Report to Society 2022

pharma.be

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

Table of contents

Foreword

The biopharmaceutical industry's main contribution to society is undeniably to develop new treatments that improve the health of patients. During the COVID-19 pandemic, much of the health system's attention went to fighting and controlling this virus. As a result, the number of newly reimbursed drugs fell drastically in 2020. In 2021, there was a sharp catch-up of cases that were put on hold by COVID-19. In particular, we note a strong increase in reimbursement of medicines for rare diseases and drugs with added therapeutic value. These offer hope to patients for whom no adequate treatment was previously available.

A long process precedes the introduction of a vaccine or a medicine on the market. In 2021, biopharmaceutical companies invested heavily in research and development and clinical trials. Eighty per cent of the 574 approved clinical trials in Belgium in 2021 were applied for by companies. The focus is mainly on cancer research. Members of pharma.be are also active in the development of Advanced Therapy Medicinal Products (ATMPs). These are breakthrough drugs based on cell, gene or tissue. By acting on them, the cause of a disease is directly addressed and there is the prospect of a complete cure.

The rapid and revolutionary developments in drug research would not be possible without intellectual property rights. They allow the invention of the company that developed the drug to be protected for a limited time. In return, information about the invention is disclosed and published so that the knowledge is shared with others. This year, pharma.be published a brochure to explain the importance of patents. Indeed, the patents on the COVID-19 vaccines came under fire, alleging they would stand in the way of a rapid global vaccination campaign. However, nothing could be further from the truth. Without the protection of intellectual property rights, expensive and uncertain research and development activities could be slowed or even cease altogether.

Caroline Ven
CEO

The biopharmaceutical sector is one of the cornerstones of the Belgian economy, creating significant additional employment in recent years. But the sector faces many challenges. With our second Report to Society, pharma.be will illustrate the added value the sector creates for patients and society. We encourage other actors in the health system and policy to join us in our efforts to perpetuate the leading position our country holds in the field of research, development and production of innovative medicines, and to give Belgian patients access to these treatments as soon as possible.

Who we are

1

1.1 For the patient's benefit

pharma.be is the ambassador of 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 your life to the fullest. Spending 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 about **42,000** people at 128 companies focused on the research and development (R&D) 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 to develop health solutions to ensure Belgium is the healthiest place to 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, or turned HIV into a manageable chronic condition

.

But science is a tool, not an end in itself. We are passionate about science but only because it 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 we 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, accredited health insurance funds, 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.

1.2 128 members

pharma.be brings together **128 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 research and development, clinical trials, production and distribution of medicines.

Together, they represent:

- → **10 %** of the contribution of the innovative biopharmaceutical industry in Belgium
- → **4,005 jobs** in 2021
- → **597** medicines on the market by 2022
- → **193,869 €** added value per employee in 2021

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 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.

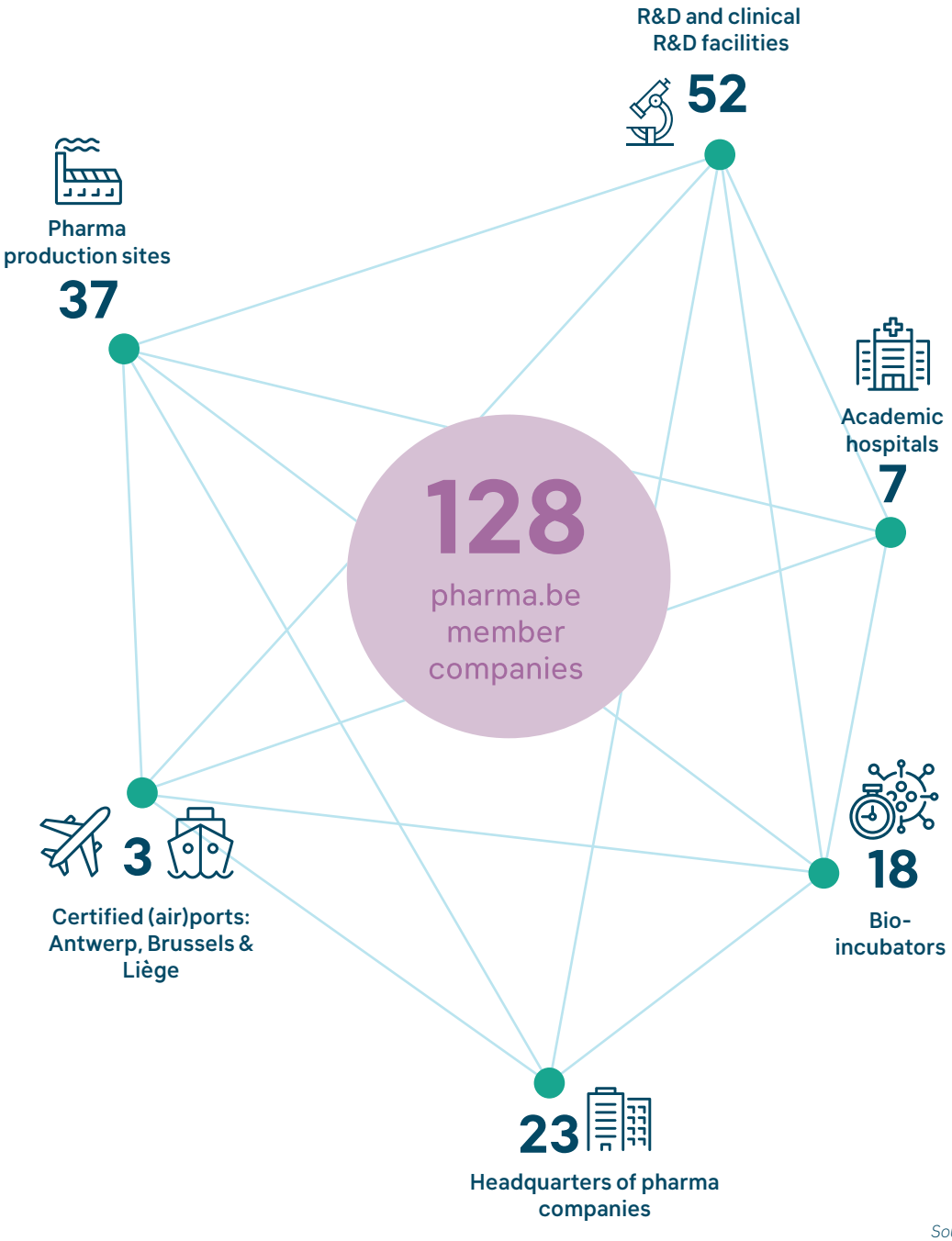
The Animal Health Group accounts for:

- → **14 members**
- → **more than 1,500** different veterinary medicines
- → **274** available immunological drugs (including vaccines) in Belgium in 2022

Discover our members

1.3 Part of a large ecosystem

The members of pharma.be are part of a Belgian biopharmaceutical ecosystem, together with universities and research institutes, teaching hospitals and pharmaceutical incubators, and also logistics players such as airports and the Port of Antwerp-Bruges, among others.

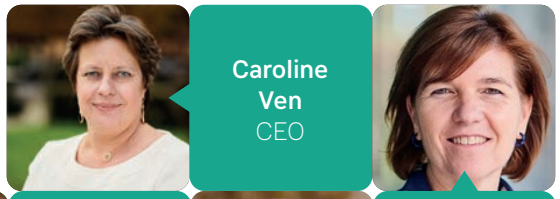


Source: pharma.be

1.4 A team of experts

The pharma.be team consists of 26 highly motivated employees with a variety of skills and expertise. They provide services to our member companies, represent them on relevant councils, committees, and advisory bodies, and promote their interests at various levels.

Meet the pharma.be team



Caroline Ven
CEO

Geert Steurs
Economics Director - Chief Economist

Herman Van Eeckhout
Political & Finance Director

David Gering
Communications Director

Ann Adriaensen
Secretary General & Public Health Director

Julie Gusman
Market Access Services Director

Marjan Willaert
Policy Advisor – Market Access

Marc Malfait
Market Access Advisor

Hanne Wouters
Market Access Advisor

Magali Audiart
Pricing & Market Access Advisor

Johan De Haes
Public & Animal Health Advisor - SME Account Manager

Nathalie Lambot
Public Health & Clinical Trials Advisor

Marie Vande Ginste
Public Health Advisor

Karen Crabbé
Economic & Health Data Advisor

Thomas Cloots
Economic Advisor

Tom De Spiegelaere
Healthcare Budget Advisor

Charlotte Weyne
Senior Legal Counsel & EU Policy Advisor

Marie-Charlotte Destrée
Legal Counsel

Chloé Legrand
Members, Partners & Office Assistant

Anne-Sophie Doms
Content Manager

Annick Vancutsem
Members, Partners & Office Assistant

Denise Blockmans
Webmaster & ICT Manager

Melanie Balcaen
Finance & HR Manager

Carine Vancutsem
Members, Partners & Office Manager

Britt Hunninck
Members, Partners & Office Assistant

Armand Voorschuur
EU Policy and Market Access Advisor

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 Frédéric Clais (Eli Lilly Benelux). Vice-Chair is An Van Gerven (Pfizer). Board members are elected at the General Assembly and hold office for a term of three years.

1 Frédéric Clais Eli Lilly Benelux, **Chair pharma.be 2 An Van Gerven** Pfizer, **Vice-Chair pharma.be 3 Renaud Decroix** AbbVie **4 Gabor Sztaniszlav** Amgen **5 Keira Driansky** AstraZeneca **6 Sally McNab** Bristol-Myers Squibb Belgium **7 Sabena Solomon** GlaxoSmithKline Pharmaceuticals **8 Maria Fernanda Prado** Janssen-Cilag **9 Brecht Vanneste** MSD Belgium **10 Federico Mambretti** Novartis **11 Marie-José Borst** Roche **12 Johan Heylen** Sanofi Belgium **13 Michael Nesrallah** Takeda Belgium **14 Willy Cnops** UCB Pharma **15 Paul Newton** Vertex Pharmaceuticals

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 members and service providers, we 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.

By 2022, 50 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 medicines, and logistics.

Discover
our partners

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 37 national associations, 38 leading pharmaceutical 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 treatments 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 innovative biopharmaceutical companies and regional and national associations across the world.

The pharma.be practical guide on medicines law

Recent years have clearly shown that public health and the pharmaceutical sector are hot topics. They are also constantly evolving, which regularly leads to new legal questions that need to be answered quickly and efficiently.

Many of the answers can be found in the Human Medicines Act, which is the basis for the regulation of medicines in Belgium. This law is one of the pillars of the legal framework within which biopharmaceutical companies operate in Belgium. It applies to medicines throughout much of their life cycle: from the application for marketing authorisation, through manufacturing and distribution, to drug safety monitoring and advertising.

But it is sometimes difficult to find complete and concrete information on which to base the application of the legal provisions to practical cases. To meet this challenge, pharma.be has published a pragmatic and clear reference work with a legal overview of pharmaceutical law.

The concept of the Practical Guide is simple: it contains a commentary on each of the sections of the Medicines Act. The commentaries are written as functionally as possible:

- → they contain concrete information on the practical implementation of the law
- → the context in which its provisions were adopted
- → their implementation by the authorities
- → as well as references to relevant doctrine and case law

The practical legal analyses are written by experts in pharmaceutical law and life sciences, most of whom are partners of pharma.be. The result shows, once again, that there is a wealth of legal expertise in Belgium on which all stakeholders in the healthcare sector can rely.

Learn more about the Practical Guide to the Human Medicines Act (in French):

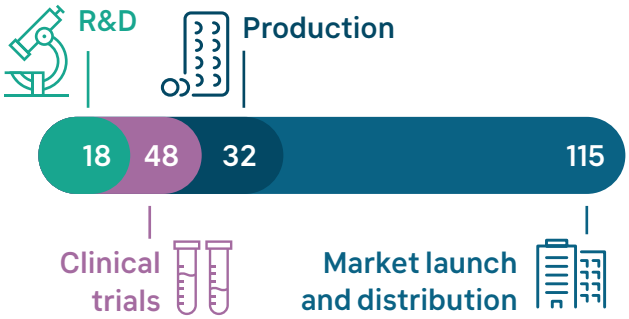
What we do

2

2.1 Operating throughout the entire value chain

As a whole, pharma.be member companies significantly contribute **to every key aspect of the biopharmaceutical value chain** (i.e. R&D and 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 strong cooperation with governments and research centres.

Number of companies in Belgium



Source: pharma.be

An integrated value chain approach comes with substantial benefits, both 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

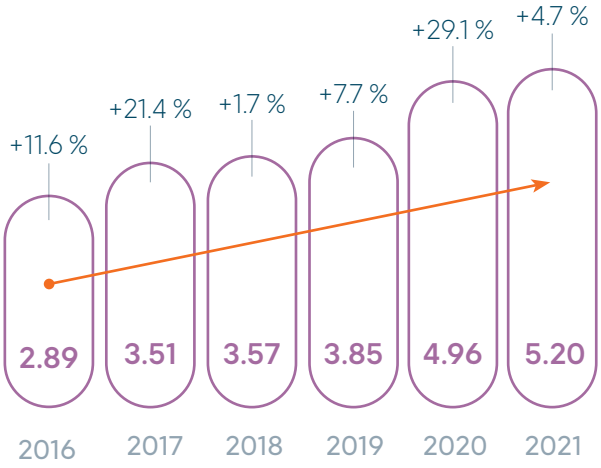
2.2.1 R&D investments in Belgium

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). However, this leading position is not a given. To maintain this position, our companies are increasingly investing in R&D:

- → In 2021, the sector invested **over € 14 million** in R&D **every day, amounting to a total of € 5.2 billion**.
- → Since 2015, investments in R&D have more than doubled. Especially in the past two years, investments increased, by more than 35 %.
- → In 2021, on average more than one patent application was filed per day in Belgium in the field of biotechnology and pharmaceuticals.
- → Since 2015, the number of patent applications in those fields has increased by almost two-thirds.

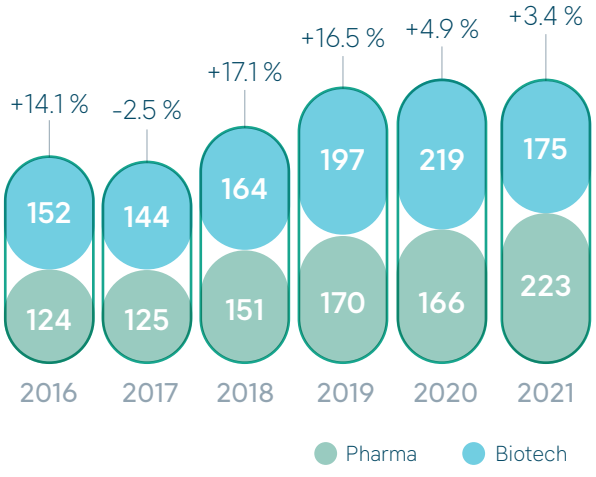
The COVID-19 pandemic temporarily shifted the focus, but meanwhile the search for innovative solutions in all therapeutic areas continues.

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 2011-2021 per field of technology

Patents on drugs and vaccines: pharma.be joins discussions on their importance for patients, society and the industry

Intellectual property rights, including patents, are a cornerstone of our innovation system. Patents temporarily give its applicant the right to protect the invention. In return, critical information about the invention must be disclosed. During the COVID-19 pandemic, a fierce debate arose over vaccine patents. Is it okay for life-saving vaccines to be protected by a patent? In general, are patents a good idea for an important industry like pharmaceuticals? Don't medicines belong to everyone?

Recognising the societal relevance of these questions, pharma.be published a brochure that frames the discussion around patents in an effort to create greater understanding about the role, need and benefits of patents. After all, the importance of patents for patients, society and the sector cannot be underestimated: they help make investments possible, facilitate cooperation with the other actors in the ecosystem, and keep the whole engine of innovation in healthcare running. Not surprisingly, the number of patent applications is one of the indicators the European Commission includes in its Innovation Scoreboard, which measures the research and innovation strength of member states. Important here is the forward-looking nature of patents. At the time of application, the potential value of an invention or innovation is often unknown. A long and often expensive development process follows, which, ultimately, may or may not be successful.

"The existence of patents in the health sector is sometimes questioned. Yet this protection of intellectual property is essential for innovation and thus for the economy and society. Belgium's position would not be what it is in life sciences without the existence of intellectual property protection worthy of the name."

Bruno Wattenbergh, Chairman Innovation Board EY Belgium
and Professor of Strategy and Entrepreneurship at Solvay Business School

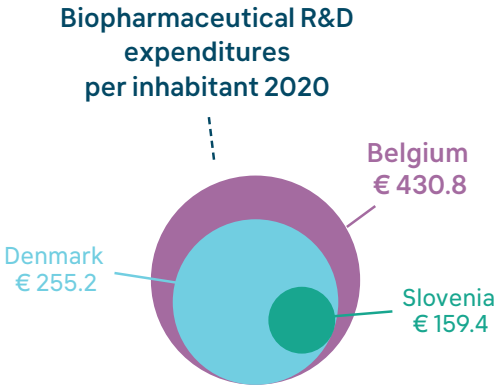
The brochure can be found here (French)

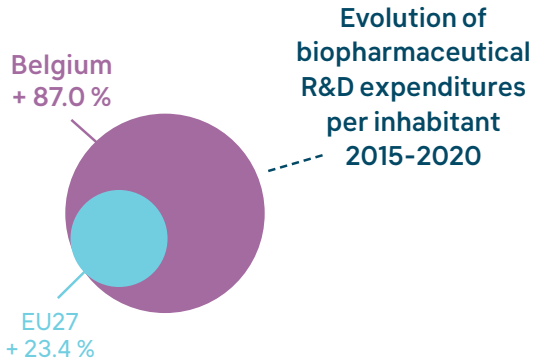
2.2.2
R&D investments compared to Europe

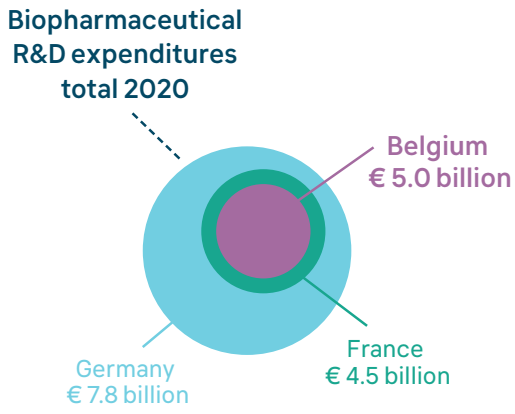
Although Belgium is a relatively small country, the people and the healthcare system can count on a proportionately high investment in biopharmaceutical innovation. **The total amount of R&D investment in the Belgian biopharmaceutical sector is comparable to that of much larger European countries**. The 2020 figures (the most recent data available) show that Belgium ranks second, after Germany, and ahead of countries such as France and Italy, while ranking only 8th in terms of population.

Looking at investment per inhabitant, Belgium is the absolute leader. Our investments in 2020 were almost 70 % higher than those of Denmark, second in the ranking, and were as much as almost three times higher than investments in Slovenia, number three in the ranking.

Over the period 2015-2020, R&D investments per inhabitant increased by more than 87 %, almost four times as much as the growth of the total EU27 R&D expenditures per inhabitant. The other top three countries in 2015, including current number two Denmark, registered nega–tive growth.







Sources: pharma.be, survey amongst members & EFPIA, The Pharmaceutical Industry in Figures, Key Data 2022

The biopharmaceutical sector as a driver for an innovative Belgium

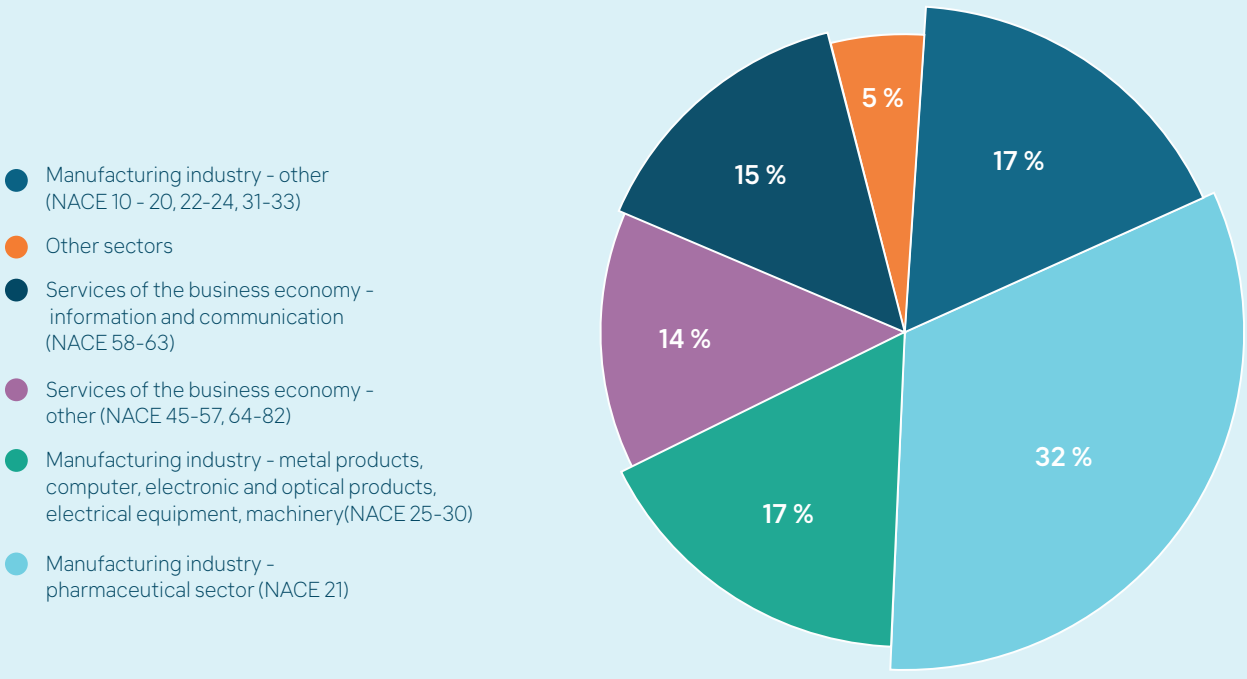
Belgium has come a long way to get to where it is today: an innovation leader, according to the European Innovation Scoreboard[1]. Years of joint efforts by knowledge institutions, companies and governments have ensured that Belgium ranks fifth within the EU in 2022. Belgium outperforms the EU average by some 29 % and follows only Sweden, Finland, Denmark and the Netherlands.

This strong innovation performance is also reflected in the figures on the share of R&D expenditures of GDP. Whereas this was less than 2.5 % in 2015, it exceeded 3 % in 2019 (the so-called Lisbon target). With a 3.5 % share of R&D expenditures of GDP in 2020, Belgium ranks first in the EU together with Sweden.[2]

The contribution of the business sector to this result is crucial, with an estimated 2.49 % share by 2020, or almost three quarters of the Belgian total[3]. Companies are thus clearly driving R&D investment in Belgium. The biopharmaceutical sector is at the forefront of this. It is the sector with by far the largest R&D investment, accounting for a third of total R&D business investment in Belgium[4].

Moreover, the sector's investment in R&D is growing faster compared to other sectors as a whole, increasing its substantial contribution year after year. The Belgian biopharmaceutical sector is therefore crucial to Belgium's exceptional performance and achievement of the Lisbon target.

SECTOR SHARE OF R&D EXPENDITURES BY THE MANUFACTURING INDUSTRY



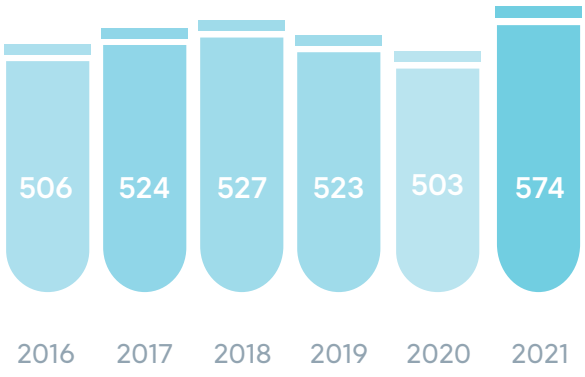
Source: Belspo, Total intramural expenditure for R&D

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**. This also provides valuable new insights into the treatment or prevention of diseases. Clinical studies are therefore an important source of inspiration for new basic scientific research. At the same time, clinical trials **provide patients with free and early access to the latest treatments** even before they are commercially available on the market.

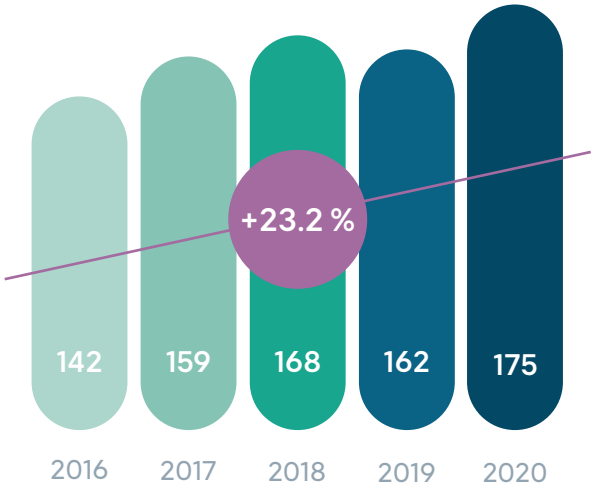
In **2021**, Belgium also confirmed its position as European leader in clinical trials, **with 574 authorised clinical trials, 80 % of which were initiated by biopharmaceutical companies**. This leading position is the result of a combination of various elements: the large number and accumulated expertise of the biopharmaceutical companies, the quality of the scientific community, the infrastructure of research centres and hospitals, a high-level of scientific community, state-of-the-art research and hospital infrastructure, and the level of expertise of researchers and the authorities involved, particularly the Federal Agency for Medicines and Health Products (FAMHP).

Number of authorised clinical trials



Source: FAMHP data

Evolution of CTAs for cancer in Belgium



Source: Deloitte report "Belgium as a clinical trials location in Europe – key results 2020"

The large number of clinical trials shows that biopharmaceutical companies keep investing in our country to find new solutions for a wide range of therapeutic areas. Studies on treatments for viral diseases and disorders of the nervous system are among the top three clinical studies in Belgium. Ranking number one is the research into drugs to fight cancer.

For example, 175 clinical trials were launched in Belgium in 2020 to treat cancer, or just under 15 new trials per month. 19 % of the clinical trials conducted in Europe in 2020 to test cancer drugs occurred in Belgium.

Clinicaltrial.be: a portal site for clinical trials

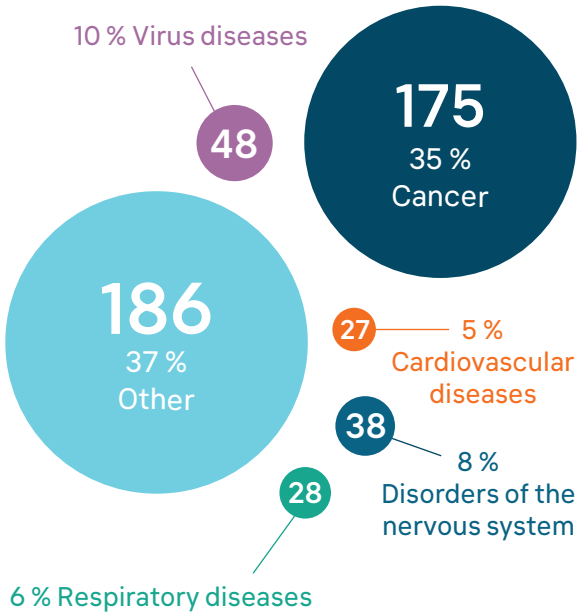
New technologies and breakthroughs follow each other at lightning speed in the biopharmaceutical sector (see also 3.1). It is crucial that patients have access to these innovations as soon as possible. Clinical trials can play a major role in this. However, the prerequisite is that doctors and patients are aware of what studies are running, which is not the case today. That is why Patient Centrics - Esperity is currently working on a clinical trial portal site, clinicaltrial.be.

Pooling information on clinical studies seems obvious, but there are many aspects involved. At the European level, there is an official database that lists all approved clinical studies; however, the information is only in English and it is not always easy to navigate the extensive data. In turn, the FAMHP database is limited to clinical trials in Belgium, which may not be as useful for patients with a rare disorder who may benefit from looking across the border.

Many actors are also involved: besides pharmaceutical companies, research institutes or hospitals, and even individual researchers set up clinical studies. Information dissemination can be equally diverse: by the companies, via hospital portals, or by patient organisations that try to bundle everything by condition. Crucial, of course, is also the reliability of the data. A single official source is needed to provide all approved information to the various stakeholders. The database of the European Medicines Agency (EMA) seems a logical source, but the drawback is that the EMA limits itself to studies of drugs. Tests of medical devices cannot be found in the database, even though they can significantly improve patients' quality of life.

So, the need for comprehensive yet clear and easily accessible information on clinical trials is high. Patient Centrics - Esperity has taken up the challenge and, among other things, is developing the portal clinicaltrial.be together with industry, patients and academia. The portal is compiling information on clinical studies in Belgium and abroad, and makes it available in French and Dutch.

Proportion of CTA's for selected disease areas in Belgium (2020)



Source : Deloitte report "Belgium as a clinical trials location in Europe – key results 2020"

It is important for both patients and their physicians that there is clear, accessible and preferably centralised information about all ongoing clinical trials in Belgium. The situation is not optimal today. This is why pharma.be supports initiatives to set up a portal site offering official information on approved studies in Belgium in French and Dutch (see box).

"Some people want to participate in clinical trials out of pure altruism, in other cases it's about patients with a particular medical need. For example, they suffer from a rare disease for which no medication exists, or the medication they are currently taking has too many side effects or insufficient effect. We believe that clinical trials, if medically justified, should become a treatment option in their own right. Doctors should always remain the point of contact for patients seeking more information about studies, but the portal can help people with a medical need ask questions."

Mitchell Silva, CEO of Patient Centrics - Esperity

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 National Institute for Sickness and Disability Insurance (NIHDI) so that patients do not have to pay the full cost.

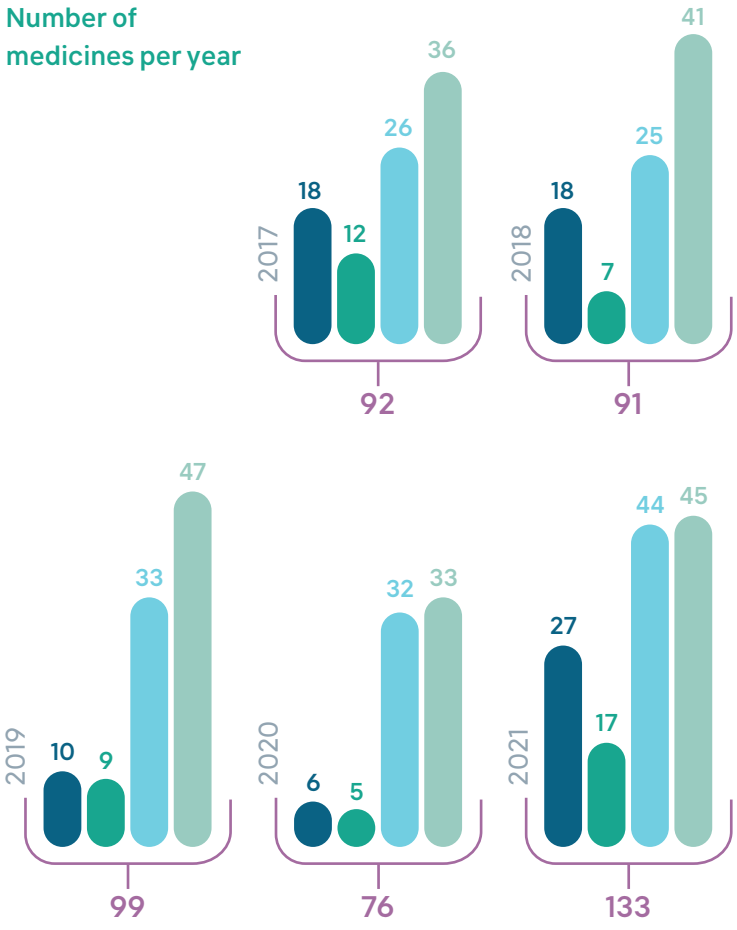
Below, we provide more information on the evolution of the number of newly reimbursed medicines in Belgium. In chapter 3, we will focus on their added value.

2.4 .1 According to type

The total number of newly reimbursed medicines increased from 2017 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.

In 2021, the number of reimbursed medicines just about doubled compared to 2020 thanks to a catch-up of applications that were put on hold in 2020. The impact is striking for medicines with added therapeutic value and orphan drugs.

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.

- Innovation with ATV
- Orphan disease
- Me-too medicines
- New indication
- All medicines

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 2021. More than half of these were new cancer medicines or immuno-modulatory agents (ATC L). In addition, more new medicines became available for infectious diseases (ATC J), blood disorders (ATC B), diseases related to the alimentary tract and metabolism (ATC A) and diseases of the respiratory system (ATC R).

ATC classification	Number of medicines reimbursed in 2021	ATC groups	Examples of pathologies
A	9	Alimentary tract and metabolism	Diabetes, hepatic porphyria, hereditary tyrosinemia
B	10	Blood and blood-forming organs	Haemophilia A, thrombocytopenia, beta-thalassaemia
C	0	Cardiovascular system	Heart failure
D	0	Dermatology	Atopic dermatitis
G	0	Genitourinary system and sex hormones	Uterine fibroids
H	2	Systemic hormonal preparations (excluding sex hormones and insulins)	Growth retardation
J	12	Anti-infectives for systemic use	HIV infections, bacterial infections, hepatitis B
L	72	Antineoplastic and immunomodulating agents	Spinal muscular atrophy, osteoporosis, etc.
M	5	Musculoskeletal system	Spinal muscular atrophy, osteoporosis, etc.
N	8	Nervous system	Migraine, epilepsy, severe depression, amyloidosis…
P	0	antiparasitic products, insecticides and repellents	Anthelmintics
R	9	Respiratory system	Cystic fibrosis, asthma, obstructive airway diseases
S	3	Sensory organs	Hereditary retinal dystrophy, diabetic macular oedema
V	3	Various	Hyperkalemia, contrast medium

Source: pharma.be

3 Our added value

The innovations of the biopharmaceutical industry improve health outcomes in patients, increasing life expectancy and improving quality of life[5]:

- → Over the past 20 years, the number of premature deaths for diseases common in Belgium, such as **COPD (chronic obstructive pulmonary disease), stroke, heart failure and type I diabetes**, has fallen by 8 % to 40 % thanks to the drugs that are the main treatments for these diseases.
- → In the field of **cardiovascular diseases**, mortality has fallen by 45 % since 2000. Thanks to new drugs, deaths have fallen by 4,000 a year.
- → In the field of **diabetes**, 70 new treatments have been introduced in the past 20 years. This has led to a significant improvement in patients' quality of life.
- → Nowadays, HIV/AIDS is no longer a fatal disease but a chronic one that can be controlled with medication. About 90 % of treated patients can lead normal professional lives.

But innovative medicines also add value in many other areas: fewer operations and hospitalisations, for example, or shorter sick leave. Sometimes work incapacity can be avoided altogether, in other cases a patient can return to work more quickly after treatment. Indirectly, family and friends can also return to full-time work more quickly because the patient requires less care. All this creates a positive effect on the labour market. It also immediately reduces costs for the government and creates added value for the economy and society.

In this chapter, we elaborate on the added value that the biopharmaceutical sector creates for **patients, the healthcare sector and society**. We illustrate this with examples of medicines that were newly reimbursed in 2021. We also briefly look ahead to promising (r)evolutions in the biopharmaceutical sector. However, the story does not stop there. Our sector is also an important driver of our **knowledge economy**. Employment and export figures were already impressive and have only continued to grow in 2021. This is reflected in the positive cost-benefit analysis of our sector for the Belgian government.

3.1 A positive impact for patients, healthcare sector and society

3.1.1 Added value of newly reimbursed medicines

In 2021, many new drugs received approval for reimbursement (see 2.4), providing significant added value for patients. Following are some examples of therapeutic added value recognition by the Commission for the Reimbursement of Medicines (CTG), and orphan drugs.

Short bowel syndrome with intestinal failure

Short bowel syndrome with intestinal failure, or SBS-IF, reduces bowel function below the minimum required for absorption of macronutrients, water and electrolytes. This makes it necessary for the patient to receive intravenous supplementation. SBS-IF often results from (partial) removal of the small intestine because of a vascular event, Crohn's disease, surgical complications or congenital disorders[6].

To survive, patients with SBS-IF need long-term parenteral nutrition (PN). This is nutrition administered through a catheter directly into a vein. The administration takes place on average five nights a week. Prolonged PN not only affects the patient's quality of life but is also associated with serious complications, such as the risk of infection and sepsis, thrombosis and liver disease[7].

Since 2021, a drug for SBS-IF has been reimbursed. It is an analogue of a natural growth hormone GLP-2, which plays an important role in the structure and function of the small intestine and the absorption of macronutrients, water and electrolytes. Thanks to this drug, patients need less PN, both in volume and number of days. In some cases, patients no longer need PN[8, 9, 10].

One or more days of "freedom" from PN means patients are not tied to their infusion and can do other things. Real World Data show that the quality of life of these patients improved significantly[11].

Acute myeloid leukaemia

Acute myeloid leukaemia (AML) is a rare, serious and malignant disease of the white blood cells in the bone marrow[12]. AML interferes with normal blood formation. Patients have non-specific symptoms such as weight loss, fatigue, fever, night sweats, loss of appetite and increased susceptibility to bleeding, bruising and infections[13]. Several gene mutations are diagnosed in AML patients; with the FLT3 mutation identified in about 30 % of patients. AML is a rapidly progressing disease and patients often relapse after treatment[14]. The prognosis after relapse is unfavourable; less than 30 % of patients are alive one year after relapse[15].

Since 2021, there is a new orphan oral drug for the treatment of adult AML patients with the FLT3 mutation who relapse after, or no longer respond to, previous treatment(s). This new treatment achieves a median survival gain of 3.7 months versus standard treatment (9.3 months compared to 5.6 months), while maintaining the same quality of life for these critically ill patients[16].

Moreover, a complete or partial response to treatment occurs in more patients (34.0 % compared to 15.3 % with standard treatment). This allows more patients to proceed to stem cell transplantation (25.5 % vs 15.3 %)[17], currently the only possible curative treatment for AML. The oral route of administration also allows treatment in the home setting, increasing patient comfort and reducing the number of hospital visits.

Cutaneous T-cell lymphomas

Cutaneous T-cell lymphoma (CTCL) is a cancer of the white blood cells in the skin[18, 19]. It is a rare, serious and potentially fatal disease, affecting about 240 people per million in Europe[20].

Two subtypes of CTCL account for about two-thirds of cases: mycosis fungoides (MF) and Sézary syndrome (SS)[21, 22].

MF usually develops and spreads slowly and is characterised by skin symptoms, including dry or scaly patches, skin rashes and, in some cases, skin tumours[23]. SS is much more aggressive and is potentially associated with abnormal blood levels. SS causes very severe itching, total redness of the body (erythroderma) and intense skin flaking[24, 25, 26].

CTCL is often difficult to diagnose and can be confused early on with skin conditions such as eczema and psoriasis.

With chronic skin conditions, sleep disorders, psychosocial problems, stigmatisation and impact on mental health are significant. Even at an early stage, the disease can have a significant impact on the patient's daily life. Working or studying becomes difficult and normal daily activities are restricted. CTCL can also be quite stressful for caregivers.

Today, thanks to new scientific breakthroughs, we have systemic therapies that address the underlying cause of CTCL. This increases progression-free survival and improves the overall response and quality oflife of people living with this disease.

Amyloid transthyretin cardiomyopathy

Amyloid transthyretin cardiomyopathy (ATTR-CM) is a disabling stacking disease. Proteins produced by the body are folded into the wrong shape, clumping together to form amyloid fibres, and cause damage to the heart muscle. This leads to cardiac arrhythmias and heart failure, among other things. If ATTR-CM is not treated, the prognosis is very bleak, with a limited survival time. The hereditary form affects about one in 100,000 Europeans. The age-related wild-type form is more common and is estimated to affect up to one in four people over the age of 80[27].

The syndrome is difficult to recognise and is often diagnosed late. This is because the condition does not follow a set pattern and causes a variety of symptoms, even outside the heart. For example, tingling in hands and fingers due to carpal tunnel syndrome is a warning sign but is not usually associated with a patient's unexplained heart failure[28].

Timely detection of ATTR-CM is extremely important for patients[29], especially now that diagnostics and treatment options are improving. Since 2021, an innovative drug has been reimbursed that aims to reduce protein accumulation, thereby delaying disease and functional limitations and increasing survival[30]. At the same time, patients' quality of life improves and they are less likely to be hospitalised[31].

Previously, there was only symptomatic treatment and organ transplantation, but due to age, concurrent diseases and donor shortage, most patients with ATTR-CM did not qualify for transplants[32]. Thus, the new drug is an important step forward and fills a high medical need.

Multiple myeloma

Multiple myeloma or Kahler's disease is a form of cancer in the bone marrow. Every year in Belgium, about 1,000 people, mostly over 55, receive this diagnosis. In patients who do not qualify for bone marrow transplantation, the average life expectancy is between 3.5 and 6 years[34].

The treatment of multiple myeloma is aimed at prolonging life and preventing relapse, while maintaining maximum quality of life. In recent years, this has evolved significantly thanks to the use of new drugs and drug combinations. In 2021, reimbursement was approved for the addition of a new drug to an existing combination in patients not previously treated.

This new combination reduces the risk of relapse or death by 47 % to 58 %[35, 36]. It also significantly improves quality of life[37, 38]. This is particularly important because within haematological cancers, patients with multiple myeloma have the worst quality of life[39].

In addition, new forms of administration can also increase the quality of treatment. For instance, instead of a long-term injection, a subcutaneous variant became available. This reduces patient time in hospital[40] and will also make home treatment possible in the future.

Ovarian cancer

Around 800 women in Belgium are affected by ovarian cancer every year[41]. The mortality rate is high due to its deep anatomical location, which usually leads to late diagnosis. Patients relapse very often, which is often fatal[42]. Genetic abnormalities (mutations) in the tumour can affect the response to treatment[43].

In 2021, a new drug was reimbursed in Belgium that adds significant value to the maintenance treatment of advanced ovarian cancer. It is the first drug that significantly reduces the risk of relapse or death in women with advanced ovarian cancer who respond to first-line chemotherapy, regardless of their mutational status[44]. A 3.5-year follow-up shows that, compared with placebo, this drug offers 34 % lower risk of relapse or exacerbation[45]. It also provides an overall higher survival rate, with a 24-month survival rate of 84 % compared with 77 % in the placebo group[46].

The drug is administered orally once a day, offering a convenient regimen for the patient[47]. Moreover, a personalised starting dose based on body weight and platelet count reduces haematological side effects[48].

Acute hepatic porphyria

Acute hepatic porphyria (AHP) is a very rare hereditary disorder caused by genetic mutations in heme biosynthesis[49]. Typically, AHP involves acute neurovisceral attacks accompanied by severe and diffuse abdominal pain. These seizures can be potentially fatal and lead to emergency hospital admission. These attacks are also often the cause of chronic symptoms that have a negative impact on daily functioning and patients' quality of life[50].

RNA interference, discovered in 1998 and awarded the Nobel Prize in medicine in 2006, offers unprecedented possibilities for treatments through the mechanism of gene silencing. It is on this mechanism of action that a new AHP treatment is based; and that has been reimbursed since 2021. It is the second representative of this new class of drugs[51]. By targeting the gene at the origin of the disease, this treatment can virtually completely suppress AHP attacks[52]. Previously, no pharmaceutical treatment succeeded in preventing seizures and had no effect on other chronic symptoms.

AHP attacks, and the associated severe disability, entail significant public costs, both at the healthcare level and at the economic level (unemployment benefits, disability, etc.). Additionally, due to the impact on working time, they reduce tax revenues. Thus, countering AHP attacks can save around € 1,700,000 per person[53].

Hereditary retinal dystrophy due to mutations of the RPE65 gene

Retinal dystrophy due to mutations in the RPE65 gene is a rare inherited disorder of the retina that occurs in an estimated 40 patients in Belgium. The RPE65 gene is responsible for making all-trans-retinyl isomerase, an enzyme necessary for the normal functioning of retinal cells. A mutation in both copies of the gene leads to a slow deterioration of vision.

Patients face increasing difficulties in avoiding obstacles, especially in low light conditions. This has a significant impact on their quality of life, mental health and development[54]. Many patients lose their sight before the age of 16. The majority are completely blind before they turn 40[55].

The gene therapy, which has been reimbursed for children and adults since 2021, consists of a virus containing normal copies of the RPE65 gene. Through a single injection into the eye, this drug releases the RPE65 gene into the cells of the retina so that they can produce the missing enzyme. This helps the cells in the retina function better and slows the progression of the disease. Only patients with enough viable retinal cells are eligible for this treatment[56, 57]. Vision recovers fairly quickly after the procedure and is protected from deterioration again for a significant period of time[58].

> *"For the first time, people with hereditary retinal disease will have access to a therapy that protects them from blindness. Today, this is a small group of patients but this is an important first step for people with inherited eye disorders."*
>
> *Prof. Bart Leroy, Medical Head of Ophthalmology at Universitair Ziekenhuis (UZ) Gent*

Spinal muscular atrophy

About 550 to 600 children with spinal muscular atrophy (SMA) are born each year in Europe. In Belgium, there are about 10. SMA is a rare, devastating genetic disease that leads to progressive muscle weakness and paralysis. Left untreated, SMA in its most severe forms can lead to permanent ventilation or death in 90 % of cases before the age of two[59, 60]. SMA is caused by a defect in a functional SMN1 gene. This leads to a progressive and irreversible loss of motor neurons, impairing motor functions[61, 62].

Since December 2021, doctors in Belgium have the opportunity to treat eligible SMA patients with a single dose gene therapy instead of lifelong treatment. This is an important milestone for patients. When administered as early as possible, this treatment can improve motor functions such as sitting, standing, walking as well as swallowing and breathing.

This innovative treatment directly addresses the underlying genetic cause of SMA. The gene therapy replaces the function of the missing or non-working SMN1 gene and provides significant clinical progress. It also improves patients' motor functions and quality of life. This was unseen in the natural history of the disease and persists today, more than five years after administration[63].

Anaemia due to β-thalassemia or myelodysplastic syndrome

Anaemia occurs when the production of red blood cells is disturbed. Anaemia occurs in the rare inherited genetic disorder β-thalassemia and in the mostly incurable haematological cancer, myelodysplastic syndrome (MDS), among others. The symptoms of anaemia are diverse and can range from fatigue and shortness of breath to eventual heart failure.

Administration of red blood cells through blood transfusion plays an important role in the treatment of patients with anaemia due to β-thalassemia and MDS. However, blood transfusions present several challenges for patients and healthcare providers. For instance, patients spend several hours in hospital during blood administration. With regular transfusions, complications also often occur, such as heart and liver diseases due to excessive iron levels, or infections and transfusion reactions that can be life-threatening[64].

A drug that can reduce the need for transfusions in patients with anaemia related to β-thalassemia and MDS has been available since 2021. The new drug promotes the production of red blood cells in the bone marrow. This reduces symptoms, decreases the need for blood transfusions as well as the risk of complications due to transfusions[65, 66].

Flu vaccination

Every year, approximately a half a million people in Belgium are affected by flu. On average, one in 1,000 flu patients develop complications requiring hospitalisation. More than 90 % of the deaths are among people over 65[67]. These older adults are often professionally active, pursuing hobbies and supporting families and our society through volunteering, caring and mentoring. All these roles are of great value to our society and economy.

Today, standard-dose quadrivalent vaccines (SD) are on the market. Although they are effective, the immune response to SD flu vaccines is less optimal in adults aged 65 years and older compared to healthy young adults[68]. One strategy to improve influenza protection in people over 65 is to adjust the antigen dose[69].

The new vaccine contains four times the amount of antigens of the other SD vaccines on the market. In a controlled, randomised clinical trial, the clinical efficacy was shown to be better than that of influenza vaccine at the standard dose for the prevention of biologically confirmed influenza in people over 65[70]. There was also a reduction or avoidance of cardiorespiratory co-morbidities and mortality[71].

Osteoporosis

Osteoporosis is a common, chronically progressive disease. It is characterised by low bone mass and deterioration of the architecture of the bone, which increases the risk of fractures. Bone loss in women accelerates during and after menopause due to oestrogen deficiency.

It is estimated that in 2019 there were some 4.3 million new bone fractures in the European Union due to frailty. This means 11,705 fractures per day or 487 per hour. Fractures resulting from osteoporosis have a negative impact on patients' quality of life and also contribute to increased morbidity and mortality. The risk of fractures increases exponentially with age. Osteoporosis is a major public health problem in developed countries, where the population is getting older. In Belgium, only 34 % of patients are treated[72].

A better understanding of how bone regulation works has allowed the development of a new drug that stimulates bone formation and reduces bone breakdown. The aim is to treat severe osteoporosis in postmenopausal women at high risk of fractures. Clinical studies after three years show that this new targeted treatment provides a marked increase in bone density and reduced risk of fractures, in addition to improving patients' quality of life[73, 74, 75].

"There is a need for innovative osteoporosis medication that greatly and rapidly reduces the risk of fractures in patients at imminent risk of fracture and will reduce the high socio-economic burden of osteoporotic fractures."

Dr Evelien Gielen - Professor of Gerontology and Geriatrics at Universitair Ziekenhuis (UZ) Leuven and president of the Belgian Bone Club

Migraine

Migraine has a significant impact, both on family life and on social and professional life. In Belgium, 45 % of migraineurs report having to cancel family or social outings[76] and more than 1,650,000 working days are lost every year because of migraine[77, 78, 79].

Since mid-2021, the class of antibodies against Calcitonin Gene-Related Peptide (CGRP) has been available to Belgian patients to prevent migraine.

Prof Jan Versijpt (Clinical Head of Neurology, Universitair Ziekenhuis (UZ) Brussel) and Mik Ver Berne of the headache association Head-Stuk talk about "a complete change in the lives of patients and neurologists." The effect in daily life is even more striking than what clinical studies predicted. Not only does the number of days with headache decrease significantly from baseline, but there was also a reduction in headache intensity, anxiety and depression scores commonly seen in migraines, as well as reduced painkiller use. Perhaps even more important for patients' lives, is the noticeable improvement in daily functio-ning (MIDAS, Migraine Disability Assessment) and quality of life[80, 81, 82].

"I was scared to schedule social activities with family and friends. I always lived with the terror that I would have to cancel."

Els, Patient

"I had to interrupt my studies years ago because I suffered too much from migraines. As a result, I always felt that I did not reach my full potential. If I had that medication then, things would have gone differently."

Annelies, Patient

> *"These reimbursements will change the lives of thousands of people whose daily lives are affected by this disabling condition... (It is) a great benefit for the quality of life of the person concerned but also for society, as migraine often leads to work absenteeism."*
>
> *Minister Frank Vandenbroucke, June 2021* [83]

Paediatric Hodgkin lymphoma

PD-1/PD-L1 inhibitors can restore the function of immune cells in the tumour microenvironment by inhibiting the interaction between PD-1 and its binding partner. As a result, there is an enhanced immune response against the tumour[84, 85].

In 2021, the first PD-1/PD-L1 inhibitor was approved for use in a paediatric indication, in patients as young as three years old with the classic form of Hodgkin lymphoma[86]. This is a haematological cancer[87]. The majority of patients with classical Hodgkin lymphoma can maintain long-term control of the disease by first-line chemotherapy, but some patients relapse or do not respond to first-line treatment. For these patients, rescue treatment is difficult and if it also fails, the prognosis is very unfavourable because the remaining treatment options are inadequate and have additional side effects[88].

Patients treated with anti-PD-1 have a higher survival rate compared to standard treatment without the cancer worsening. Their quality of life also improves[89].

Although few paediatric patients have classic Hodgkin lymphoma, the approval of the PD-1/PD-L1 inhibitor in these patients who relapse or fail to respond to restorative treatment represents an important milestone in immunotherapy and opens options in the fight against paediatric cancers.

NTRK gene fusion driven cancer

Since 2021, a new drug has been reimbursed in Belgium for the treatment of NTRK gene fusion (neurotrophic tyrosine receptor kinase) driven cancer. Because NTRK gene fusions are rare, NTRK gene fusion-driven cancer is a rare disease with a high medical need. The disease is determined by a specific gene change, independent of tumour type, that can occur anywhere in the body, both in children and adults[90, 91]. It is necessary to detect this gene change to find the right patient for whom this targeted, personalised treatment may be of interest.

The new treatment blocks the action of the TRK fusion proteins and can thus slow or stop the growth of the cancer, regardless of its location in the body. The drug may also help shrink the tumour[92]. It is the first cancer drug for which an indication independent of tumour type has been approved.

This innovative drug represents a major advance in the fight against cancer because it treats the underlying cause of tumours.

Clinical trials have shown a rapid, effective and durable response, with a favourable safety profile and a significant impact on patients' quality of life[93]. Moreover, it is an oral treatment, meaning patients can simply take it at home and do not need to visit the hospital, which is often the case with current treatments such as chemotherapy. Therefore, this targeted therapy has a major impact on the daily lives of patients and those around them, as well as on the healthcare budget.

Diffuse large-cell B-cell lymphoma

Diffuse large-cell B-cell lymphoma (DLBCL) is an aggressive type of lymphoma and affects over 850 Belgian patients each year[94]. About two out of three DLBCL patients can be cured in first-line treatment with chemo-immunotherapy, but in case of resistance or relapse, DLBCL leads to rapid progressive deterioration of health status and an unfavourable prognosis[95].

For several years, a new form of immunotherapy has been reimbursed in Belgium that offers DLBCL patients the prospect of longer survival and even a real chance of a cure. In this new form of therapy, CAR-T cell therapy, T cells are first isolated from the patient's blood in order to be equipped with a special antenna or CAR (Chimeric Antigen Receptor). This CAR can recognise and attack the lymphoma cells. The T cells are re-administered to the patient. In this way, the patient's own immune system is modified to target the cancer cells.

For the newly reimbursed indication, as a third-line treatment for refractory or relapsing DLBCL, clinical studies show that CAR-T cell therapy represents a clear improvement. Whereas the prognosis after two previous lines of treatment was previously very unfavourable, with a median survival of only 6.3 months[96], for CAR-T cell therapy, it has been shown that over 42 % of patients were still alive after five years and 92 % of these patients did not need additional treatment afterwards, suggesting a potential cure[97]. On this basis, CAR-T cell therapy has rapidly become the new standard of care within this indication. Efficacy and safety within other types of lymphoma and blood cancer are being further investigated.

Mucoviscidose

Mucoviscidosis, also known as cystic fibrosis, is a rare, genetic, multi-organ disorder[98]. About 1,350 people are living with cystic fibrosis in Belgium.

Mucoviscidosis is caused by a fault in the CTR gene (CTR stands for cystic fibrosis transmembrane conductance regulator). This gene codes for the CFTR protein, which is important for regulating water balance in the body. Failure or malfunction of the CFTR protein leads to the production of sweat with a high salt concentration and of mucus in the body that is very thick and tough[99].

Mucoviscidosis starts from birth and can lead to lung damage, pancreatic, digestive and reproductive problems, among others. Mucoviscidosis has a significant impact on patients' quality of life and often leads to early death[100].

Until recently, the standard treatment for Belgian cystic fibrosis patients focused on controlling symptoms. The newly reimbursed treatments target the underlying cause of the disease and improve the amount and/or quality of the CFTR protein in the body[101].

These treatments are associated with improvements in lung function, body mass index, lung incidence and quality of life. These treatments allow patients to do simple actions that most people take for granted, such as carrying their child to bed or walking a kilometre without stopping to cough[102].

These treatments have been reimbursed in Belgium since 2021 for a significant group of patients, for some as young as two years old.

> *"In the end, it gives much hope to my father and my family, but also to other patients in the same situation."*
>
> *Louise De Koninck, daughter of Constant De Koninck, DLBCL patient*

The Lazarus Therapy

Cancer drugs bring hope

Many clinical trials in Belgium involve cancer drugs, and the vast majority of newly reimbursed drugs in 2021 are also for cancer. This is not surprising as cancer is a major cause of death. **Fortunately, new cancer drugs bring hope, which is reported not only in professional journals but also in the mainstream press.**

For example, on the occasion of the 27th annual Children's Cancer Day on 2 October 2022, organised by the Foundation Against Cancer, the non-profit organisation National Children's Cancer Day, and the Planckendael animal park[103], almost 250 children and their families were able to enjoy a day without worries after a terrible diagnosis that still affects far too many. Fortunately, cancer in children (under 15) is rather rare in Belgium (less than 1 % of all cancers). In 2019, 330 new cases were registered (Cancer Registry Foundation). The most requent cancers are leukaemia, lymphomas and tumours of the central nervous system. Together, they account for more than half of all cancers in children. Over the years, the care and management of these children has greatly improved. The cure rate has also improved remarkably over the past 40 years, thanks in part to innovation in drug treatment. On average, 80 % of all children with cancer are cured, compared to less than 50 % in the 1970s. So there is room for hope!

The team of Prof Dr Bart Neyns of the Vrije Universiteit Brussel (VUB) also made the press[104] with the results of innovative immunotherapy drugs in advanced and metastatic skin cancer (melanoma) in Belgian patients. These results are nothing short of spectacular. Metastases in stages 3 and 4 (the most severe diagnoses) were previously always fatal due to a lack of treatments, now, thanks to the innovative immunotherapy drugs, 29 % of patients are still alive after five years, with a limited chance of relapse. Thus, it is estimated that around 750 patients in Belgium with advanced and metastatic skin cancer have had their lives saved since the use of these immunotherapy drugs in 2010[105].

These survival rates are consistent with results from clinical trials of these drugs and other international studies. The study was conducted based on the results of all treated patients with stage 3 and 4 melanomas at Universitair Ziekenhuis (UZ) Brussel between May 2010 and March 2022. These outcomes are hopeful for all affected patients and a substantial improvement over the period before these drugs were introduced.

3.1.2
Promising (r)evolutions in the biopharmaceutical sector

ATMPs

Gamechanger, breakthrough, revolution: these are all terms associated with ATMPs. The name itself says it all: ATMPs or Advanced Therapy Medicinal Products are a long way ahead of the treatments we know today. This is mainly because ATMPs focus on the cause of a disease, while conventional medicines are more likely to treat the symptoms. Thanks to gene therapy, for example, a defective gene can be replaced by a fully intact gene, in certain cases. This obviously increases the chances of an effective cure.

What are ATMPs?

ATMP stands for Advanced Therapy Medicinal Product. ATMPs differ markedly from traditional medicines in the way they are made and administered, and in the benefits they provide. Broadly speaking, there are three categories of ATMPs:

- → **Cell therapy** uses externally cultured body cells to treat the patient or restore the impaired function of a particular organ.
- → **Tissue therapy** goes even further: cells are brought together to reproduce a completely new piece of tissue.
- → In **gene therapy**, the function of a patient's defective gene is restored by administering a healthy copy of the gene.

Not only do ATMPs provide higher cure rates in certain diseases, they also bring greater patient comfort. After all, administration often only has to be done once. For patients who otherwise have to visit the hospital weekly for their treatment, for example, this has a particularly positive impact on their daily lives and those of their family and friends. In addition, side effects are usually much less than with traditional treatments. All this means that patients can often return to a normal life and return to work or school thanks to ATMPs.

The benefits also translate into an increase in the QALYs of these therapies compared to traditional therapies. QALY stands for Quality-Adjusted Life Year, an extra year of life in good health. A study of drugs that became available between 1992 and 2017 showed that cell and gene therapies yielded an average QALY gain of 5.78 compared with 0.49 and 0.43 QALYs for chemical (small) and biological molecules, respectively[106, 107].

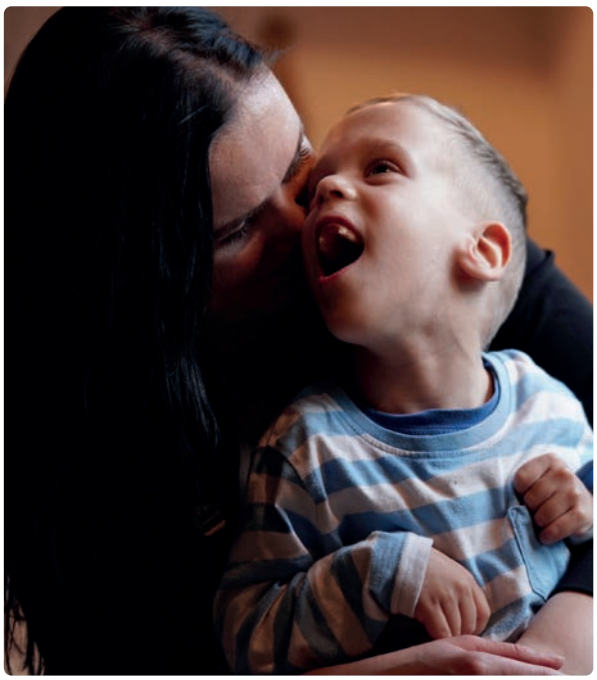
Another study on gene therapies currently under development estimates that they will yield an average of 5.12 QALYs per person treated from 2020 to 2034[108]. These figures illustrate the great potential of gene therapies in terms of health gains compared to chronic treatments.

Thus, the individual and family impact of ATMPs is significant. Socially, too, ATMPs make a significant difference because patients can return to normal functioning and productivity. In the longer term, ATMPs can also mean savings for the healthcare system because they only need to be administered once. On the other hand, however, ATMPs are unquestionably expensive today.

After all, the manufacturing process is not only very innovative but also extremely complex and completely tailored to the individual patient. This inevitably entails a high production cost.

Access to, and reimbursement of, ATMPs are not evident today because our current healthcare system is not geared towards them. It is precisely the lifelong effect of ATMPs, which makes all the difference for patients and society, that causes problems here. The high one-off cost is a pain point and has to be weighed against long-term savings. Moreover, the full (lifetime) effect of an ATMP is almost impossible to capture in a clinical trial, which is a stumbling block in accessing and reimbursing ATMPs.

pharma.be has set up a think tank (see box) to help pave the way for ATMPs because we are convinced that we are only at the beginning of the revolution. Within the EU, 16 ATMPs are currently approved. These mainly target rare diseases for which few or no treatments exist today. However, we expect 10 to 20 per year to be given the green light soon, even for very common diseases. Because there, too, medical needs remain high. For diabetes, for instance, many drugs exist that keep it under control, but the disease persists. Depending on the type of diabetes, gene or cell therapy could provide a complete cure.



Precision medicine

ATMPs are tailor-made for individual patients, providing a great example of one of the most striking and promising trends in medicine: precision or personalised medicine.

By 2021, personalised medicine already accounted for 35 % of the total number of new drugs approved by the Federal Drug Administration (FDA). So the days of one type of treatment being used very **broadly seem to be over. Treatments are becoming more targeted and thus logically more effective.**

Today, personalised medicine is still limited to a relatively small number of diseases. They are already being used in cancer treatment in particular with great success. Not only are they more effective than conventional drugs, their side effects are often also more limited. Traditional chemotherapy, for example, kills all cells that multiply rapidly, including normal cells. This brings drastic side effects.

The therapy also does not benefit all patients, as cancer cells are not always sensitive to chemotherapy. In precision medicine, doctors first look for very specific characteristics of the cancer in the individual patient, for example through a piece of tumour tissue. Based on this, a tailor-made treatment is initiated. In this way, side effects can be minimised and success rates maximised.

In the longer term, more and more diseases will qualify for this kind of customisation. In fact, hundreds of clinical trials are already running today around this kind of innovative treatment. We have only uncovered the tip of the iceberg.

As with ATMPs, we need to make sure that our healthcare system is ready to support the huge potential of precision medicine so that patients in Belgium have easy access.

ATMPs: pharma.be prepares the future together with other stakeholders

The members of pharma.be are active in the development of ATMPs, both in Belgium and internationally. They are keen to get these innovative drugs to patients in a broad, sustainable and efficient way. However, our current healthcare system is not yet adapted to these new transformative and often one-off treatments. To achieve this, an open dialogue with all stakeholders is needed.

The ATMP Think Tank, established in January 2021, aims to encourage and actively contribute to this dialogue. Only through close cooperation can we move mountains for patients, so that they can benefit from this new generation of promising treatments and technologies.

Between April and September 2021, pharma.be organised 14 dialogue sessions with a large group of Belgian stakeholders on the opportunities and challenges for ATMPs in Belgium. Participating stakeholders were academics, policymakers, the FAMHP, the NIHDI, hospitals, patient organisations, doctors, scientific institutions such as Sciensano, health insurance funds and other umbrella organisations.

Based on this dialogue, pharma.be developed a white paper with clear recommendations on the regulatory framework and reimbursement of ATMPs in Belgium. Based on these recommendations, pharma.be again actively engaged in dialogue with relevant stakeholders in 2022 to underline the importance of these reforms.

An overview of our recommendations:

- → We need a **modern regulatory framework** in which Belgium maintains its position as a **pioneer in clinical trials**.
- → We need to optimise procedures so that patients in Belgium have **faster access** to breakthrough drugs.
- → Clinical and budgetary uncertainties can be addressed by temporarily reimbursing ATMPs under **outcome-based agreements**. This allows us to give patients access to ATMPs while collecting additional evidence on the effectiveness (outcomes) of the ATMP. Because the patient's health outcome is central, the government has the option to pay for drugs only for those patients for whom they have been shown to be effective.
- → For some ATMPs, spreading the high initial investment costs over several years can help avoid a spike in drug budget spending (**staggered payments**).
- → Some **evaluation criteria** in the Belgian reimbursement procedure need to be adapted if we want to capture the full clinical, economic and societal value of ATMPs.
- → ATMPs require very specific care. The administration of some ATMPs will therefore be done in a limited number of specialised centres in Europe. We therefore need to prepare for access to **cross-border care** for ATMPs for which there is no approved centre in Belgium.

You can access the full white paper online

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 above) contribute substantially to the Belgian knowledge economy, underpinning our welfare state.

3.2.1 The economic value of the biopharmaceutical industry

EMPLOYMENT

In Belgium

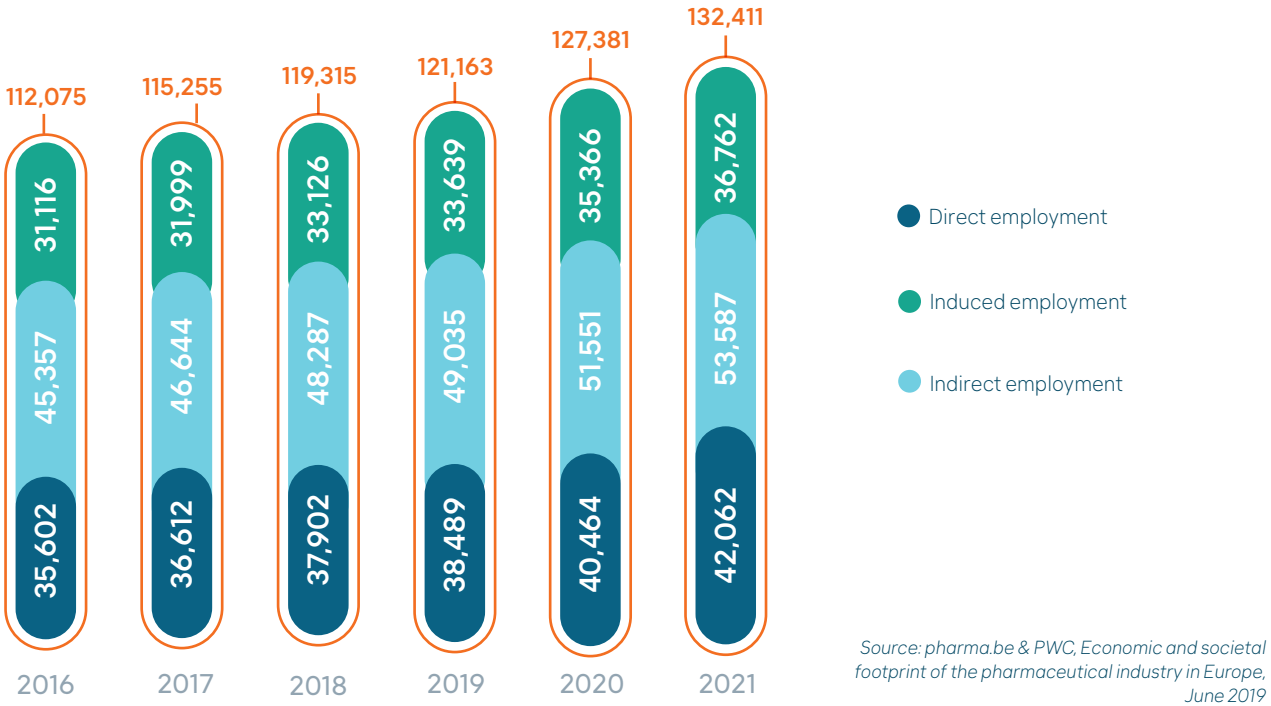
Thanks to our biopharmaceutical industry's leading position worldwide, employment in the industry in Belgium is growing.

Since 2015, the number of employees increased by about a quarter, to reach 42,062 people in 2021. We saw particularly strong growth in the last two years.

This growth is clearly higher than in the overall manufacturing industry in Belgium, where employment increased by only 3.0 % over the same period. In 2021, the biopharmaceutical industry alone accounts for almost 9 % of direct jobs in the manufacturing industry in Belgium. The sector also provides no less than 53,587 indirect jobs and 36,762 induced jobs. This means that for every job created in the Belgian biopharmaceutical industry, two other jobs are created. In this way, the sector accounts for more than 130,000 jobs in total.

In Europe

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



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

An illustration of the indirect employment impact: transporting medicines

Drugs produced in Belgium need to be transported, often worldwide. Belgium is also a hub for drug imports, which are then often further transported from Belgium to the rest of Europe. This transport of medicines creates additional, indirect employment associated with the activities of the biopharmaceutical sector in Belgium.

Last year, we focused on pharma transport and associated investments by Brussels Airport, Liège Airport and Port of Antwerp-Bruges.

Logistics group H.Essers has also been expanding its pharma logistics operations since 2006. It built a specialised logistics cluster near its headquarters in Genk, christened pharma valley. This was expanded in 2022 with a new transhipment site, a € 20 million investment, as the transport of pharmaceuticals grows by an average of 8 % every year.

H.Essers' pharma logistics operations involve significant employment. In Belgium, it employs about 900 people, a number that has doubled in five years. In terms of profile, this represents about a third white collar (in, among other things, customer relationship management, operational management, planning, customer service and quality control), a third blue collar (operators at the transhipment site and in warehouse management) and a third drivers. All are trained according to European Good Distribution Practice guidelines that ensure the quality of life sciences and healthcare products during distribution.

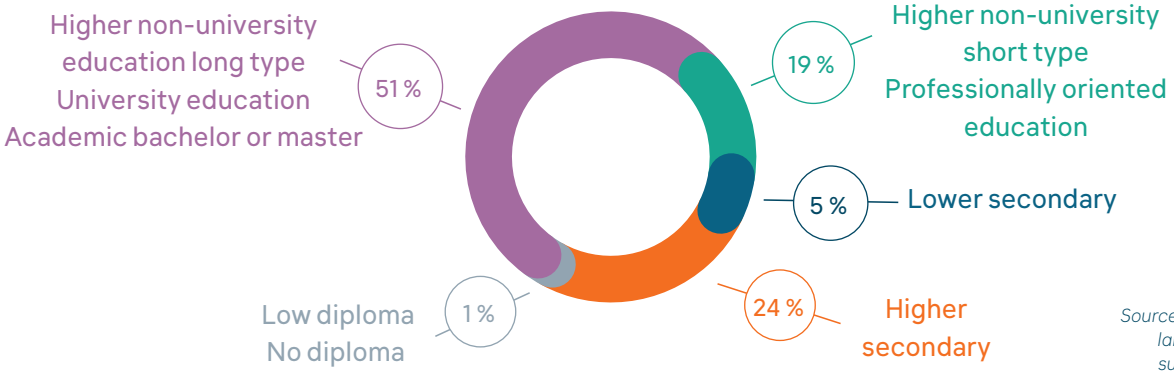
Another pharma valley expansion is planned from 2024, which will increase employment by another 200 workers.

A diverse sector

The sector not only generates a large number of jobs but also a wide variety of jobs. The Belgian biopharmaceutical landscape is very diverse, ranging from small start-ups to highly innovative biotechnology companies and medium-sized family businesses to local subsidiaries of multinational corporations and large manufacturing companies. This diversity is also reflected in employment. SMEs represent almost 90 % of the market in numbers, accounting for about a quarter of employment within the sector.

The companies within the sector are diverse, but so are the job profiles the industry needs, from non-specialised to highly skilled workers. Although in this knowledge-intensive sector, there are considerably more highly educated employees than in other sectors, with around 70 % of employees holding a higher education degree. In terms of the total working population, this is about half. This amounts to 40 % in the manufacturing industry in general and to approximatively 55 % in the chemical industry.

Distribution of profiles in the biopharmaceutical sector in 2021



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
2021	51	48	46	63

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
2021	13	29	17	23

Source: pharma.be

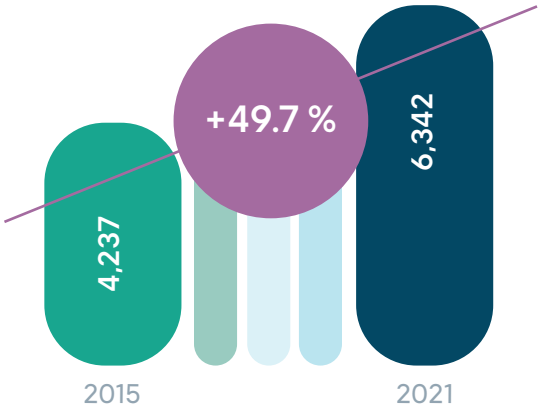
In terms of gender diversity, the biopharmaceutical sector is fairly gender balanced. By 2021, the proportion of female employees rose to 51 %. Female researchers are in the majority, with 63 % in 2021. Compared to the previous year, we see a particularly striking increase in the number of women on corporate boards. There had already been some catching up in previous years. This was even more pronounced in 2021, with an increase in the amount of female directors to 46 % compared to 38 % in 2020.

The sector is also diverse in terms of the number of non-Belgian workers employed. Between 2018 and 2020, the number of non-Belgian employees rose from 8 % to 14 %, before stabilising at 13 % in 2021. They are also relatively more represented in management, with a share evolving from 15 % to 29 %. Last year, a quarter of board members were non-Belgian employees, but this has fallen back to 17 %. Finally, the share of non-Belgian employees active in research has increased even further and even more significantly in 2021, to 23 %.

A strong foundation

In Belgium, the industry 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. Since 2015, this group has grown by half. This brings the total number of researchers to 6,342. They are the cornerstone of the biopharmaceutical industry and contribute substantially to its success.

Increase in the number of researchers in 4 years



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

pharma.be reflects on talent challenges

Because of the significant increase in employment in the sector as well as technological evolutions, it is becoming increasingly challenging for biopharmaceutical companies to find the right talent. This also applies to other sectors that mainly need technical or scientific profiles, the so-called STEM profiles[109], such as the chemical and IT sectors.

pharma.be is helping to think of possible ways to fill these staffing needs. At the Observatory for the Pharmaceutical Industry, of which pharma.be is a member along with several other stakeholders, a study is under way on attracting and retaining local and international talent. Locally, the question is how to guide more young people to STEM courses. How do we make them more mobile in our ecosystem and how do we better align their curricula with technological evolutions in the sector? Internationally, we are looking at how we can make Belgium more attractive to foreign talent and how we can keep that talent here.

In addition, we obviously focus on lifelong learning within our companies: how can we keep people active for longer and how can we make the interaction between academic platforms and our companies possible and more attractive? In early 2023, the Observatory will formulate its recommendations.

"We all see that the world is changing rapidly and profoundly, which is why it has never been more important to work in a multidisciplinary way. We all need to work on that, in the business world but especially in education. For example, IT and data science are two separate programmes, which exchange and communicate little with each other. As a result, students only get part of the story, without the broader context. The question is: 'How do we make these courses broader and more relevant so that they better meet the needs of the strongholds of the Belgian economy including the biopharma sector?'."

Sonja Willems, President of the Pharmaceutical Industry Observatory

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.

2021 was no exception. More so, due to the crucial role Belgium played in making COVID-19 vaccines available. It was a year of **exceptional export growth**. Whereas overall Belgian exports improved by about a quarter after the weak corona year 2020, the pharmaceutical sector managed to grow by more than half.

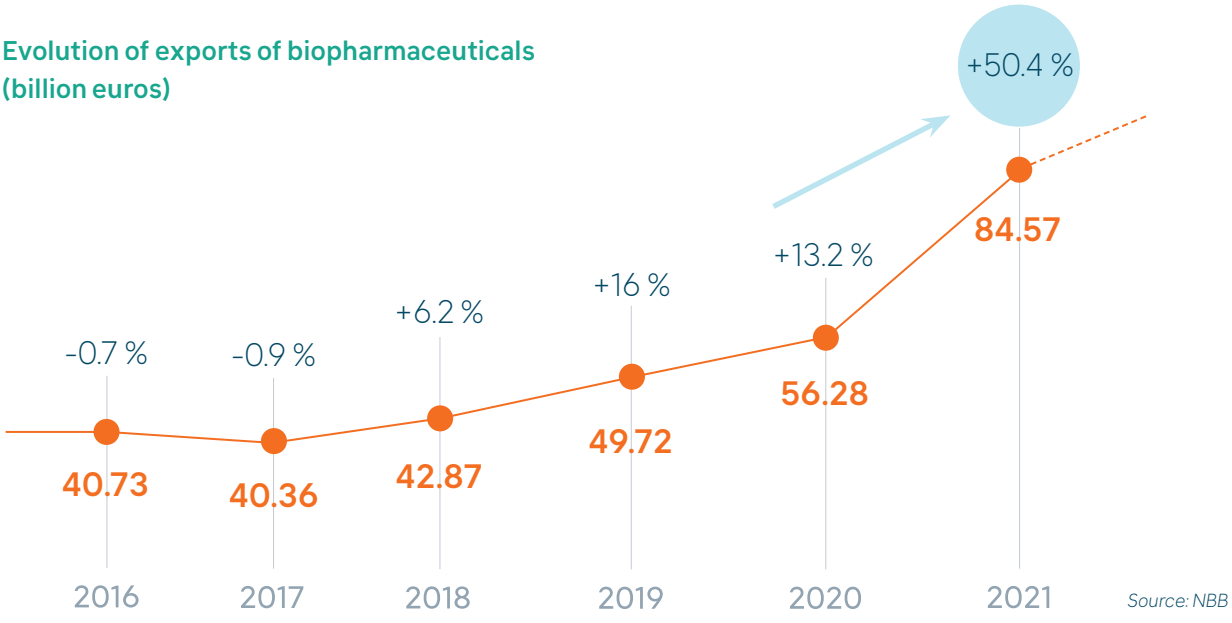
Biopharmaceuticals represented almost a fifth of total Belgian exports in 2021. The sector made an extremely important contribution to Belgium's positive trade balance of € 14.3 billion. The biopharmaceutical sector has the largest surplus, with a contribution of € 23.3 billion. Without the industry, Belgium would have to present a negative trade balance. This proves that the sector is one of the pillars of the Belgian economy, even during and after the difficult COVID-19 period.

Facing Europe and the world

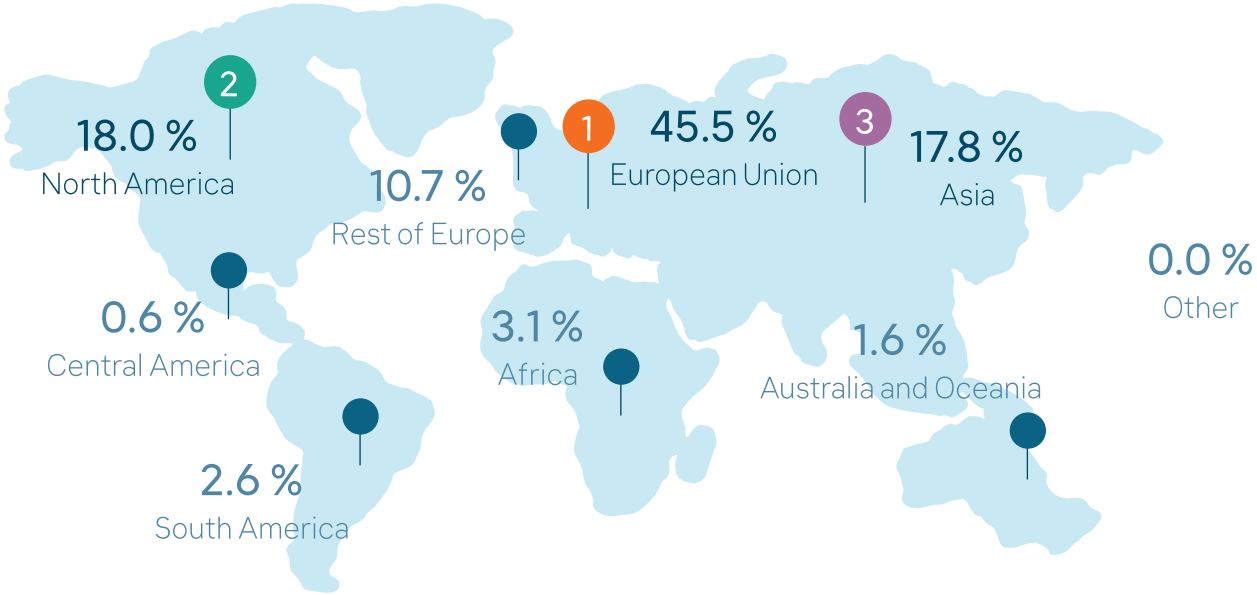
In a global perspective, Belgium is doing very well. In terms of total exports of biopharmaceuticals, Belgium is only behind Germany within the EU. If comparing the number of exports with the number of inhabitants, Belgium also ranks second, after Ireland. In total, almost a fifth of total EU pharmaceutical exports are shipped from Belgium. Germany is Belgium's main trading partner, with a 17.5 % share, followed by the US with 16 %.

Belgium is clearly an international hub for the export of biopharmaceuticals and thus can also play a role in global public health. This was made all the more clear by Belgium's impact in the search for a solution to the COVID-19 crisis. Thanks to the presence of highly developed pharmaceutical production facilities, Belgium was a key player in the development and large-scale production of vaccines. This is also reflected in the export figures.

Evolution of exports of biopharmaceuticals (billion euros)



Source: NBB

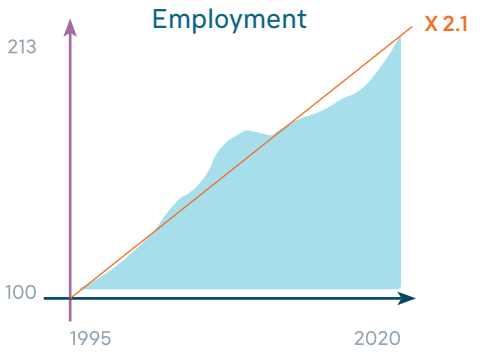


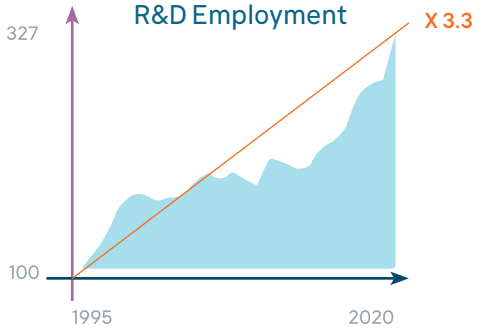
The biopharmaceutical sector has been showing a strong economic growth trajectory

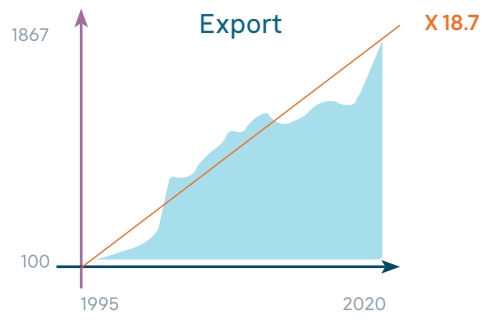
In recent years, the biopharmaceutical sector has managed to post great results. But this is certainly nothing new. The sector has been successful for many years and has long occupied an important place in the Belgian economic landscape, as the graphs show.

In terms of employment, it has more than doubled. In the case of R&D employment, we are even talking about a factor 3. The sector achieved the highest growth over the years in exports. Few sectors can present such an exceptional report. It is undeniably an exceptional result, which clearly shows the evolution Belgium has gone through to become the European biopharma valley it is today.

Evolution of the sector in 25 years







3.2.2
Cost-benefit analysis for the Belgian government

The direct economic impact of a strong biopharmaceutical sector in Belgium may be clear by now, but the sector also has a positive impact on public finances, as shown in the following calculation based on 2020 statistics.

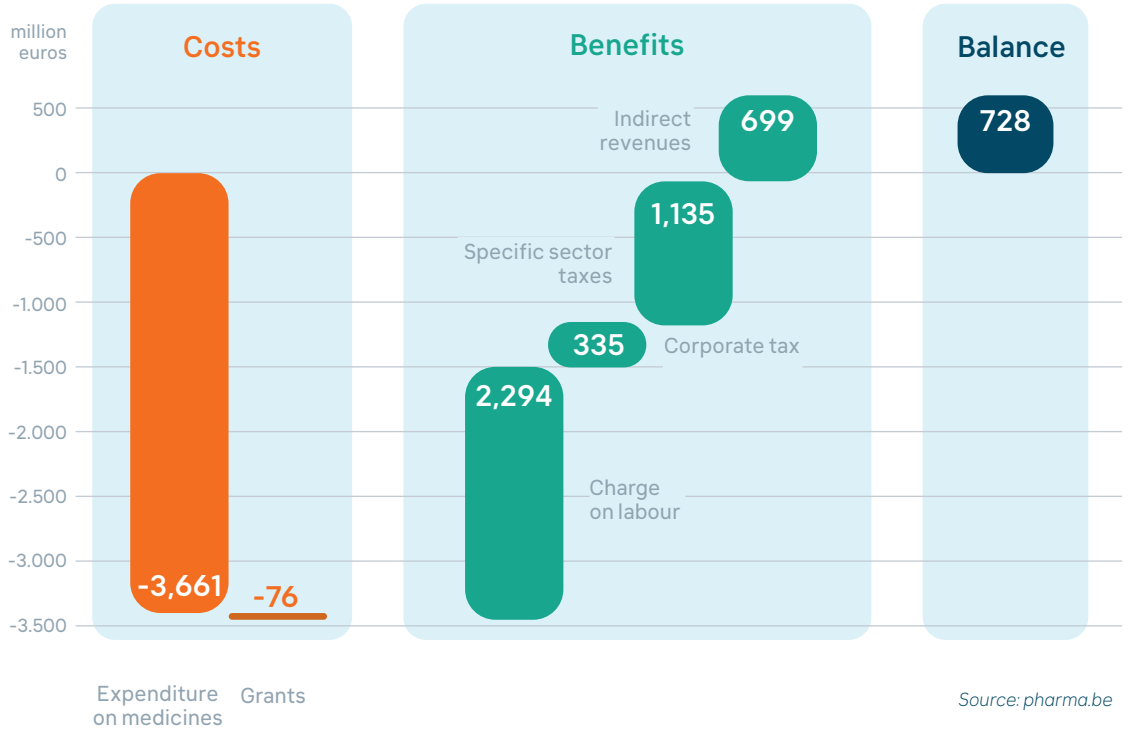
To make this cost-benefit analysis (see also appendix 1), we first take into account the costs incurred by the government for medicines. These costs are reimbursed by the NIHDI and include expenditures on all reimbursed medicines. Government subsidies for the biopharmaceutical industry are also included here. In total, these expenditures amount to € 3.74 billion.

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

1. taxes on labour, amounting to almost € 2.3 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, revenues for the government amount to € 4.46 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 our Belgium's income is substantially higher than the expenditure. The surplus amounts to € 700 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 on the market and beyond, biopharmaceutical companies work closely with healthcare professionals (HCPs) and the healthcare industry. These interactions are not only legitimate, they are also necessary. After all, as the first point of contact with patients, HCPs can provide invaluable expertise. This is crucial so the biopharmaceutical industry can develop increasingly effective treatments for patients.

Additionally, biopharmaceutical companies have a responsibility to inform HCPs about new treatments so that every patient can receive the best possible treatment. The companies share objective and scientific information, in particular information on indications, expected outcomes and possible side effects. This ensures the correct use of medicines.

Interactions between healthcare providers and the biopharmaceutical industry are regulated by law to ensure the independence of the parties. Interactions always start from a position of knowledge sharing and the aim to promote scientific research or improve patient treatment.

PHARMA.BE'S CODE OF DEONTOLOGY

The biopharmaceutical industry must comply with extensive legal requirements, such as pharmaceutical legislation, competition legislation, intellectual property and data protection legislation and anti-corruption regulations. **Our member companies also voluntarily commit to the additional standards in pharma.be's Code of Deontology.**

This Code provides a framework for developing sustainable relationships with healthcare partners. The Code defines the requirements to be met by the industry and supports companies' commitment to operate in a professional, ethical and transparent manner.

The Code applies to various activities of pharmaceutical companies:

- → information and promotion relating to medicines
- → interactions with healthcare providers, healthcare organisations and patient organisations

Procedure when the provisions of the Code are breached

In case of doubt about compliance of a pharma.be member with the Code, any individual or legal entity may lodge a complaint with the Secretariat of the Code of Deontology. This complaint is initially handled by the Deontology and Pharmaceutical Ethics Committee (DEF Committee). If the decision is appealed, it will be recorded by the Board of Appeal.

These deontological bodies are independent of pharma.be and are composed of:

- → a chairman, lawyer by training, who is not active in the pharmaceutical industry
- → a member representing the pharmaceutical industry (human or veterinary products), depending on the product/issue
- → a non-industry member representing either the medical or pharmaceutical sector, or the scientific or academic community

This composition reflects a strong commitment to externalise self-regulation procedures in the pharmaceutical sector. The input of representatives of all partners in the health sector and of objective lawyers (including former magistrates of the highest courts) offers a clear advantage in terms of independence and aims to further professionalise this type of procedure.

The Deontology Code

You can request a hard copy at : deonto@pharma.be

Once the complaint has been filed, the parties concerned shall first exchange their arguments in writing before defending their position in a hearing before the relevant deontological body.

If a breach of the Code is found, the DEF Committee or the Board of Appeal orders the immediate cessation of the challenged practice. They may also impose the following:

- → corrective measures, such as adapting the promotional material, adding a notice of rectification or communicating the decision to the medical and/or pharmaceutical sector
- → accompanying measures, such as transparency or readability recommendations
- → financial safeguards in the form of the payment of compensation to the King Baudouin Foundation
- → the publication of the decision in certain scientific journals

This procedure is detailed in articles 58 to 83 of pharma.be's Code of Deontology.

In 2021, two cases were settled by the DEF Committee. A third was referred to the Board of Appeal, which ruled in March 2022.

Interested parties may request an extract of these decisions at deonto@pharma.be. However, communication of an extract of a decision always requires the prior agreement of the parties involved.

Bureau for Control on Written Communication (BCWC)

There is a second deontological procedure within pharma.be: the Bureau for Control on Written Communication (BCWC). Its specific purpose is to monitor communications from our member companies to healthcare providers about the medicines they market.

What is the BCWC?

On 1 May 2010, pharma.be launched this new initiative with the aim of improving the quality of information provided by our member companies to healthcare providers.

An independent body, the **BCWC**, was set up to monitor the quality of information and check that it is in line with pharma.be's Code of Deontology and with laws and regulations. This project of self-regulation is unique in the world.

Why do pharmaceutical companies provide information to healthcare providers?

(Bio)pharmaceutical companies invest on average 10 to 12 years in R&D of a new innovative medicine. During this process, they build a great deal of expertise and gather a wealth of scientific information, which they make available to healthcare providers, giving them sufficient prior knowledge to guide their patients and encourage the appropriate use of drugs.

How does the procedure work?

Every month, the BCWC randomly selects five medicines from five different member companies of pharma.be. These companies are contacted and provide the Bureau with a copy of all written communication about the drugs, aimed at healthcare providers.

The BCWC, composed of a lawyer, a physician and a pharmacist, analyses and checks whether these communications comply with the legislation on drug advertising and pharma.be's Code of Deontology.

Want to know more about this? You can find the BCWC's detailed procedure in articles 46 to 57 of our Code of Deontology.

The deontological platform Mdeon

Deontology and self-regulation transcend the workings of our association. The pharmaceutical industry (including pharma.be) and the medical and dental technology sector are all members of the deontology platform Mdeon, alongside associations of doctors, pharmacists, veterinarians, dentists, nurses, physiotherapists, paramedics, hospital technicians and wholesale distributors.

This platform aims to establish a quality framework for interactions between healthcare providers and pharmaceutical and medical technology companies. In particular, it intervenes at scientific events in which healthcare providers participate to keep abreast of the latest developments in their field (e.g., international conferences or meetings of researchers).

In some cases, funding for healthcare providers' participation in such scientific meetings requires a visa. Mdeon is responsible for granting these visas, as a guarantee of compliance with legislation and deontology.

Mdeon manages the betransparent.be platform (see below).

The legal basis for Mdeon's actions is Section 10 of the Medicines Act of 25 March 1964.

Code of Deontology can be found here

What next?

Based on the BCWC's report, companies can adjust their communications to better comply with legal and deontological provisions.

In addition, the BCWC produces a report every year summarising their evaluations and providing recommendations. Member companies of pharma.be can use these reports as best practices for developing promotional materials aimed at healthcare providers.

You can request a digital version of the 2021 report at deonto@pharma.be. Through this initiative, our member companies recognise and take responsibility for sharing quality scientific information about the medicines they market.

The BCWC helps guarantee the third ethical principle included in the introduction to our Code of Deontology: "Member companies strive to ensure that the information in advertising materials reflects a proper balance between the risks and benefits of their medicines and supports their proper use. Advertising is ethical, accurate, balanced and must not be misleading."

"Every month, five members of pharma.be are invited to provide the BCWC with their written communication on a particular drug intended for healthcare professionals. BCWC members act completely independently when evaluating these communications. The added value of this monitoring procedure lies in the fact that it continues to draw companies' attention to the legal and ethical framework as our modes of communication evolve. Through these recommendations, the BCWC aims to contribute to quality written communication among companies. The conclusions provide companies with practical guidelines for compliance."

Marc Van Grimbergen, Chairman BCWC

For more information, read the brochure "Health Ethics" (in French).

Five conditions scientific events must meet:

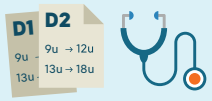
What says the law

Mdeon

Prior approval from the Visa Bureau of Mdeon for congresses that run over several days. Composition of the Bureau: 1 lawyer, 1 member from the health sector and 1 member from the pharmaceutical industry

Scientific Nature

meets a medical need, no relaxation



Precise locations and dates

without any confusion as to the scientific nature

Capped meals, hotels and travels, including abroad

only for healthcare professionnals

Healthcare professional: Economy
Speaker: Business Class allowed

Max.
€ 40/lunch
€ 80/diner

Max.
€ 250 per night

Partners not covered

Compensation limited to the official duration of the congress

extension to a private capacity must be paid for by the healthcare professional

*Compensation only allowed if it is not possible to arrive the morning of the congress or return the evening of the congress

No quid pro quo

extension to a private capacity must be paid for by the health-care professional

Source: brochure "Health Ethics" (in French)

ENSURING TRANSPARENCY IN THE INTEREST OF PATIENTS

If we want to get the most out of an ecosystem such as the Belgian healthcare system, we need to build bridges between the different actors and ensure optimal cooperation between them. This is particularly true for the pharmaceutical industry and healthcare providers, healthcare organisations and patient organisations. They interact and cooperate in various areas of their activities:

- → Pharmaceutical companies partner with healthcare providers and healthcare organisations to share their expertise and exchange knowledge, enable healthcare providers to participate in scientific meetings, conduct scientific research and inform the medical community about the various treatment options available.
- → Pharmaceutical companies work with patient organisations to learn more about how patients experience their disease in order to develop treatments even better suited to their needs. They also support patient organisations in their educational work and community building.

These forms of collaboration are essential for medical advances and for optimal patient care.

These collaborations are subject to a strict legal framework to ensure the independence of the various parties involved. This framework includes the obligation of transparency to the public. Transparency is crucial for the pharmaceutical sector. More transparency ensures better understanding of interactions and to answer legitimate questions from the public about them.

Since 2017, pharmaceutical and medical technology companies have been documenting and publishing certain financial information about their interactions with healthcare providers, healthcare organisations and patient organisations through the platform www.betransparent.be.

An overview of the Transparency Register in 2022

The figures published in 2022 refer to the 2021 operating year:

- → A total of € 255.4 million worth of cooperation with healthcare actors was published. This is an increase of 33 % compared to corona year 2020 and 3 % compared to 2019, pre-corona.
- → Most of the collaborations - € 174.3 million or 68 % of the total amount - relate to scientific research. These are mainly collaborations in the context of clinical studies. This is because Belgium is a leader in clinical studies in Europe. Our healthcare providers and hospitals have an excellent reputation worldwide.
- → The other forms of cooperation include:
  - participations in scientific events (€ 27.1 million), which must be pre-approved by Mdeon through a visa procedure
  - donations and grants to support healthcare (€ 21.4 million)
  - fees from service contracts (€ 19.5 million)
  - contributions to patient organisations (€ 13.1 million)

This mainly concerns European patient organisations that have their base in Belgium because of the presence of the European institutions.

	2021
Scientific research	€ 174,254,150
Scientific events	€ 27,129,289
Donations and grants to support healthcare	€ 21,381,575
Services and consultancy	€ 19,524,385
Other fundings (PO)	€ 13,131,161

€ 255,409,559

Source: www.betransparent.be

Status after five years of Transparency Register

In 2022, the legal framework for transparency of interactions has existed for five years. So, time to take stock.

In April 2022, some critical articles appeared about the betransparent.be platform. These gave the impression that the industry deliberately disclosed the information in a complicated manner and it was reported in an incorrect or unclear way. pharma.be reacted immediately, as did other parties, and initiated a dialogue with the journalists.

As co-manager of the platform, pharma.be is open to improving the transparency and the accessibility of published data. On pharma.be's initiative, members of the betransparent.be platform (managed within Mdeon) examined the extent to which they could improve the platform, in line with the goals in the Sunshine Act[110].

The following improvements have been approved within Mdeon:

- → Improving the search engine by integrating the following features:
  - cross-sectional searches based on beneficiary name only (all categories of beneficiaries and years combined)
  - easy switch between calendar years within a search result
  - cross-referencing within the same search result
- → Enable the export of search results to an Excel file
- → Reporting of the total amounts for a beneficiary in the search result
- → Extending the validity period of captchas to three hours
- → Modernising the website

In the longer term, the extent to which substantive improvements can also be made to achieve even better transparency will be explored. This will require close cooperation with the FAMHP and the cabinet of the Minister of Social Affairs and Health; these discussions are currently being prepared internally.

> *"Collaboration between companies producing drugs or medical devices and healthcare professionals, healthcare institutions and patient associations has the potential to add value to our healthcare system. But such collaborations must be deontologically sound and completely transparent. It is necessary for the published information on such collaborations to be relevant, exact, ascertainable, and readable in order to build trust in our healthcare system and its actors. Undoubtedly, there is still room for improvement in the process launched five years ago, and transparency can be strengthened. This is what I, along with the FAMHP, will be consulting on with the Platform and the involved sectors."*
>
> *Frank Vandenbroucke, Minister of Health and Social Affairs* [111]

Those interested in learning more about the transparency obligation can consult the full activity report of betransparent.be here (in French).

4.1.2
Addressing urgent patient needs

The *compassionate use* and *medical need* programmes allow, in exceptional cases, the administration of a medicine that is under review but not yet approved by the EMA, to patients suffering from a chronic or serious disease who cannot be treated with a medicine that is already available on the market.

With new legislation in 2014, Belgium implemented European Regulation 726/2004 (Article 83) and introduced the concept of *compassionate use*. At the same time, our country took the opportunity to create a broader legal framework by also allowing emergency medical programmes.

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

- → ***Compassionate use programmes (CUP)*** cover medicines that have not yet received marketing authorisation.
- → **Emergency Medical Programmes (MNP)** involve drugs that have a marketing authorisation for a particular indication but use is being sought for an unapproved indication.

To give patients **faster and free** access to the latest treatments through these programmes, in exceptional cases, even before the registration procedure is completed, the FAMHP needs to grant a temporary authorisation or Early Temporary Authorisation (ETA).

Because the EMA has not yet granted market authorisation, the FAMHP has to strictly weigh the benefits versus the risks of the drug. If the application is approved, the company gives the new drug **free of charge** to patients who are included in the programme at the request of their treating doctor. The programmes last until the drug is available on the market for the indication concerned.

This exceptional provision is made in full transparency; all approved programmes are published on the FAMHP website[112]. Patients and healthcare providers can consult them there.

By autumn 2022, more than 60 programmes were ongoing.

Number of approved applications per year

Source: FAMPH

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. 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 and animals. That is why, throughout the entire cycle from research to production, use and disposal of medicines, there is a strong focus on avoiding contamination. To accomplish this, all participants across the value chain need to work together.

Here are some examples of our environmental and climate efforts:

Multistakeholder collection of expired and unused medicines

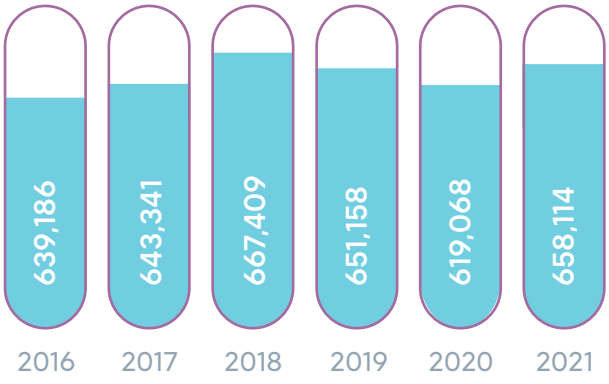
Unused or expired medicines should not be flushed down the toilet or thrown away. They must be sorted and collected separately, as they can be harmful to the environment. They can also be harmful to public health. After all, unused medicines should not be used or disposed of improperly (children playing, for example, or animals looking for food).

To encourage sorting and ensure proper collection, the biopharmaceutical sector has collaborated with various stakeholders to develop a convenient cost-free solution to the patient. Thanks to this multi-stakeholder initiative, you can simply drop off unused and expired medicines to your pharmacy. The pharmacist collects the medicines in a special cardboard box. The boxes are collected by wholesale distributors and incinerated; the thermal energy that is released during the process is reused.

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 previous year.

Thanks to this collaboration, an estimated 658,114 kg of unused and expired medicines were collected in Belgium in 2021. The table below shows that after a decline in 2019 and especially in 2020, the volume increased again in 2021. It is not easy to interpret this evolution. An increase may be positive as it may mean that fewer medicines ended up in the environment. However, a decrease may just indicate that there was less waste of medicines to begin with, which is also a good thing. The lower figure in 2020 is most probably due to COVD-19, meaning that fewer people brought their expired and unused medicines to their pharmacy.

Total amount of expired or unused medicines in kg



Source: pharma.be

Start 4 water - encouraging people to do their part through art

From 20 October to 4 December 2022, you could see the exhibition Faces of Water | Art Meets Awareness at the Brussels Bozar.

pharma.be was one of the partners in this art project, notably in the realisation of an installation by US artist Haseeb Ahmed. He has been working around wind and water for over a decade. In this exhibition, he focused on the impact of pharmaceutical pollution that, despite great efforts at prevention, ends up in our water chain.

Ahmed came to the paradoxical conclusion that a number of substances developed to support our physical health may eventually affect our ecosystems. With his art, Ahmed zooms in on this complexity and holds up a mirror to us. After all, much of the pollution in the ecosystem is in our own hands.

Also through art, pharma.be aims to encourage the public to do their part by bringing expired and unused medicines to pharmacies for safe destruction.

Discover the exhibition (in French)

E-PIL: Electronic Patient Information Leaflet

Every pack of a medicine contains a paper package leaflet with guidelines and important information for proper use of the medicine. The paper package leaflet is required by European legislation. In Belgium alone, more than 100 million drug packages are delivered every year. The environmental impact is therefore huge. Perhaps there are situations where an electronic alternative is just as safe and more sustainable.

To investigate this question, the biopharmaceutical industry launched the Electronic Patient Information Leaflet (e-PIL) pilot project in 2018. e-PIL focuses on a selection of drugs on the market in Belgium and Luxembourg whose administration is limited to the controlled environment of a hospital. In such an environment, drug packages are never delivered directly to patients without the guidance of a healthcare professional. An electronic leaflet can provide a fast, efficient and ecological alternative.

The electronic package leaflet is available from reliable sources such as the FAMHP database, the website of the Belgian Centre for Pharmacotherapeutic Information (BCFI) or the pharma.be e-compendium website. The electronic package leaflet is not only more sustainable but also offers other advantages, such as access to the latest information and the possibility of consulting the leaflet in a user-friendly and personalised way (e.g., larger font or language of choice).

The e-PIL pilot project is a first in Europe. Four years after its launch, the interim results are extremely positive and in line with previous interim evaluations. 97 % of hospital pharmacists surveyed did not experience any inconvenience from the absence of the paper package leaflet. The positive impact on the environment was also recognised by hospital pharmacists. For 95 % of the hospital pharmacists surveyed, the paper leaflet may be removed from all packaging of medicines administered in the hospital in the future.

"A structured electronic drug package leaflet is an efficient, indispensable source of information to support hospital healthcare workers in providing quality and safe patient care. When the most up-to-date version of the electronic package leaflet is always readily available via one central platform or integrated into the electronic patient record, a paper leaflet in every pack is unnecessary. This step towards a paperless hospital also contributes to ecological and sustainable healthcare."

Hospital pharmacist Thomas De Rijdt, Universitair Ziekenhuis (UZ) Gasthuisberg

Based on these positive results, the European Commission gave its approval in 2022 to extend the project until 1 August 2025 and to include more medicines in the project. By collecting more data, the initial conclusions could be confirmed and the exclusive use of the electronic package leaflet in the hospital setting could be considered for inclusion in legislation. A third call for candidates was launched to pharmaceutical companies between August and November 2022. A number of medicines were submitted for consideration. Validation of these medicines is currently ongoing by the responsible authorities in Belgium and Luxembourg. So in spring 2023, even more drugs than the current 42 will be added to the project.

You can follow this project on our website (in French)

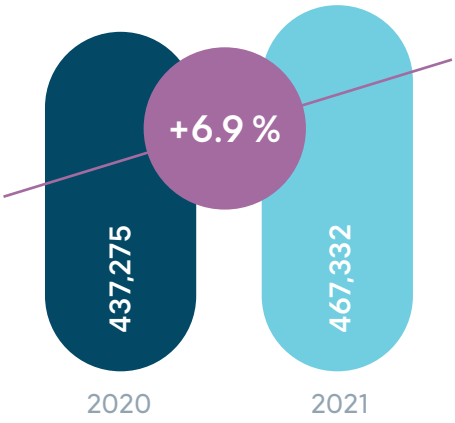
4.1.4 Caring for people and animals

Reducing animal testing[113]

The 3Rs are one of the fundamental principles in 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 2021, 467,332 animals were used in research, an increase by 6.9 % compared to 2020. 55 % of the experimental animals were mice; 13.1 % were rabbits. Dogs and cats were used to a much lesser extent (0.32 % for both species).

Number of animals used in research



Source: EU Statistical Data of all uses of animals

In 2021, the majority of laboratory animals were used for basic and applied research (72.4 %). After a decrease in 2020, the percentage in 2021 is at the same level as in 2019. 109,548 laboratory animals, or 23.4 % of the total number of laboratory animals, were used in the context of regulatory studies and routine production (quality and efficacy testing toxicity tests, etc.). Compared to 2020, this is a decrease, both in absolute numbers (127,262) and in proportion (29.1 %).

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 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 environmental health are all closely connected and affect one another. Sustainable use of antibiotics in veterinary medicine is therefore important to help safeguard public health.

More rational use of antibiotics in animals

As in previous years, pharma.be continues to actively promote policies that encourage the rational use of antibiotics. One of the ways we do this is through AMCRA (see box). After all, it is of the utmost importance for the health of both humans and animals that they can be treated with antibiotics when needed.

By raising awareness with veterinarians and livestock farmers on the rational use of antibiotics and emphasising the importance of prevention, we can limit antibiotic resistance and preserve the effectiveness of antibiotics for as long as possible.

Thanks to the efforts of all stakeholders involved in Belgium's antibiotic policy, use of antibiotic in our country decreased again by 8.4 % in 2021, after a year of stagnation in 2020. Compared to our reference year 2011, we are using almost half less antibiotics in animals. This decrease is shown in all animal species whose administration of antibiotics is monitored: there is an annual decrease of 15.3 % in pigs, 19.4 % in calves and up to 40.7 % in poultry.

In addition to these positive general figures, there is also good news regarding the "red antibiotics"[114]. We notice a decrease by as much as 42.8 % compared to the previous year. Compared to 2011, the use of these molecules has been reduced by more than 80 %.

4.2 Working together for the benefit of the patient

Health and healthcare are not the remit of one individual or one agency. It is a complex system that requires an integrated approach. Collaboration is therefore not only convenient, but also absolutely necessary for health and innovation. pharma.be is continuously working on sustainable, high-quality collaborations, with patient organisations, and when collecting data or ensuring the availability of medicines.

pharma.be helps advocate for new National Cancer Plan

With the European plan against cancer, the European Commission aims to step up the fight against the disease. This plan tackles cancer from all angles: prevention, diagnosis, treatment and survival. On 22 June 2022, pharma.be organised an information session on this together with the Foundation against Cancer.

The Belgian Cancer Centre seeks to work with all stakeholders to translate the European plan to the Belgian context. Representing the innovative pharmaceutical industry, we from pharma.be fully support this goal of working together towards a new National Cancer Plan.

pharma.be is itself an advocate of strong partnerships and collaborations. The Cancer Plan Working Group of pharma.be was pleased to invite the Foundation Against Cancer to present the Cancer Barometer. This gives a global overview of cancer care in Belgium and the priorities for the fight against cancer.

4.2.1 Working together with patient organisations

Within pharma.be, cooperation with patients is of paramount importance and, therefore, used very responsibly. In 2021, a **working group** was set up to focus specifically on topics concerning engagement with patient organisations. This working group is composed of representatives from 20 companies. The aim is to strengthen the cooperation between patient organisations and pharmaceutical companies and to formulate improvement proposals.

As actors in the same ecosystem, collaboration between pharmaceutical companies and patient organisations is a must. As in any industry, listening to the end user of products is crucial for pharmaceutical companies. After all, patients know better than anyone else the practical impact of a disease on their daily lives and those of their loved ones, and know best how a treatment can make a difference. By gathering this information, pharmaceutical companies can develop drugs that effectively meet patients' needs. In practice, this amounts to regular consultation with patients from the early stages of a study and throughout a drug's life cycle (clinical trials, awareness campaigns, improving patient knowledge, RWD collection, etc.).

Within this framework, the Patient Expert Centre (PEC) (https://www.patientexpertcenter.be/) trains Patient Experts who can speak on behalf of patients suffering from the same disease. In this way, they can provide advice to pharmaceutical companies, governments and academic institutions. **pharma.be supports this initiative and has been a member of PEC's governing body since its official launch in 2019.**

For their part, patient organisations can approach pharmaceutical companies to request support for their operations, such as setting up an awareness campaign, developing a brochure or organising an event. Chapter three of pharma.be's Code of Deontology contains the general principles and rules that companies must respect when working with a patient organisation.

The guiding principle of the working group is the will to co-create with patient organisations from the beginning. The working group therefore started contacting over 60 patient organisations to involve them in their activities. A virtual kick-off meeting was held in 2021.

This was an immediate opportunity to exchange views with patient organisations and listen to their needs. An initial discussion on areas of cooperation between industry and patient organisations was initiated. The patient organisations' enthusiastic response to this initiative clearly shows that both sides support dialogue.

An online survey was then distributed to patient organisations to find out more about their approaches, challenges and experiences when working with industry. A total of 36 patient organisations responded. Thanks to the results of this survey, we have a better idea of what we can and should do together, what are currently the greatest needs, and who has what priorities.

Survey results in brief:

→ The main challenge for patient organisations is the long-term sustainability of their association, especially in terms of funding.

→ Most patient organisations appreciate the cooperation with the biopharmaceutical sector, although they report that there are **areas for improvement**. Some examples:

- Patient organisations, like true partners, should be involved from the start and at regular intervals in projects set up by companies. Evaluation of projects should also be done together with patient organisations (e.g., feedback on activities).
- In non-competitive areas (i.e., general topics, such as disease awareness campaigns, information campaigns or surveys), companies should better coordinate and collaborate on their initiatives. This will avoid a multitude of similar projects from different companies.
- Communication from companies to patient organisations should be adapted: Dutch/French (rather than English) is preferred and clear language is needed.
- Patient organisations have a hard time finding the right contact person at a company.
- The rules around collaboration between patient organisations and biopharmaceutical companies are fragmented and do not always come across clearly. There is a need for more communication on this.
- Support for patient organisations by biopharmaceutical companies is necessary and legitimate, provided the underlying arrangements are clear, transparent and balanced.
- Smaller patient organisations have limited human resources (volunteers). Companies working with them need to take this into account (e.g., adapted response times or required workload).

Two projects are currently under development within this working group:

- → Together with the PEC, pharma.be organised the first edition of the "Patient Organisations and Pharma Initiative" on 1 December 2022 in Brussels. The aim of this event was to bring together patient organisations and pharmaceutical companies for a dialogue on how to improve cooperation. The ambition is to make this an annual event to strengthen contacts with patient organisations and continue to build mutual trust.
- → The second project deals with the difficulties faced by patient organisations in finding their way around the regulatory framework applicable to collaboration with pharmaceutical companies. The Patient Engagement working group of pharma.be is currently developing a publication for patient organisations that explains the rules and provides concrete examples.

At the same time, the working group is thinking about other long-term projects it wants to undertake with patient organisations. Co-creation remains an important starting point, which means that this long-term vision will be drawn up in consultation with patient organisations.

"Cooperation between the pharmaceutical industry and patient organisations undeniably increases the relevance of projects being developed. A crucial prerequisite for this is the independence of patient organisations. The sky-high difference in organisational form and capacity between patient organisations and pharmaceutical companies can sometimes make cooperation challenging. Moreover, the pharmaceutical industry regularly takes initiatives that ideally would be initiated by patient organisations themselves. Quite a few pharmaceutical companies develop non-competitive initiatives, such as capacity-building events and workshops, without mutual coordination. On the one hand, this sometimes leads to oversupply and pressure on patient organisations. After all, they almost always struggle with limited capacity. On the other hand, the independence of participating patient organisations would be better assured if these initiatives emanated from the pharmaceutical umbrella organisation or at least from several companies together."

Eva Schoeters - RaDiOrg

What are 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 Trial (RCT)[115].

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 medical 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.

4.2.2 Working together for relevant health data

RWD in the life cycle of a medicine

Sharing patient data can lead to valuable new insights and medical innovation. By comparing significant amounts of data, it is possible to arrive at a faster diagnosis and a tailored treatment plan. This requires a significant amount of data on health and, secondly, a lot of research. Therefore, biopharmaceutical research with RWD is present throughout the life cycle of a medicine, complementing data from clinical trials.

A health data ecosystem

FAIR data are at the basis of a health data ecosystem. FAIR stands for:

F **Findable**

to be usable, data must of course be easy to find, for example via a metadata catalogue in one place.

A **Accessible**

data must be accessible (within a predefined and transparent framework).

I **Interoperable**

databases and collections must be compatible with our Belgian e-health infrastructure so that they can be linked together.

R **Reusable**

data should be reusable for research, healthcare, and policy decisions.

There are still steps to be taken in each of these four areas. **Together with all stakeholders in the ecosystem, pharma.be wants to contribute to this**. We were therefore very happy to welcome the creation of the Belgian Health Data Authority in 2022, which is very ambitious and wants to start immediately.

pharma.be and RWD

Biopharmaceutical research with RWD leads to new health outcomes that benefit patients. This is why pharma.be has had a RWD working group since 2015, as well as a Health Data & Digitalisation task force since 2022. This taskforce supports or initiates projects and policy initiatives in health data and digitalisation.

One example is the collaboration with all Belgian hospital associations, the Association of Flemish Hospital Judges and the Belgian Association of Hospital Directors on a harmonisation of procedures and templates for the secondary use of RWD in hospitals.

In addition, our members are working to clarify and harmonise GDPR guidelines for the secondary use of personal data for research.

pharma.be also organises a yearly information session with various speakers to provide our members with insight on the latest available data, procedures and initiatives. Since we want to grow together in this new field of data and digitalisation, we also opened this event to our other partners in the "health data" ecosystem since 2022.

Finally, together with our members in the CAR-T domain and reference centres, we are working on a platform to simplify and automate the data registration of CAR-T treatments. With this project, we hope to demonstrate by the end of 2023 how data registration can be improved and simplified. This should lead to easier collection of more quality health data to be used in research by doctors, academics and pharmaceutical companies.

4.2.3 Working together for the availability of vaccines and medicines

Medicines should always be available whenever patients need them. However, in reality, medicines are sometimes 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. Therefore, we can never fully exclude the possibility that the production of medicines is delayed. 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 a medicine on patients.

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

Since early 2021, PharmaStatus has offered additional communication options. This allows pharmacists and wholesale distributors to contact a company through PharmaStatus when there are problems with the supply of a medicine. Besides the company, the FAMHP also sees these reports. If necessary, the FAMHP can provide additional information to the pharmacist or wholesale distributor. This allows for a more targeted response to an unavailable medicine.

We are also working together 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 the amount of unavailable medicines remains limited and that the impact on patients is minimal.

This cooperation led to a new royal decree in 2021 that requires wholesalers to submit a monthly statement to the FAMHP of the medicines they have in stock and how much of each medicine they have bought and sold. In this way, the government will have a better idea of the quantities of each available medicine and can act more quickly if problems occur.

Looking at the actual figures, 406 medicines were temporarily unavailable in May 2021. Although this has an impact on the patient and the healthcare provider (getting a new prescription, additional visits to the pharmacy), the impact on the continuity of treatment is limited.

In 351 cases there was at least one alternative available, and in 160 of these cases patients had even three or more alternatives. In a majority of the other cases, the patient could be helped by importing a medicine from abroad or by adjusting the treatment. Where even these solutions were not possible, the FAMHP convened a working group to formulate recommendations to ensure the care of affected patients.

pharma.be and FAMHP jointly organise the "Vaccines Symposium"

Contributing to a healthy population is the main goal of the biopharmaceutical sector. Our members not only develop innovative drugs to make sick patients healthy again but also vaccines to ensure that people do not get sick in the first place. After all, vaccination is one of the most powerful and cost-effective forms of prevention. Vaccination not only protects vaccinated people but also ensures the collective protection of the population. pharma.be is cooperating in a policy that promotes the importance of access to vaccines for the entire population.

Although Belgium scores well in terms of vaccinating children, the willingness of adults to be vaccinated is much lower. However, the health gains we can achieve in this population group by convincing them of the importance of prevention are very high.

The healthcare budget is under pressure and a government can only spend each euro once.

Collaboration is therefore essential. Hence our joint strategic commitment to promoting access to vaccines, encouraging life-long immunisation, and emphasising the importance of vaccinating adults. Within pharma.be's Public Health task force, we also have a specific Vaccines subgroup which includes all member companies active in the field of vaccines.

This group organised a two-day symposium together with the FAMHP on 10 and 12 May 2022 around the lessons to be learned from the corona pandemic in Belgium. The COVID-19 pandemic highlighted the importance of immunisation in combating infectious diseases. The authorities and the biopharmaceutical industry worked intensively together to bring safe and effective vaccines to the population. Experts from the FAMHP, Sciensano, regional authorities and academia also looked ahead at the symposium, to be better prepared for the next health crisis and to make life-long vaccination of Belgian patients as effective as possible.

Appendix 1
Methodology of cost-benefit analysis

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 breakdown of expenditures and income on which we based our analysis.

Detailed breakdown of expenditure (in thousands of euros)

Cost for the government (2020)	**3,737,128**
1.1. State expenditure on medicinal products (industry costs, excluding VAT) - NIHDI	3,661,095
1.2. Grants	76,033

State expenditure on medicines is based on the NIHDI figures of expenditure on biopharmaceuticals specialities. This expenditure is 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 government to the biopharmaceutical industry is based on the yearly financial statements of companies operating in Belgium, i.e. ASC 740 (operating grants and compensatory amounts received on behalf of public authorities), 9125 (capital subsidies granted by public authorities) and 9126 (interest subsidies granted by public authorities).

Detailed income statement (in thousands of euros)

Government revenue (2020)	**4,465,816**
2.1. Labour charges	2,294,658
2.1.1. Employer's contribution for social security	**825,209**
2.1.2. Employee's contribution for social security	**416,873**
2.1.3. Third parties withholding tax	**1,052,576**
2.2. Corporate tax	335,690
2.3. Taxes	1,135,874
2.3.1. VAT on turnover (6 % ex-factory price non-reimbursable medicines)	**154,552**
2.3.2. NIHDI taxes on turnover	**343,146**
2.3.3. Third parties withholding tax	**43,906**
2.3.4. Corporate income taxes	**594,269**
2.4. Indirect revenue from third party transactions and investments	699,595
2.4.1. Raw material and commodity purchasing, miscellaneous goods and services	**637,538**
2.4.2. Investments	**62,057**

The income from labour charges is based on the yearly financial statements of companies operating in Belgium, i.e. ASC 621 (employer's contribution to 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 use the turnover figure for non-reimbursable medicines as indicated by IQVIA. We do not take into account the VAT on reimbursed medicines since this is paid by the NIHDI to the government, having no effect on the comparison.

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

   This figure comes from the NIHDI.

3. balance sheet ASC 9148 (withholding tax)

4. balance sheet ASC 640 (corporate taxes and duties)

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

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

   The calculation based on information from the input-output tables (Federal Planning Bureau), which show the domestic demand of the bio-pharmaceutical sector to the other sectors. For each sector, we apply to this domestic demand the ratio of value added to turnover (also available in the input-output tables). We then apply the average (para)tax rate (43.1 %, OECD).

2. revenues from investments by the biopharma-ceutical industry

   To the number of investments, based on Statbel data, we apply the ratio of added value to turnover of the manufacturing industry. Then the average (para)fiscal tax rate is applied (43.1 %, OECD).

APPENDIX 2
Abbreviations

AMCRA	Antimicrobial Consumption & Resistance in Animals
ATC	Anatomical Therapeutic Chemical
ATMP	Advanced Therapy Medicinal Product
BCFI	Belgian Centre for Pharmacotherapeutic Information
BCWC	Bureau for Control on Written Communication
CDR	Commission of Drugs Reimbursement
COPD	Chronic Obstructive Pulmonary Disease
CUP	Compassionate Use Programme
DALY	Disability Adjusted Life Years
DEP Committee	Committee for Deontology and Ethics
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
E-PIL	Electronic Patient Information Leaflet
ETA	Early Temporary Authorisation
FAMHP	Federal Agency for Medicines and Health Products
FAIR	Findability, Accessibility, Interoperability, and Reusability
FDA	Food and Drug Administration
HRQoL	Health Related Quality of Life
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
MIDAS	Migraine Disability Assessment
MNP	Medical Need Programme
OECD	Organisation for Economic Co-operation and Development
R&D	Research and Development
PEC	Patient Expert Centre
PRO	Patient-Reported Outcomes
PN	Parenteral Nutrition
QALY	Quality-Adjusted Life Year
RCT	Randomised Controlled Trial
NIHDI	National Institute for Health and Disability Insurance
RNA	Ribonucleic acid
RWD	Real World Data
RWE	Real World Evidence
SmPC	Summary of Product Characteristics
Statbel	the Belgian statistical office
STEM	Science, Technology, Engineering Mathematics

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Acknowledgements

This Report to Society would not have been possible without the collaboration of the pharma.be colleagues who provided the content and carefully proofread successive print versions, the pharma.be members who provided a description of their newly reimbursed medicines, the stakeholders who were willing to provide a quote, Conny Van Gheluwe of Sproke who was responsible for the copywriting and dotWEB for the layout of this report.

NPO - BE 0407.622.902 - RPR Brussel - Legal deposit: D/2023/4021/01
Responsible publisher: Caroline Ven | Terhulpsesteenweg 166 Chaussée de La Hulpe , 1170 Brussels, Belgium
www.pharma.be | info@pharma.be
VAT BE 0407.622.902 - Company number 0402.622.902

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