995; for metastatic skin cancer, the five-year survival rate has also multiplied by a factor of 10, from 5 % to 50 %. [57]

→ **Patients with other types of cancer**, such as testicular cancer, breast cancer and children with leukaemia, **also live longer**. [58]

The Belgian Cancer Registry likewise reports an accelerated increase in survival rates for cancer patients.[59] The figures show that from 2013 onwards, the three-year survival rate for all cancer types is rising faster than in the previous years. The progress observed in cancer survival is explained by an increase in early cancer detection, as well as the development of innovative biopharmaceuticals.

Despite the positive results achieved in recent years, there is still huge progress to be made in the fight against cancer within a relatively short time frame, thanks mainly to further research into existing treatments and upcoming new medicines.

Thus, it has been calculated that by introducing innovative immunotherapy, we could gain 11 000 life years in the next five years, including 9,500 healthy life years.[60] In Belgium, the reimbursement of innovative immunotherapies has already resulted in 9 705 additional quality-adjusted life years (QALY).[61] It is expected that immunotherapy will lead to a further reduction in the number of deaths from cancer in the years to come.

In addition, targeted treatment tailored to the patient (Personalised Healthcare) will yield considerable gains in the number of years of life. The same goes for gene therapy and cell-based treatments. These innovations are likewise expected to come with improved care and with substantial socio-economic benefits .

3.2 A positive impact on the economy

Belgium's unique biopharmaceutical hub is world-class, and a leader in the development of revolutionary medicines and vaccines. In addition to the added value for patients, **the healthcare system and society, our strong biopharmaceutical industry also provides a direct economic return and a positive impact on public finances.**

In terms of employment, the biopharmaceutical industry generates no less than 130,000 jobs (direct, indirect and induced jobs). The sector also occupies an important place in terms of exports, significantly strengthening Belgium's positive trade balance. In addition, the significant investments in R&D and clinical studies (see sections 2.2 and 2.3) contribute substantially to the Belgian knowledge economy, underpinning our welfare state.

3.2.1 The economic value of the biopharmaceutical industry

EMPLOYMENT

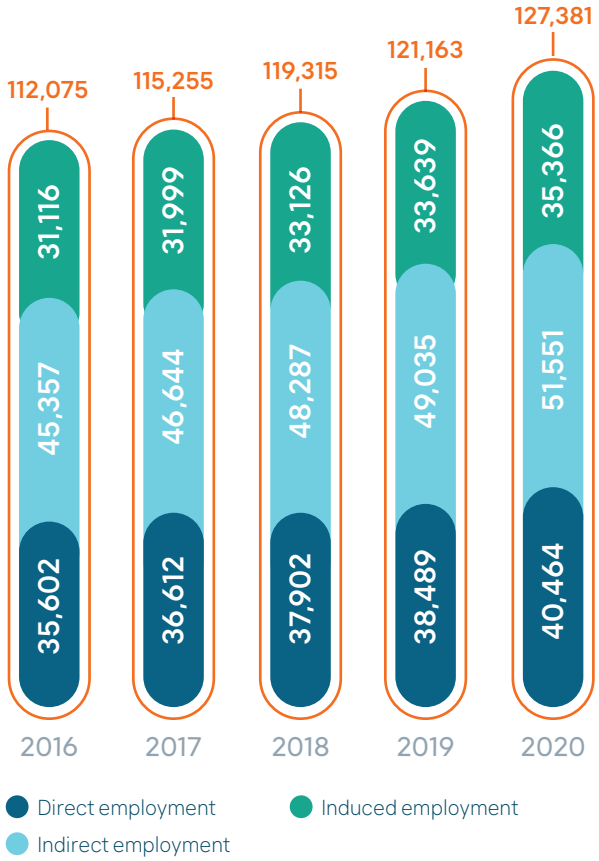
In Belgium

Thanks to our biopharmaceutical industry's leading position worldwide, employment in the industry in Belgium is growing.

Over the past five years, the number of employees increased by 18.7 % to 40,464 people. 2020, the COVID-19 year, accounts for about one third of this growth.

Employment growth in the Belgian biopharmaceutical industry is higher than in the total manufacturing industry, which is declining by 0.6 %.

The biopharmaceutical industry alone accounts for more than **8.5 % of the direct jobs in the manufacturing industry in Belgium**. The sector also provides no less than 51,551 indirect jobs and 35,366 induced jobs. This means that for every job created within the Belgian biopharmaceutical industry, two other jobs are created. In this way, the sector accounts for a total of almost 130,000 jobs.



Source: pharma.be & PWC, Economic and societal footprint of the pharmaceutical industry in Europe, June 2019

In Europe

The importance of these figures becomes even clearer when you put them in the European context. Belgium ranks third, both in terms of the share of total employment and of employment in the manufacturing industry.

A diverse sector

The sector not only generates a **large number of jobs** but also a wide variety of jobs. The Belgian biopharmaceutical scene is very diverse, ranging from small start-ups, to highly innovative biotechnology companies and medium-sized family-owned businesses, to subsidiaries of multinational corporations and large manufacturing companies. This diversity is also reflected in employment. Small- and medium- sized enterprises represent almost 90 % of the market, accounting for some 27 % of employment or approximately 11,000 jobs.

The companies are diverse, but so are the job **profiles** the industry needs, from non-specialised to highly skilled workers. However, in this knowledge-intensive sector, there are considerably more highly educated employees than in other sectors, with just under 70 % of employees holding a higher education degree. This amounts to 37 % in the manufacturing industry in general, and to approximately 50 % in the chemical industry, which corresponds to the share in the total working population.

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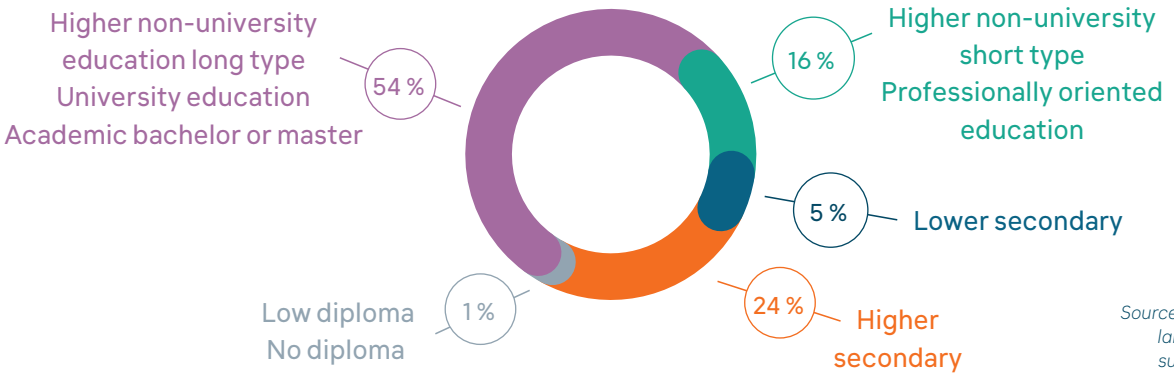
Distribution of profiles in the biopharmaceutical sector in 2020



Source: STATBEL labour force survey 2020

Share of women

%	Total	In management	In cb	In research
2018	49	46	29	57
2019	49	47	35	57
2020	48	47	38	60

Source: pharma.be

Share of non-Belgian employees

%	Total	In management	In cb	In research
2018	8	15	21	10
2019	11	21	19	13
2020	14	28	25	16

Source: pharma.be

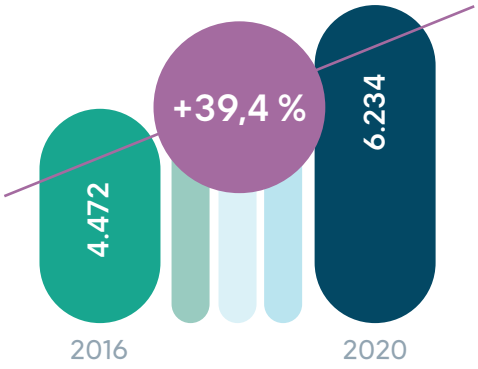
In terms of **gender diversity**, the biopharmaceutical sector is fairly gender balanced. In the past three years, the sector has employed a total of just under 50 % women. Female researchers are in the majority, with 60 % in 2020. On corporate boards, however, women are still underrepresented, although they are catching up. In 2020, the share of female board members had increased to 38 %.

The sector is also diverse, and increasingly so, in terms of **non-Belgian employees**. Between 2018 and 2020, the number of non-Belgians increased from 8 % to 14 %. In 2020, they were more represented in management, with a share of 28 %, an increase of 13 %. One in four board members in 2020 were non-Belgians, compared to one in five in 2018. Finally, the share of non-Belgian employees active in research also increased significantly, from 10 % to 16 %.

A strong foundation

In Belgium, the sector can draw on **a large pool of qualified workers**, thanks to the presence of 12 universities, which provide strong education and a stable inflow of highly qualified and productive workers. Many of these highly skilled workers are employed as researchers in R&D. Over the past four years, this group has grown by almost 40 %. This brings the total number of researchers to 6 234. They are the cornerstone of the biopharmaceutical industry and contribute substantially to the industry's success.

Increase in the number of researchers in 4 years



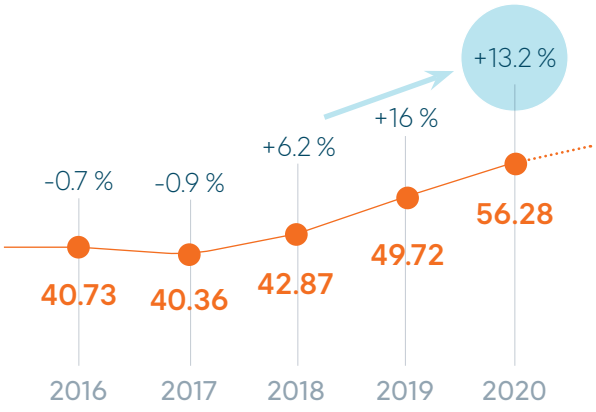
Source: pharma.be, member companies doing fundamental research in Belgium

GLOBAL EXPORT

In Belgium

Thanks to expertise in export, infrastructure, and a high level of connectivity with the rest of Europe and the world, Belgium is an attractive country in which to invest and develop new activities. Year after year, this is reflected in the industry's excellent export rates.

Evolution of exports of biopharmaceuticals (billion euros)



Source: NBB

Even in 2020, when Belgian exports in total dropped by 8 %, the biopharmaceutical sector was one of the only sectors to boost its position by no less than 13 %.

In 2020, biopharmaceuticals accounted for more than 15 % of Belgium's total exports. In addition, the sector made a huge contribution to Belgium's positive trade balance of €21 billion, 44 % (€9.2 billion) of which was accounted for by biopharmaceuticals. This clearly demonstrates that the sector is one of the pillars of the Belgian economy, even during the difficult COVID-19 period.

This strong growth in export is not new. Export rates have increased by more than 10 % for the second year in a row.

In Europe and the world

Belgium is also strong in a global perspective. In terms of total exports of biopharmaceuticals within the EU, Belgium is only surpassed by Germany and Ireland. **In total, 14 % of the EU biopharmaceutical export was shipped from Belgium**.

Belgium exports all over the world. With a share of 24 %, the USA is the most important trading partner.

As a result, Belgium also has an impact on global public health. This was demonstrated by Belgium's leading role in the urgent search for solutions to mitigate the COVID-19 pandemic. Thanks to the presence of highly developed biopharmaceutical production facilities, Belgium was a key player in the development and large-scale production of vaccines. This is also reflected in the export statistics.

COVID-19

Biopharmaceutical transport full speed ahead

In the race against time to get biopharmaceutical products to patients as quickly as possible, our pharma-certified airports played a crucial role. The increased transport of medicines and vaccines through these airports illustrates the positive impact of the thriving biopharmaceutical industry on the Belgian economy. The Port of Antwerp is likewise committed to the transport of medicines and raw materials for the production of biopharmaceuticals.

Brussels Airport[62]

Compared to 2019 (before the pandemic), total pharma transport (import and export) at Brussels Airport grew by 17 % in 2020. Meanwhile, pharma transport accounts for some 8 % of the total airfreight at Brussels Airport, almost twice as much as at any other European airport. Twenty-five of the 100 logistics companies at Brussels Airport are specialised in handling medicines and vaccines.

This is extraordinary performance for such a challenging year. The COVID-19 vaccines, of course, had something to do with this. Today, 350 million COVID-19 vaccine doses have left the European Union via Brussels Airport, accounting for half of the European global export of COVID-19 vaccines. There are also numerous connecting flights from China carrying Sinovac or Sinopharm vaccines, using Brussels Airport as a hub to transport the vaccines to South America and Africa. Finally, there are also COVAX flights to African countries with dose donations from EU member states.

To sustain this growth, Brussels Airport continuously invests in infrastructure and equipment. Brussels Airport now has 30,000 m^2 of temperature-controlled storage space. Four additional Airside Pharma Transporters have been brought in to meet the growing demand for an unbroken cold chain. Brussels Airport is also investing heavily in digitalisation and strategic partnerships with other airports worldwide to create pharma corridors.

Liege Airport[63]

Compared to 2019, freight tonnage at Liege Airport grew by more than 60 % in 2020. Here too, the biopharmaceutical industry was responsible for the significant increase.

Liege Airport is the preferred airport of both the World Food Programme and UNICEF. Liege Airport collaborates with both organisations in the context of humanitarian and healthcare logistics (biopharmaceutical or other). Liege Airport is also one of the links in the COVAX chain for the transport of vaccines and supplies around the world.

Liege Airport has more than 36.000 m^2 of temperature-controlled storage space. Many operators are specialised in biopharmaceuticals and handle these types of goods on a daily basis.

Port of Antwerp[64]

The Port of Antwerp is the first maritime port in the world to operate under the standard of the European Good Distribution Practice (GDP) rules throughout the logistics chain, including container terminals. GDP is designed to guarantee the quality of life sciences and healthcare products throughout the distribution process.

The port of Antwerp has 63.000 m^2 of warehouses that comply with the GDP guidelines, 8 000 plugs for refrigerated containers, and a worldwide connectivity with more than 1.000 destinations. This puts the port in an excellent position to play a major role in the distribution of life sciences and healthcare products. That is why the Port of Antwerp has drawn up GDP guidelines for the deep-sea freight and port logistics of these temperature-sensitive products.

#togetheragainstcovid19

3.2.2
Cost-benefit analysis for the Belgian government[65]

The direct economic impact of a thriving biopharmaceutical sector in Belgium may be clear by now, but the sector also has a positive impact on public finances, as shown by the following calculations based on 2018 statistics.

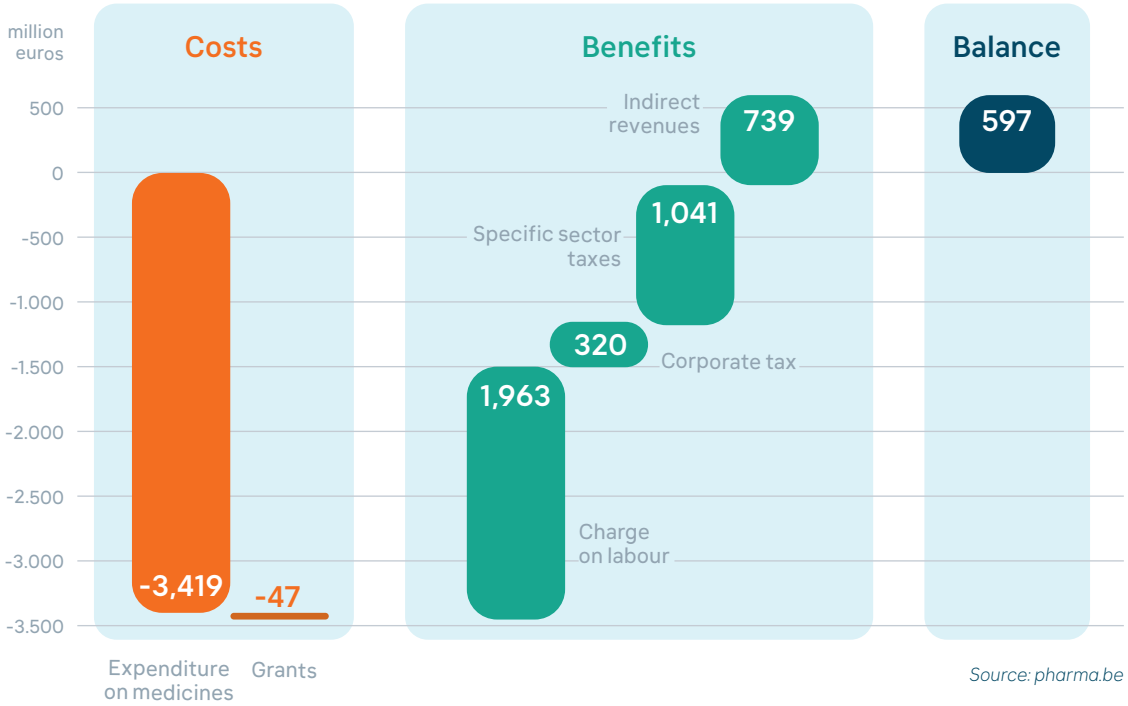
To make this cost-benefit analysis (see also appendix 1), we will first take into account the costs incurred by government for medicines. These costs are reimbursed by the NIHDI and comprise the expenditures for all reimbursed medicines. Government subsidies for the biopharmaceutical industry are also included. In total, these expenditures amount to €3.47 billion.

The biopharmaceutical industry, however, also generates significant revenues for the government, including:

1. taxes on labour, amounting to almost €2 billion
2. sector-specific levies (such as turnover tax)
3. corporate taxes
4. revenues linked to the economic chain created by the biopharmaceutical sector

In total, the revenues for the government amount to €4.06 billion.

Cost-benefit analysis of the biopharmaceutical sector for public finances



Source: pharma.be

The comparison between expenditure and income for the government shows that the biopharmaceutical sector's contribution to Belgium's income is substantially higher than the expenditure. The surplus amounts to almost €600 million. This is a unique position and the envy of many other countries.

4 Our approach

4.1 We take responsibility

4.1.1 Following strict ethical standards

Throughout the R&D process to the launch of a new medicine and beyond, biopharmaceutical companies work closely with healthcare professionals (HCPs) and the healthcare industry. These interactions are not only legitimate, but they are also necessary.

After all, as the first point of contact, HCPs can provide invaluable practical expertise. This is crucial for the biopharmaceutical industry to develop effective treatments for patients.
Biopharmaceutical companies, on the other hand, have a responsibility to inform HCPs about new treatments so that each patient can have the very best treatment. The companies share objective and scientific information, in particular information about the mechanism of action, therapeutic indications, expected outcomes and possible adverse events. In this way, the safe and effective use of medicines is ensured.

The interactions between HCPs and the biopharmaceutical industry are particularly well documented in legislation. Interactions always start from knowledge sharing and are aimed at promoting scientific research or improving the treatment of patients.

Obligation of transparency

Transparency regarding interactions with HCPs is of the utmost importance to the biopharmaceutical industry. More transparency provides better insights into the interactions and meets the growing social expectation.

Since 2017, biopharmaceutical and medical device companies have been required to document and annually publicise certain financial information about their interactions with healthcare providers, healthcare organisations (HOs) and patient organisations (POs). You can find this information at **www.betransparent.be**.

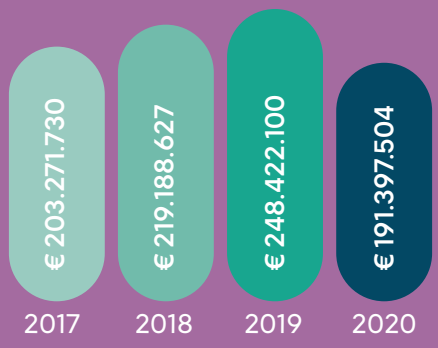
Evolution 2017-2020 of investments in interactions

These interactions include:

1. R&D, including investments in clinical trials in Belgian hospitals
2. contributions to the cost of participating in or organising scientific events as part of the continuing education and training of HCPs
3. donations and grants that support healthcare
4. fees, payments, and reimbursement of expenses for services and consultancy, scientific lectures and participation in scientific advisory boards

This table shows companies' investments per type of interaction and the evolution of investments since Mdeon was designated (see below) by the Sunshine Act:

Evolution of total investments Annual Report BeTransparent



Source: BeTransparent

The impact of COVID-19 in 2020 is clear. Investments in scientific events alone are down by half compared to 2019.

pharma.be as a leader in ethics

Even before this transparency was legally mandated, our Code of Deontology (see below) contained an obligation of transparency. After all, pharma.be has been leading the way in ethics for 50 years. In 1976 we were the first industrial association to demand members to comply with a strict code of deontology.

pharma.be puts transparency and accessibility for all patients first, at all times. Thus, we often take a pioneering role in ethical matters, which are then formalised by legislation, such as:

- the introduction of a **visa** procedure **for sponsoring participants or organisers of scientific events**
  This visa procedure is now followed up by the deontological platform Mdeon. (see below)

- **the publication of financial information about interactions** with HCPs, healthcare organisations and patient organisations
  Before this was imposed by law, our members were already committed to transparency.

- **implementation of a ban on gifts**
  Our Code of Deontology prohibits all gifts to HCPs, even when they are of negligible value. Member companies may provide HCPs with informational or educational materials, but only under strict conditions. In this, our Code of Deontology goes one step further than the law, which permits small-value gifts regarding the practice of the medical profession.

To optimally inform the public and other stakeholders, we developed a brochure in 2020 with infographics on ethical topics such as advertising of medicinal products, the interactions of biopharmaceutical companies with HCPs, healthcare organisations (HOs) and patient organisations (POs), and donations and grants. You can consult the brochure here.

You can download the Code of Deontology here:

The pharma.be Code of Deontology

Our Code of Deontology reflects our commitment to ethics. The biopharmaceutical industry must comply with extensive **legal requirements**, such as laws on medicines, competition, intellectual property, data protection, and anti-bribery. In addition, our members voluntarily commit to the **additional standards** set out in pharma.be's Code of Deontology.

This Code provides a framework for building sustainable relationships with healthcare partners. It defines the requirements that the sector must meet and supports the commitment of companies to work in a professional, ethical, and transparent way. Compliance with the Code is a condition of pharma.be membership.

The Code of Deontology applies to various activities of biopharmaceutical companies, including:

- **information and promotion** of medicinal products

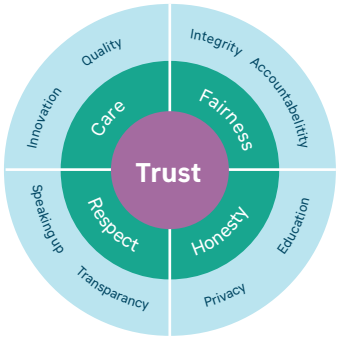
- **interactions** with HCPs, HCOs and POs

pharma.be strives to adapt this deontological framework to a constantly changing world, so that we can continue to guarantee quality, transparency and accessibility throughout all evolutions and trends involving the biopharmaceutical sector. At the General Assembly of 13 May 2020, we approved a modified version of the Code of Deontology.

Main changes are:

- **integration** of the pharma.be ethical principles

- **strengthening** the rules for interactions with POs



Source: IFPMA

Procedures

Putting deontological guidelines on paper is one step, putting them into practice is another. That is why, with a view to quality control, we have developed various procedures to support our members in their interactions within the healthcare sector.

Procedure for advertising and providing information on medicinal products

In 2010 pharma.be launched the Bureau for Control on Written Communication (BCWC). The aim of this independent body is to improve the quality of written information intended for HCPs.

The 2020 BCWC report can be requested via **deonto@pharma.be**.

Complaint procedure

Any individual or legal entity observing a violation of the rules of deontology as laid down in our Code of Deontology may file a written complaint with the Secretariat. The Committee for Deontology and Ethics in the Pharmaceutical Industry (DEP Committee) will mediate these complaints. Any appeal made against decisions taken by the DEP Committee will be adjudicated by the Chamber of Appeal.

When the DEP Committee or the Chamber of Appeal declares that a violation is established, it will impose an appropriate measure.

In 2020, one complaint was filed with the Secretariat. The dispute was settled amicably.

Mdeon, a common ethical platform

Mdeon is an illustration of how professional associations in the healthcare sector take action in the field of ethics through self-regulation.

- *23 May 2006*: launch of the non-profit organisation Mdeon by 12 professional associations from the healthcare sector, including pharma.be
- *Members*: 29 affiliated professional associations in 2020. As a founding member, pharma.be participates in the Board of Directors and the Executive Committee of Mdeon.
- *Objective*: to create, in a proactive manner, a quality framework for the promotion and information about medicinal products and medical devices and dental technology companies

Designated tasks by the FAMHP:

- **Visa procedure**
  Any producer or supplier of medicinal products or medical devices wishing to invite a HCP to take part in a scientific event which takes place during several consecutive calendar days, is required to have a prior visa.
- **Collection and publication of data within the context of the Sunshine Act**
  Companies that put medicines or medical devices on the Belgian market are required to report to the FAMHP the premiums and benefits that they grant to persons who prescribe, deliver or administer medicines (including hospitals) as well as to patient organisations.

Mdeon provides access to this information via the Belgian Transparency Platform **www.betransparent.be**.

As a member of the Board of Directors and Executive Committee, pharma.be helps ensure smooth daily operations of Mdeon, particularly with regard to the visa procedure and betransparent.

In 2020 Mdeon also started working on simplifying the betransparent.be search engine and introduced an urgency procedure for submitting a visa application. Preparations were also made to update the Articles of Association.

COVID-19
The impact on Mdeon

In 2020, the year of the COVID-19 pandemic, visa applications decreased by an approximately of 80 % as of March. As Mdeon's income almost entirely consists of contributions from businesses for visa applications, revenue fell dramatically. Thus, Mdeon's operations and the self-regulation it represents were compromised.

It was therefore decided to (temporarily) increase the contribution required for a visa application, in addition to cost cutting. The uploading of data in betransparent, which used to be free of charge, was made subject to payment as well. Through these interventions the financial independence of Mdeon could be safeguarded for the future.

#togetheragainstcovid19

4.1.2
Meeting urgent patient needs

Thanks to compassionate use and medical need programmes, a medicine that has not yet been approved by the European Medicines Agency (EMA) because the authorisation procedure is ongoing, can be administered to patients suffering from a chronic or serious illness who cannot be treated with a medicine that is already available on the market.

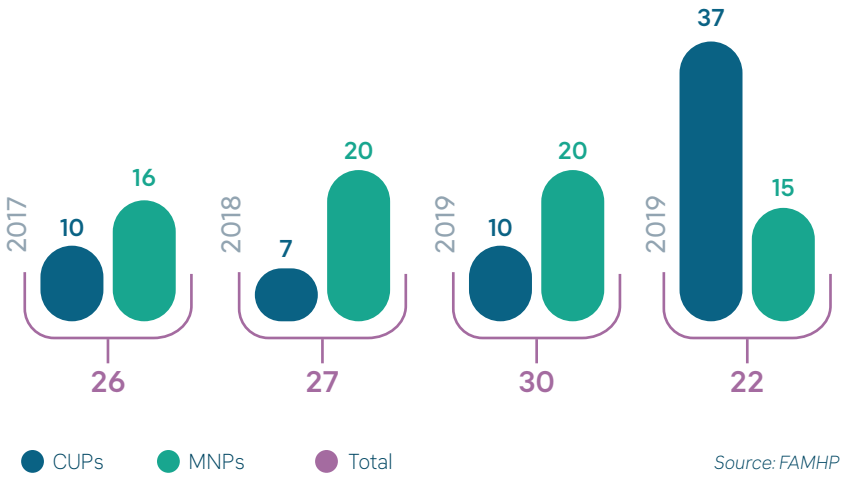
In 2014, Belgium implemented Regulation (EC) No 726/2004 (Article 83) through a Royal Decree and introduced the concept of compassionate use. Our country used this opportunity to create a broader legal framework, allowing medical need programmes as well.

The main difference between these two programmes has to do with marketing authorisation:

→ **Compassionate use programmes** (CUP) encompass medicines that do not yet have a marketing authorisation.

→ **Medical need programmes** (MNP) encompass medicines that already have a marketing authorisation for one indication but are used for a second or third, unapproved indication.

Number of approved applications per year



Source: FAMHP

Early Temporary Authorisation (ETA)

In exceptional cases, innovative medicines can be given early temporary authorisation. In this way, patients in need can have faster access to the newest treatments, even before the registration process is complete.

A biopharmaceutical company can submit an application to the FAMHP for a medical need or a compassionate use programme to obtain an ETA for a particular medicine. This is only possible in exceptional cases, when the medicine is used in the treatment of a serious or fatal illness for which there is no therapeutic alternative.

In these cases, as no market authorisation has been granted by the EMA, the FAMHP has to carefully weighs the medicine's benefits and risks. If the application is approved, the company will provide the new medicine free of charge to patients who are admitted to the programme upon a request submitted by their treating physician. The programmes are ended when the medicine is commercially available for the indication in question.

This exceptional authorisation is done in full transparency. All approved programmes are published on the FAMHP website.[66] Patients and carers can consult them there.

By summer 2021, there were more than 60 programmes up and running.

4.1.3 Caring for the environment and climate

Our members not only prioritise ethical standards, but environmental concerns are also high on their agendas. Thus, they strive to reduce the carbon footprint of their activities in Belgium and in the rest of the world.

They also actively work to prevent pollution. Pharmaceutical substances can be released into the environment during, for example, the production of medicines and their use by humans or animals. That is why, throughout the entire cycle from research to production, use and disposal of medicines, there is a strong focus on pollution prevention. To accomplish this, all participants across the value chain need to work together.

Green pharma conference

On 23 January 2020, pharma.be and Deloitte organised a conference on green pharma. There are plenty of opportunities for biopharmaceutical companies to reduce their carbon footprint, both in R&D, production, distribution, and in daily operations. As the use cases at the conference showed, companies try and make the most of these opportunities.

The conference attendees were presented with a wide range of best practices: reducing water consumption, using residual heat from production processes to heat the offices, rethinking packaging, eliminating plastics, opting for multimodal transport and a green fleet, and launching initiatives to free up resources for staff initiatives on sustainability.

Here are some examples of the industry's efforts to protect the environment and climate:

Multistakeholder collection of expired and unused medicines

Unused and expired medicines should not be flushed or thrown away. They need to be sorted and collected separately, as they can be harmful to the environment. They can also be harmful to public health. After all, unused medicines should not be

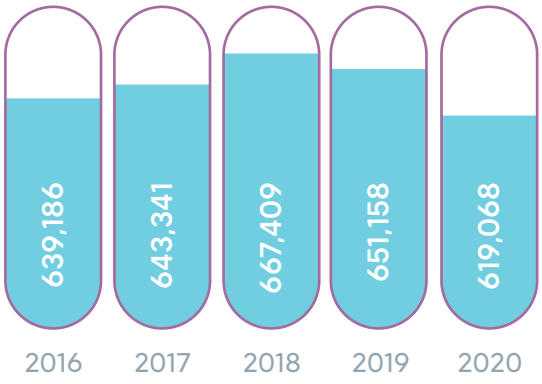
used or disposed of improperly (by children playing, for example, or animals looking for food).

To encourage sorting and to ensure proper collection, the biopharmaceutical sector has collaborated with **various stakeholders** to develop a convenient, cost-free solution for the patient. Thanks to this multi-stakeholder initiative, people can drop of their unused and expired medicines at their pharmacy. The pharmacist collects the medicines in a special cardboard box. The boxes are collected by a wholesale distributor and incinerated, and the thermal energy that is released during this process is being recovered.

The biopharmaceutical industry bears the costs of the cardboard boxes and incineration, including transport costs from the wholesaler's distribution centre to the incinerator. These costs are allocated based on the number of medicines sold to the ambulant healthcare sector in the prior year.

Thanks to this collaboration, an estimated 619,068 kg of unused and expired medicines were collected in Belgium in 2020. In the table below, you will see that this volume is lower than in previous years, whereas between 2016 and 2019, the volume steadily increased. It is not easy to correctly interpret this evolution. An increase may be positive because as it may mean that fewer medicines ended up in the environment. But then, a decrease may indicate that there was less wastage of medicines to begin with, which is also a good thing. The lower figure in 2020, though, is most probably due to COVID-19, meaning that fewer people brought their expired and unused medicines to their pharmacist.

Total amount of expired or unused medicines in kg



Source: pharma.be

E-PIL: Electronic Patient Information Leaflet

Each package of medicines comes with a paper leaflet containing guidelines and important information for the proper use of the medicine. These patient information leaflets are required by European legislation. In Belgium alone, every year more than 100 million packages of medicines are distributed. Hence, the impact on the environment is enormous. There may be situations in which an electronic alternative might prove to be just as safe while being more sustainable.

To investigate this, the biopharmaceutical industry launched the Electronic Patient Information Leaflet (e-PIL) pilot in 2018. E-PIL focuses on a selection of medicines on the market in Belgium and Luxembourg that are only administered within the controlled environment of a hospital. In such an environment, the packages never end up with the end-users, the patients. **In this case, an electronic package leaflet may offer a fast, efficient, and eco-friendly alternative**.

E-PIL makes the electronic leaflet available through reliable sources such as the FAMPH database, the website of the Belgian Centre for Pharmacotherapeutic Information (BCPI) or our own e-compendium website. Not only is the electronic leaflet more sustainable, but it also offers other advantages such as access to the latest information and the possibility to consult the leaflet in a user-friendly and personalised manner (e.g. larger font size or language of choice).

E-PIL is a first in Europe. Two years after its launch, the interim findings are quite positive, to say the least. 98 % of the hospital pharmacists surveyed had not encountered any problems due to the absence of the paper leaflet. The European Commission has therefore extended its approval. The project will now run till 1 August 2022 and will be applied to a larger selection of medicines. Currently 172 biopharmaceutical companies are participating, including 14 of our members, with a total of 42 medicines.

You can follow the project on our website:

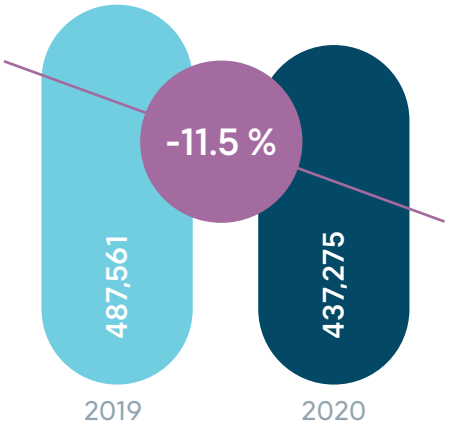
4.1.4
Caring for people and animals

Reducing animal testing[67]

The 3Rs are one of the fundamental principles of animal research, obliging researchers to **Reduce** the number of animals used in experiments, to **Refine** practices to minimise animal suffering and, where possible, to avoid or **Replace** animal research with non-animal methods. The biopharmaceutical industry is firmly committed to these principles.

In 2020, 437 275 animals were used in research, a decrease by 11.5 % compared to 2019. 57.6 % of these animals were mice; 16.2 % were rabbits. Dogs and cats were used to a much lesser extent (0.35 % and 0.06 % respectively).

Number of animals used in research



Source: EU Statistical Data of all uses of animals

In 2020, the majority of laboratory research animals were used for basic and applied research (66.2 %); in 2019, this share still amounted to 71.6 %. In 2020, 127,262 animals, or 29.1 %, were used in the context of regulatory studies and routine production (quality and efficacy testing, toxicity tests, etc.). Compared to 2019, this is an increase, both in absolute numbers (115,267) and in proportion (23.3 %).

More rational use of antibiotics in animals

Excessive use of antibiotics can lead to bacteria becoming resistant. There are various mechanisms through which resistance is exchanged between animals and humans. It would be wrong, however, to ban the use of antibiotics in animals as sick animals have a right to be treated and it is our duty to provide appropriate care.

Moreover, this goes beyond animal welfare; it is also about responsible and safe food production for humans. By only administering antibiotics to animals that really need them, we can limit antibiotic resistance and preserve the effectiveness of antibiotics for as long as possible.

That is why we are setting up various actions to limit antibiotic resistance. We are investing in training and raising awareness with veterinarians and livestock farmers. We also organise and support symposia, poster campaigns, the e-formularium and the e-learning module, 'Proper use of antibiotics'. We also conduct research into alternatives to antibiotics, co-finance data collection by AMCRA (see below) and participate in European initiatives.

A new four-year vision for AMCRA

pharma.be has re-committed , together with 21 other signatories, to the AMCRA four-year vision. The first joint action plan in the fight against antibiotic resistance ran from 2014 to 2020. Three objectives were set (with 2011 as reference year):

1. 50 % less use of antibiotics by 2020
2. 75 % reduction in use of the most critically important antibiotics by 2020
3. 50 % reduction in medicated feed by 2017

Despite all efforts, two of the three targets were not met:

1. In 2020, after six years of decrease in a row, there was a slight increase again in the total use of antibiotics. Consequently, between 2011 and 2021, the use dropped by only 40.2 % instead of 50 %.
2. In 2020, the use of the most critically important antibiotics also increased. As a result, only a 70.1 % reduction was achieved, instead of 75 %.

The fight against antibiotic resistance is clearly not over. That is why pharma.be, together with the other partners of AMCRA, has developed a new four-year vision. The 2021-2024 vision focuses on minimising antimicrobial prescriptions for all animal species and by all veterinarians.

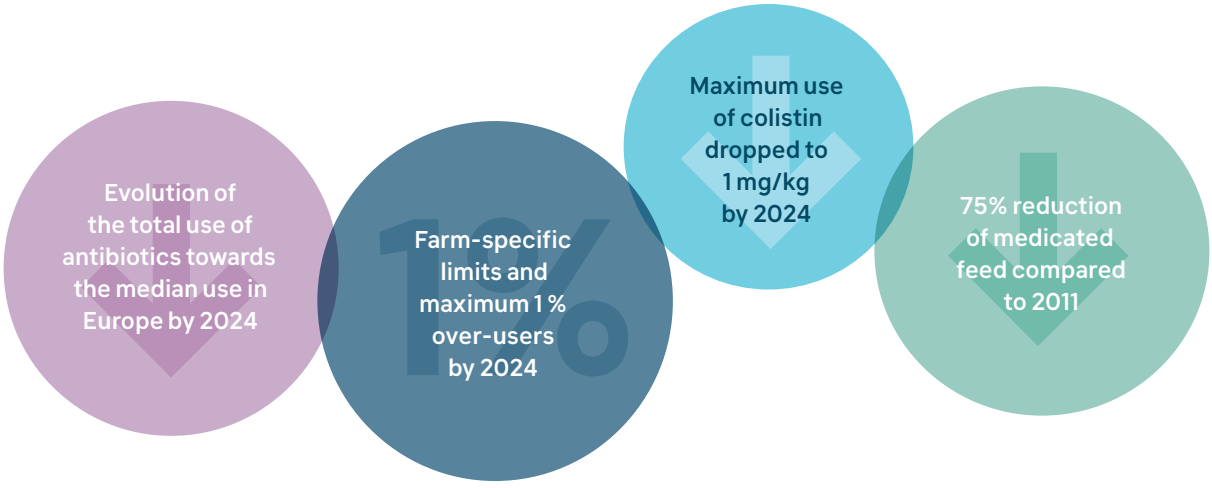
Four main objectives are set:

Who or what is AMCRA?

AMCRA stands for **Antimicrobial Consumption & Resistance in Animals**. AMCRA is a federal knowledge centre dedicated to the reduction of antibiotic resistance and antibiotic use in animals in Belgium. The organisation collects and analyses relevant data and uses these data to raise awareness with veterinarians and animal owners and to provide targeted advice.

It is no coincidence that **the Animal Health Group of pharma.be was one of the co-founders of AMCRA** in 2012. AMCRA's objectives largely reflect the vision of our own organisation.

pharma.be aims to ensure that sick animals in Belgium can be treated with high-quality veterinary medicines. The One Health concept is key in this respect: animal health, human health and environment health are all closely connected, and affect one another. Sustainable use of antibiotics in veterinary medicine is, therefore, important to help safeguard public health.



4.2 Working together for the benefit of the patient

The COVID-19 crisis has demonstrated once again that health and healthcare are not the responsibility of one individual or one agency. It is a complex system that requires an integrated approach. Registration and analysis of data are crucial in this respect.

Therefore, collaboration is not merely convenient, it is a prerequisite for health and innovation. That is why pharma.be is making a continuous effort to build sustainable, high-level collaborations, whether in terms of collecting data or ensuring the availability of medicines.

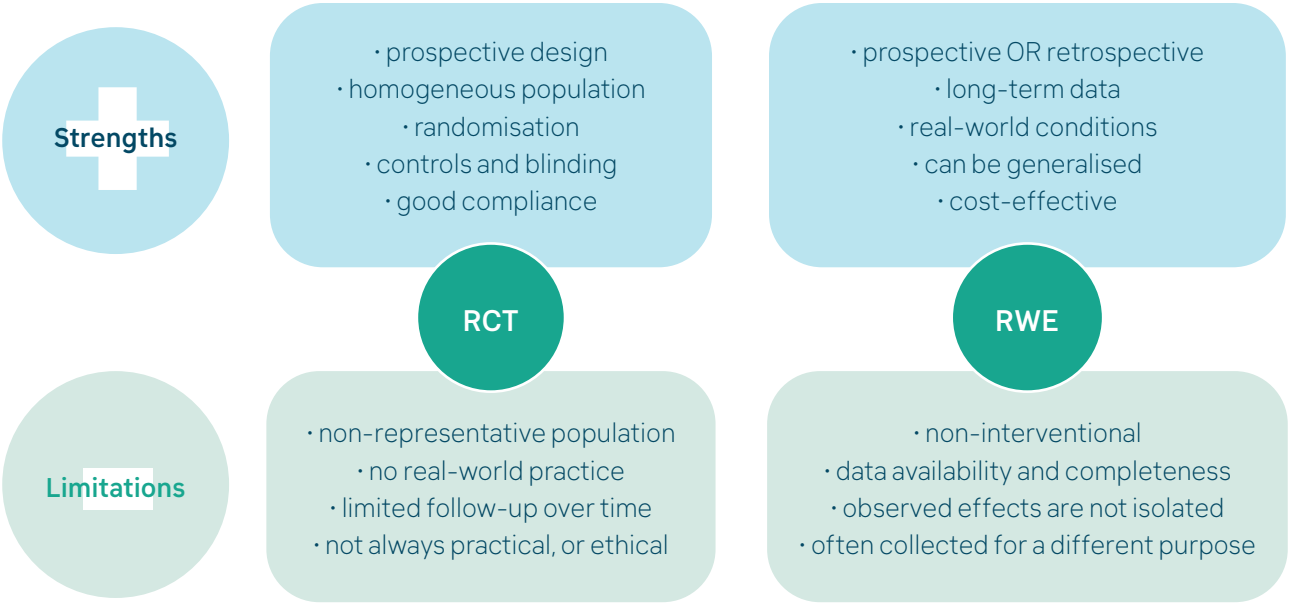
4.2.1 Working together for relevant health data

Real World Data and Real World Evidence

Real World Data (RWD) is an umbrella term for data on the effects of health interventions (such as safety or effectiveness) that are not collected in the context of highly controlled **randomised clinical trials (RCTs)**.[68]

RWD may include, for example, clinical and economic outcomes, administrative data, patient-reported outcomes (PROs) and health-related quality of life (HRQoL). RWD are collected from a wide variety of sources, including patient registries, electronic health records or health insurance databases.

The US Food and Drug Administration (FDA) defines **Real World Evidence (RWE)** as the clinical evidence regarding the use and potential benefits or risks of a medical product derived from analysis of RWD. RWE complements traditional clinical trials to provide validation in everyday clinical practice.



RWD in the life cycle of a medicine to the benefit of the patient

In addition to data from clinical trials, biopharmaceutical research also uses RWD throughout the life cycle of a drug. These RWD studies lead to more insights and better treatments to the benefit of the patient.

Some examples of the use of RWD:

R&D phase

- to understand how a disease works or other epidemiological studies to develop new treatments for unmet medical needs
- to improve a clinical trial design or to identify the population and to speed up patient recruitment
- to perform genetic testing or virtual drug design to accelerate the development of new medicines or to get the right medicine to the patient faster (personalised medicine)

Reimbursement phase

- collecting information on the patient population, cost-effectiveness and outcomes in order to maximise patient access to the new innovative medicine

Outcome phase

- reporting information on safety, treatment adherence and active patient follow-up to improve future innovations
- re-use of collected RWD to optimise the patient's treatment trajectory

A health data ecosystem

Data are at the basis of all biopharmaceutical research. Studies can only be realised because HCPs register data about the patient. These data are then anonymised and made available for research. That research leads to the development of new or improved treatments for patients. And the treatment outcomes, in turn, create new data.

In this way, a 'health data ecosystem' is created in which each partner contributes to registering, collecting, making available, analysing and, finally, translating the best possible data into an improvement in healthcare.

The leading role in this ecosystem is not reserved for data collected within the strict context of a laboratory. All kinds of RWD can be relevant for the development of effective treatments and for making well-informed decisions.

Along with other stakeholders, pharma.be is building this ecosystem of RWD health data that gives a boost to Belgian biopharmaceutical sciences, academic research and, above all, health outcomes.[69]

pharma.be and RWD

As RWD are a crucial innovation resource and thus ultimately benefit patients and healthcare, we put in extra effort to inform our members about RWD and to make RWD available.

Each year we organise an information session on RWD for our members and partners. During this session, database owners present their databases and show attendants how they can access and use these health data. We also showcase international use cases and invite Belgian policymakers to present the newest policy plans for health data. The focus of these sessions is on potential collaborations and the creation of added value.

RWD or outcomes managers of biopharmaceutical companies share their insights and best practices of RWD databases and RWD projects within our RWE working group. This working group gathers practical examples and experiences and provides input to improve the collection and FAIRification of health data in Belgium. The working group has built outstanding expertise and vision in the past few years, sharing it with Belgian policymakers and other stakeholders.

4.2.2 Working together for the availability of medicines

Medicines should always be available whenever patients need them. In reality, however, medicines sometimes are temporarily not available. This has to do with the complex production process and the various quality control checks. These checks are crucial if we want to guarantee the quality and safety of our medicines. Because of this, we can never fully exclude the possibility that the production of medicines is delayed. Therefore, we will never be able to guarantee 100 % availability of a medicine.

That is why pharma.be, together with the FAMHP and all stakeholders within the distribution chain, is looking for solutions to minimise the impact of non-availability of medicines on patients.

This means, in the first place, **being transparent and providing clear information about unavailable medicines**. The FAMHP's online application FarmaStatus plays an important role in this. Thanks to FarmaStatus, doctors, pharmacists and patients can easily check how long their medicine will be unavailable and why. Through FarmaStatus, the FAMHP can also provide alternatives for unavailable medicines. Finally, using FarmaStatus, wholesale distributors, pharmacists and companies can work together to find solutions if a medicine is unavailable in a pharmacy or at a wholesale distributor.

Together, we are also looking for ways to ensure that medicines destined for the Belgian market actually benefit Belgian patients. Where possible, the regulatory framework is being adapted to avoid the temporary unavailability of medicines without any negative impact on quality and safety. All this is intended to make sure that the number of unavailable medicines remains limited and that the impact on patients is minimal.

Looking at the actual figures from June 2020, **514 medicines were temporarily unavailable**. Although this has an impact on the patient and carer (getting a new prescription, extra visits to the pharmacy), there is very little impact on the continuity of treatment. **In 384 cases there was at least one alternative available**, and in 340 cases patients had three or more alternatives. **There was only one case of critical unavailability**. In this case the FAMHP launched a working group to formulate recommendations to guarantee the care of the patients concerned.

Scan me for more information!

4.2.3
Working together with patient organisations

Collaboration with the patients themselves is, of course, central at all times and all places:

1.
Since 2019, pharma.be has been a member of the **Patient Expert Center** (PEC). The PEC aims to improve the quality of life and healthcare experience of patients. The PEC realises this by coordinating the training of experts, by experience, to become accredited patient experts, together with patient organisations in various therapeutic areas.

2.
In Belgium there is no specific regulatory framework for collaborations between patient organisations and the biopharmaceutical industry. That is why pharma.be and EFPIA have drawn up **sector-specific guidelines**. In our Code of Deontology (see 4.1.1) there is a chapter on interactions with patient organisations. It contains the general principles to be respected by companies when working with a patient organisation.

Furthermore, since 2020, all rules for interactions with HPCs and HOs are also applicable to interactions with patient organisations.

3. In 2020, a **global review** was launched on the involvement of patients in the activities of biopharmaceutical companies. For this purpose, we have set up a special working group at pharma.be.

APPENDIX 1

Cost-benefit analysis methodology

In **3.2.2** we provided a summary of the cost-benefit analysis of the biopharmaceutical industry for the Belgian government. Below are the detailed statements of expenditure and income on which this analysis was based.

Detailed breakdown of expenditures (in duizend euro)

Costs for the government (2018)	**3,466,453**
1.1. State expenditure on medicinal products (industry costs, without VAT) - NIHDI	3,418,964
1.2. Grants	47,488

State expenditure on medicines is based on the NIHDI figures of expenditures on biopharmaceutical specialties, composed of the ex-factory price of medicines, distribution costs and VAT. In this analysis, we only take into account the ex-factory price, excluding distribution costs and VAT.

The amount of grants paid by the State to the biopharmaceutical industry is based on the financial statements of companies operating in Belgium, i.e. ASC 740 (operating subsidies and compensatory amounts received from public authorities), 9,125 (capital subsidies granted by public authorities) and 9,126 (interest subsidies granted by public authorities).

Detailed income statement (in duizend euro)

Revenues for the government (2018)	**4,063,265**
2.1. Labour charges	1,963,096
2.1.1. Employers' contribution for social security	**724,831**
2.1.2. Employees' contribution for social security	**375,539**
2.1.3. Third parties withholding tax	**862,726**
2.2. Corporate tax	320,229
2.3. Taxes	1,040,651
2.3.1. VAT on turnover (6 % ex-factory price non-reimbursable drugs)	**120,104**
2.3.2. NIHDI taxes on turnover	**399,283**
2.3.3. Third parties withholding tax	**33,836**
2.3.4. Corporate income taxes	**487,427**
2.4. Indirect revenue from third party transactions and investments	739,288
2.4.1. Raw material and commodity purchasing, miscellaneous goods and services	**697,263**
2.4.2. Investments	**42,025**

The income from labour charges is based on the financial statements of companies operating in Belgium, i.e. ASC 621 (employers' contribution for social security), 620 (remuneration and direct social benefits, part of social security) and 9147 (withholding tax on professional income). The same applies to corporate taxes. Here it concerns ASC 670 (income taxes).

Taxes are divided into four elements:

1. VAT on non-reimbursable medicines
   To calculate this, we used the turnover figure for non-reimbursable drugs as indicated by IQVIA. We do not take into account the VAT on reimbursed drugs since this is paid to the government by the NIHDI, having no effect on the comparison.

2. the taxes companies pay to the NIHDI based on their turnover

3. balance sheet ASC 9148 (withholding tax)

4. balance sheet ASC 640 (business taxes)

In addition to direct revenues, there are also indirect revenues for the government:

1. revenue generated by the biopharmaceutical industry's domestic purchases of raw materials, commodities, miscellaneous goods and services

   The calculation is based on information from the input-output tables (Federal Planning Bureau), which show the domestic demand of the biopharmaceutical sector for the other sectors. For each sector, we apply to this domestic demand the ratio of added value to turnover (also available in the input-output tables). We then apply the average (para)fiscal tax rate (44.9 %, OECD).

2. *revenue from investments by the biopharmaceutical industry*

   To the number of investments, based on Statbel data, we apply the ratio of added value to turnover for the manufacturing industry. Then the average (para)fiscal tax rate is applied (44.9 %, OECD).

APPENDIX 2
List of abbreviations

AD	Atopic Dermatitis
AMCRA	Antimicrobial Consumption and Resistance in Animals
API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Chemical
ATV	Added Therapeutic Value
BCPI	Belgian Centre for Pharmacotherapeutic Information
CHD	Coronary Heart Disease
COPD	Chronic Obstructive Pulmonary Disease
CUP	Compassionate Use Programme
DALY	Disability Adjusted Life Years
DEP Committee	Committee for Deontology and Ethics in the Pharmaceutical Industry
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
E-PIL	Electronic Patient Information Leaflet
ETA	Early Temporary Authorisation
FAIR	Findability, Accessibility, Interoperability, and Reusability
FAMHP	Federal Agency for Medicines and Health Products
FDA	Food and Drug Administration
GDP	Good Distribution Practice
HCC	Hepatocellular Carcinoma
HO	Healthcare Organisation
HCP	Healthcare Professional
HRQoL	Health-Related Quality of Life
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
NIHDI	National Institute for Health and Disability Insurance
MNP	Medical Need Programme
OECD	Organisation for Economic Co-operation and Development
PAD	Peripheral Artery Disease
PEC	Patient Expert Centre
PO	Patient Organisation
PRO	Patient-Reported Outcomes
QALY	Quality-Adjusted Life-Year
RCT	Randomised Controlled Trial
RWD	Real World Data
RWE	Real World Evidence
SmPC	Summary of Product Characteristics
Statbel	the Belgian statistical office

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ASBL/VZW — 0407.622.902 — RPR Brussel — Legal deposit: D/2021/4021/09
Responsible editor: Caroline Ven, Chaussée de La Hulpe 166 - Terhulpensesteenweg, 1170 Brussels, Belgium
VAT BE 0407.622.902 — Company number 0402.622.902
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