Report to Society

2023

pharma.be

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

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Foreword

Caroline Ven
CEO pharma.be

Mid-2023, pharma.be, as the umbrella federation of innovative pharmaceutical companies, released its memorandum for the next European, federal and regional elections to be held in June 2024. The credo is "for a healthy Belgium". After all, the biopharmaceutical industry is a powerful driver for the health of our country's citizens and patients but contributes also to economic prosperity. This is demonstrated once again by the achievements pharma.be can present in this third "Report to Society".

Also in 2023, our country maintained a leading position within the European Union in terms of R&D, production and exports. Although Belgium has only 2.6 % of the EU population, the biopharmaceutical industry accounts for 7.8 % of jobs, 18.7 % of exports and 19.3 % of R&D investment in the EU. This ranks the sector third, second and first in Europe, respectively.

Because of this top position, it is important for our country to assert itself at European level on important files ahead, such as the revision of European pharmaceutical regulations and intellectual property rights. Especially when Belgium chairs the European Council in the first half of next year.

The current federal government has rightly included our country's competitiveness as a priority in the "Belgium health and biotech valley - today and tomorrow" project, but we also call for more attention to the European reform proposals. If our country wants to strengthen innovation, it must continue to take measures that encourage scientific progress. Without incentives for innovation and the protection of intellectual property rights associated with it, many of the medicines and vaccines we have today would simply not exist.

And those treatments do impact patients. In 2022, 95 new medicines were reimbursed. About half were new treatments against cancer or immunomodulatory agents. In addition, relatively more new medicines also became available against cardiovascular diseases, and of the respiratory system.

The stakes are high in the coming period. The European umbrella federation (EFPIA) of the innovative biopharmaceutical industry, has commissioned an impact analysis of the European Commission's existing proposals. The latter would significantly weaken Europe's attractiveness for future investment. If the European position weakens, Belgium loses all the more given our top position.

We ask the next federal and regional governments to pay structural attention to the impact of policy measures on the competitiveness and leverage of the pharmaceutical industry, which is one of the key drivers of a healthy country and population.

Belgium is among the most prosperous countries in the world, and we want to keep it that way in the future. The biopharmaceutical industry can and will continue to make an important contribution to the challenges facing our country.

I hope you enjoy (re)discovering the many activities in this fascinating sector.

Who we are 1

1.1 Focus on the patient

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

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 these needs. They define the way we live our lives. They drive us in everything we do, every single day.

We directly employ about 43,000 people at 127 companies focused on the research and development (R&D) of innovative medicines and vaccines.

For us, health is central: we want the best possible life for everyone in Belgium. That is why our mission is to make Belgium the healthiest place through health solutions. To grow up, live, work and live out your 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 means, not an end in itself. Science is our passion, but only because it allows us to make a positive impact on lives. We are the people who care for others.

The world is changing at a rapid pace: including new diseases and viruses, an ageing population and evergrowing digitalisation. And there are numerous new questions. 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 won't rest. 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 With 127 members

pharma.be brings together **127 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 turnover of the innovative biopharmaceutical industry in Belgium
- **5,881 jobs** in 2022
- **643** medicines on the market in 2022
- **403,379 euro** added value per employee in 2022

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**
- About **1,000** employees by 2022

Discover our members

1.3 As 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, as well as 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 **28 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

Ann Adriaensen
Secretary General & Public Health Director

Herman Van Eeckhout
Political & Finance Director

Geert Steurs
Economics Director
Chief Economist

Patricia van Dijck
Political & Medical Director

Julie Gusman
Market Access Services Director

David Gering
Communications Director

Marjan Willaert
Policy Advisor Market Access

Hanne Wouters
Market Access Advisor

Filipo Serra
Market Access Advisor

Magali Audiart
Pricing & Market Access Advisor

Marie Vande Ginste
Public Health Advisor

Johan De Haes
Public & Animal Health Advisor
SME Account Manager

Nathalie Lambot
Public Health & Clinical Trials Advisor

Karen Crabbé
Economic & Health Data Advisor

Thomas Cloots
Economic Advisor

Tom De Spiegelaere
Healthcare Budget Advisor

Charlotte Weyne
Senior Legal Counsel & European Policy Advisor

Willy Cnops
Life Science Advisor

Armand Voorschuur
European Policy & Market Access Advisor

Annick D'Hont
Compliance & Legal Advisor

Anne-Sophie Doms
Content Manager

Denise Blockmans
Webmaster & ICT Manager

Melanie Balcaen
Finance & HR Manager

Carine Vancutsem
Members, Partners & Office Manager

Chloé Legrand
Members, Partners & Office Assistant

Annick Vancutsem
Members, Partners & Office Assistant

Britt Hunninck
Members, Partners & Office Assistant

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' terms of office are valid for three years. They are elected at the General Assembly.

1 Frédéric Clais Eli Lilly Benelux **Chair of pharma.be**, **2 An Van Gerven** Pfizer **Vice-Chair of pharma.be**, **3 Renaux Decroix** AbbVie, **4 Gabor Sztaniszlav** Amgen, **5 Keira Driansky** AstraZeneca, **6 Sally McNab** Bristol-Myers Squibb Belgium, **7 Emmanuelle Boishardy** GlaxoSmithKline Pharmaceuticals, **8 Maria Fernanda Prado** Janssen-Cilag, **9 Katrien De Vos** MSD Belgium, **10 Federico Mambretti** Novartis, **11 Marie-José Borst** Roche, **12 Johan Heylen** Sanofi Belgium, **13 Michael Nesrallah** Takeda Belgium, **14 Xavier Hormaechea** 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 2023, 54 organisations had partnered with pharma.be. These organisations are active in various fields of expertise such as pricing and reimbursement, medicine 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. The direct members include 37 national associations, 40 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.

What we do 2

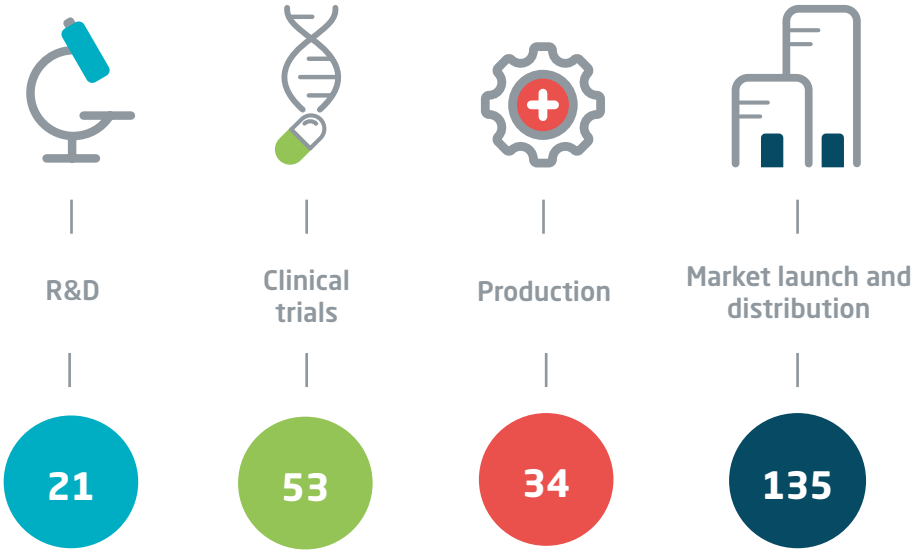
2.1 Operating throughout the entire value chain

Together, the pharma.be member **companies hold strong positions in Europe in every key aspect of the biopharmaceutical value chain**, from R&D and clinical trials over production to medicine marketing and distribution. This is due to a unique combination of a well-developed ecosystem, highly skilled workforce and strong cooperation with governments and research centres.

The benefits of an integrated approach to the value chain are great, both for patients, their environment and healthcare, and for the economy. This was abundantly clear during the COVID-19 pandemic. The Belgian biopharmaceutical sector was able to fully meet the challenge, from research and production to the introduction of innovative solutions for patients.

In this section, we focus on the innovation activities of our member companies in Belgium towards better solutions for patients: how much they invest in R&D, the clinical trials they conduct here, and the new medicines for which our companies have applied for and received reimbursement. We also pay specific attention to rare disease challenges. In chapter 3, we will look at the added value of these activities for patients, the healthcare system and society, and their economic return.

Number of companies in Belgium



Source: pharma.be

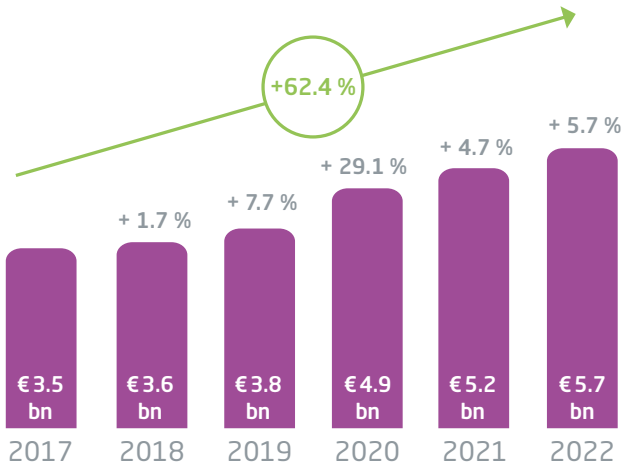
2.2 Research & Development as drivers of innovation

2.2.1 R&D investments in Belgium

We have no natural resources in our country, but all the more knowledge. Research and development (R&D) are not only in Belgium's DNA, but are also at the heart of the biopharmaceutical industry. The sector delivers a lot of important innovations every year. The added value is immediately very visible, as we live longer and better thanks to these innovations.

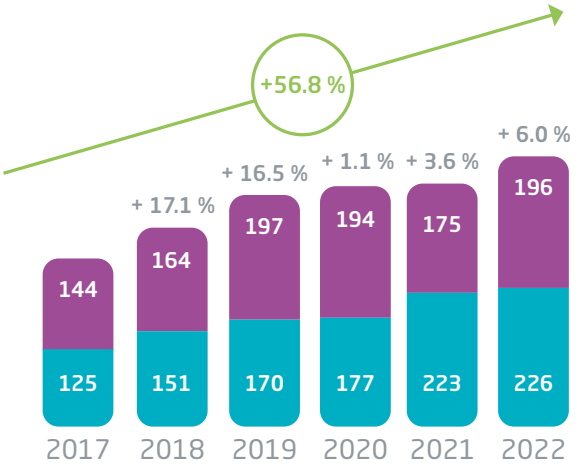
- In 2022, the sector invested over 15 million euros in **R&D every day**, amounting to a total of **5.7 billion euros**.
- Over the past 25 years, investment in R&D has increased fivefold. Over the past five years, investments increased by no less than 62 %.
- In 2022, on average **more than one patent application was filed per day** in Belgium in the field of biotechnology and pharmaceuticals. These applications are crucial for the sector because the protection provided by patents is a prerequisite for continued investment in the very expensive and long-term research programmes.
- Since 2017, the number of patent applications in those fields has increased by almost 57 %. This growth was some three times higher than the growth in all technology domains combined. In 2022, for example, the sector accounted for **over 16 % of the total number of patent applications** in Belgium. This makes the biopharmaceutical sector an absolute leader in innovation.

Evolution of R&D investment in Belgium (billion euros)



Source: pharma.be, members' survey

Evolution of patent application in Belgium



Source: European Patent Office, European patent applications 2011-2021 per field of technology

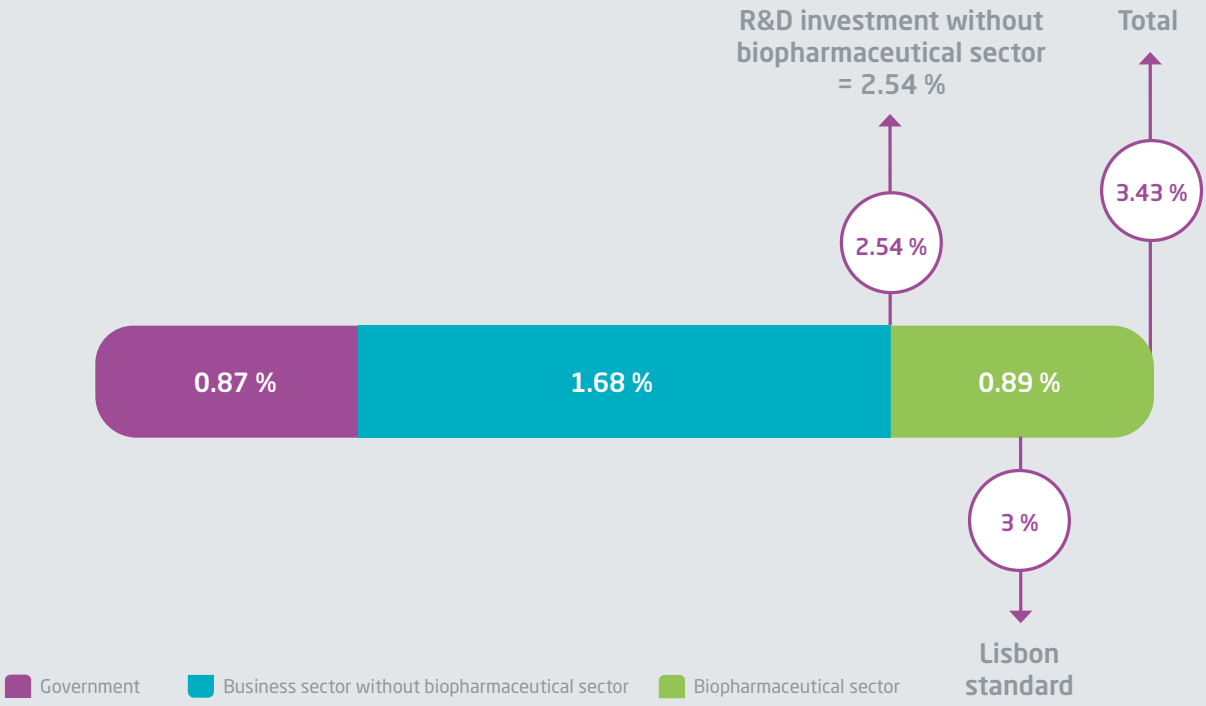
What if the biopharmaceutical sector did not invest in R&D in Belgium?

The fact that Belgium is an "innovation leader", as defined in the European Innovation Scoreboard 2023[1], is largely due to the biopharmaceutical sector. If, when calculating the Summary Innovation Index for a number of dimensions considered at sector level*, we set the biopharmaceutical sector's figures to zero, we see that Belgium scores significantly lower. The score would drop from 125.8 to 122.3. This would mean that Belgium is no longer among the 5 innovation leaders, more precisely the countries with a score higher than 125 % of the EU average. **In other words, it is thanks to the Belgian biopharmaceutical sector that Belgium is today at the forefront of innovation within Europe.**

We come to a similar conclusion when we look at the so-called Lisbon standard. To keep up with international developments, it was agreed in 2000 that European governments and companies should together spend 3 % of GDP annually on R&D by 2010[2]. Belgium has managed to meet this standard since 2019, reaching 3.4 % of GDP for 2021. Of this, 2.5 % was accounted for by the business sector[3]. The biopharmaceutical sector accounts for just over a third of these investments by the business sector and thus accounts for 0.8 % on its own in the Lisbon standard[4]. Put differently, Belgium would arrive at an R&D investment rate of 2.5 % of GDP if there were no biopharmaceutical R&D investments. **Belgium would not meet the Lisbon standard in that case.**

* It deals with the following dimensions: R&D expenditure in the business sector, non-R&D innovation expenditures, innovation expenditures per person employed in innovation-active enterprises, PCT patent applications and medium and high-tech product exports[5].

Distribution of R&D investment in 2021 (% GDP)



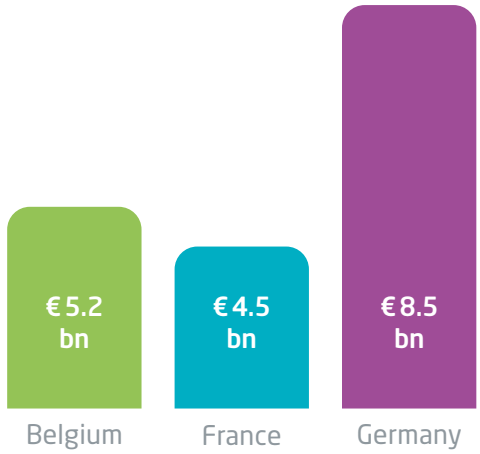
2.2.2 R&D investments compared to Europe

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.** In terms of R&D investment in 2021, the latest year available, Belgium should only be behind Germany, while we are ahead of France. Placing this result in perspective, the Belgian biopharmaceutical sector invested more in 2021 than Italy, Denmark, Spain and Sweden - numbers 4 to 7 - combined, while Belgium only ranked in 8th place in terms of population.

Looking at investment per inhabitant, Belgium is definitely in the lead. Our investments in 2021 were almost 2.5 % 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. **Between 2017 and 2021, Belgian R&D investment per capita increased by more than 45 %**, more than three times the growth rate of total R&D investment per capita in the EU27. No other country with a significant amount of R&D investment per capita realised such strong growth. The no. 2, Denmark, even recorded significantly negative growth.

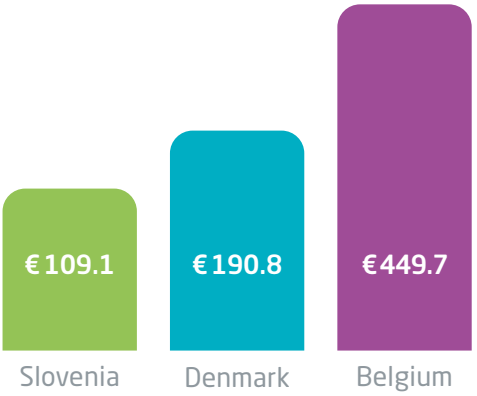
These impressive figures show that innovations cannot be taken for granted. New, innovative medicines require a particularly large amount of time and resources. The biopharmaceutical sector is therefore the most R&D-intensive industry. Not only in Belgium, but also in Europe, the Belgian biopharmaceutical sector is increasingly important in terms of R&D.

Total biopharmaceutical investment 2021



Growth of biopharmaceutical investment in R&D per capita

Biopharmaceutical investment in R&D per capita 2021



Source: pharma.be, enquête onder leden & EFPIA, The Pharmaceutical Industry in Figures, Key Data 2023

2.3 Clinical trials for new therapies

Clinical trials are a key phase in the development of new vaccines or medicines. Through clinical trials medicines are tested for safety and efficacy in humans. This also provides valuable new insights into the treatment and prevention of diseases. Clinical studies are therefore an **important source of inspiration for new fundamental scientific research**. At the same time, clinical trials provide **patients with free access** to the latest treatments even before they are available on the market.

It is certainly always useful to participate in clinical trials. I am convinced that if I had never entered clinical studies, I would not have evolved with clinical science. I was one of the first to participate in the studies with antibodies. Subsequent evidence suggests that these medicines are a good solution. As a participant in the clinical trials, I enjoyed the scientific advances even before the commercialisation of the medicine. I have already had the benefit of a medicine that is not yet available to other people. I do not regret participating in clinical trials because I am sure it is thanks to those clinical trials that I am still here today.

Jean-Pierre Blondeel,
Patient and Chairman Hodgkin & Non-Hodgkin vzw

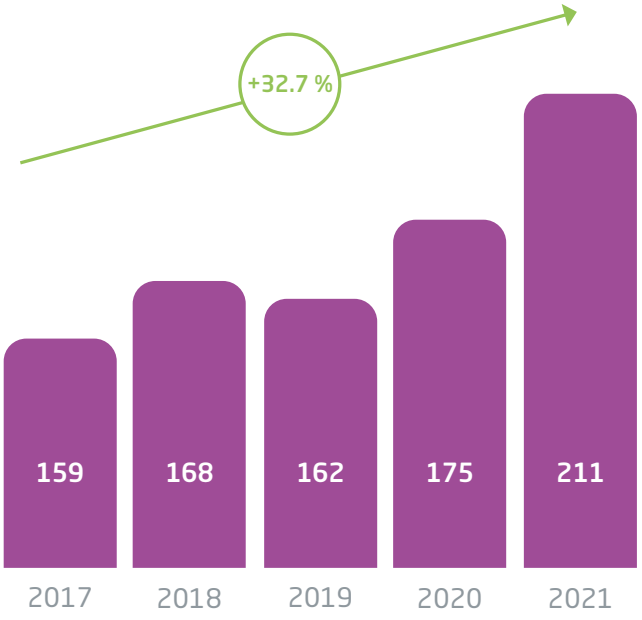
Watch his testimony

In 2022, Belgium once more confirmed its position as European leader in clinical trials, with 474 authorised clinical trials, 80 % of which were initiated by companies. Consequently, the biopharmaceutical sector is a driving force for clinical trials in Belgium. The fact that Belgium is at the forefront is the result of an interplay of several elements: the strong presence and accumulated expertise of biopharmaceutical companies, the quality and knowledge of the scientific community, the infrastructure of research centres and hospitals, and the level of expertise of researchers and of the competent authorities, in particular the Federal Agency for Medicines and Health Products (FAMHP).

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 medicines to fight cancer.**

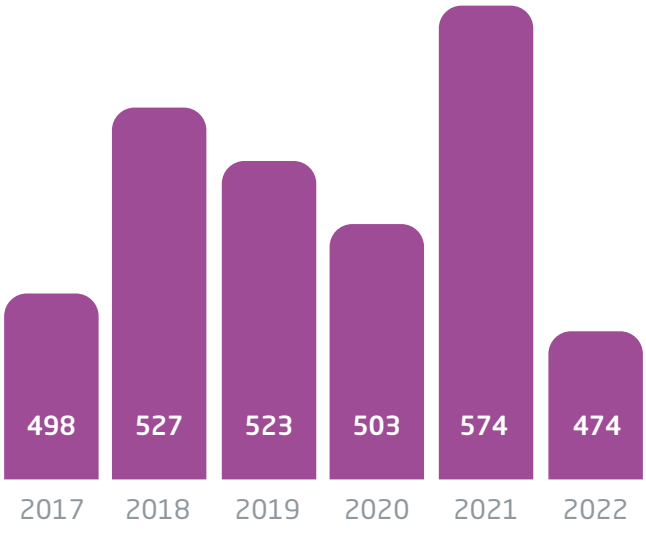
For example, 211 clinical trials were launched in Belgium in 2021 to treat cancer, or just under 18 new trials per month. 20 % of the clinical trials conducted in Europe in 2021 to test cancer medicines occurred in Belgium.

Evolution of cancer clinical trial applications in Belgium (2017 - 2021)



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

Number of approved applications for clinical trials



Source: FAMHP data

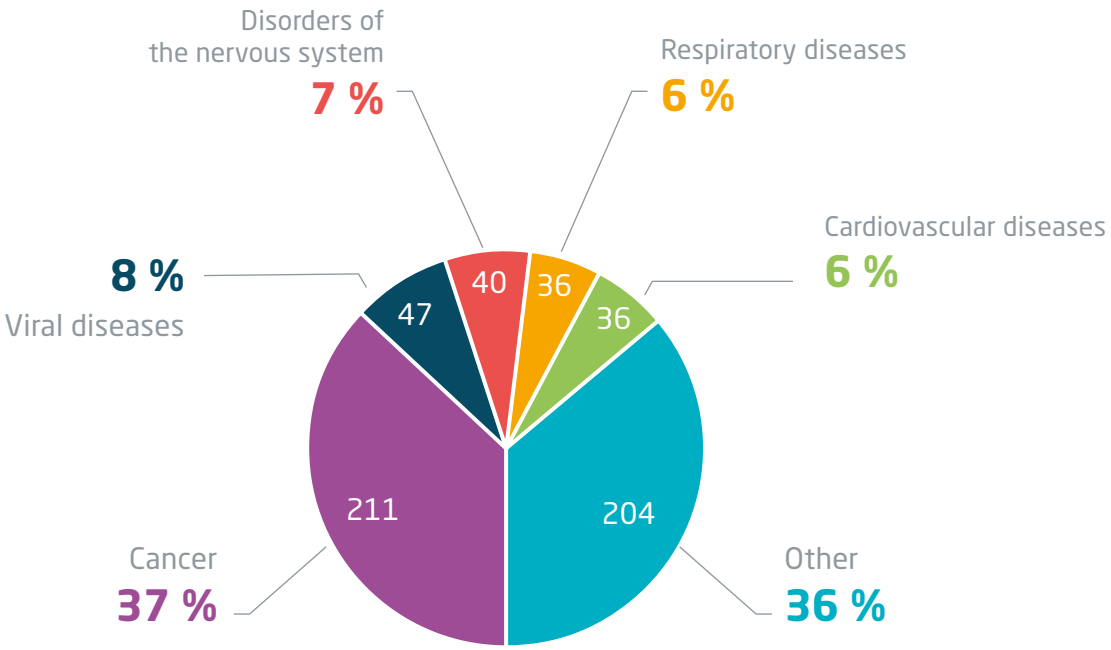
Clinicaltrial.be: a portal site around clinical trials

It is important for both patients and their treating doctors that there is clear, accessible and preferably centralised information about all ongoing clinical trials in Belgium. However, patients report that at diagnosis, they are not always aware of the possibility of participating in a clinical trial. Information on clinical trials is often only available in English and is also difficult to understand. Today, we also see a lot of fragmentation of information, including through all kinds of companies, hospital portals or through patient organisations trying to bundle everything for one disease. It was therefore essential to have a single official source that could provide all approved information in an appropriate language to the various stakeholders. Patient Centrics - Esperity has therefore created a unique web portal in collaboration with patient organisations, hospitals and the biopharmaceutical industry: clinicaltrial.be.

After more than two years of development, this platform was officially launched on 20 May 2023, on the occasion of International Clinical Trials Day, as part of an awareness campaign #ThanksToScience highlighting the importance of clinical trials in improving patients' quality of life.

clinicaltrial.be

Share of clinical trial applications in Belgium by disease domain (2021)



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

2.4 Newly reimbursed medicines

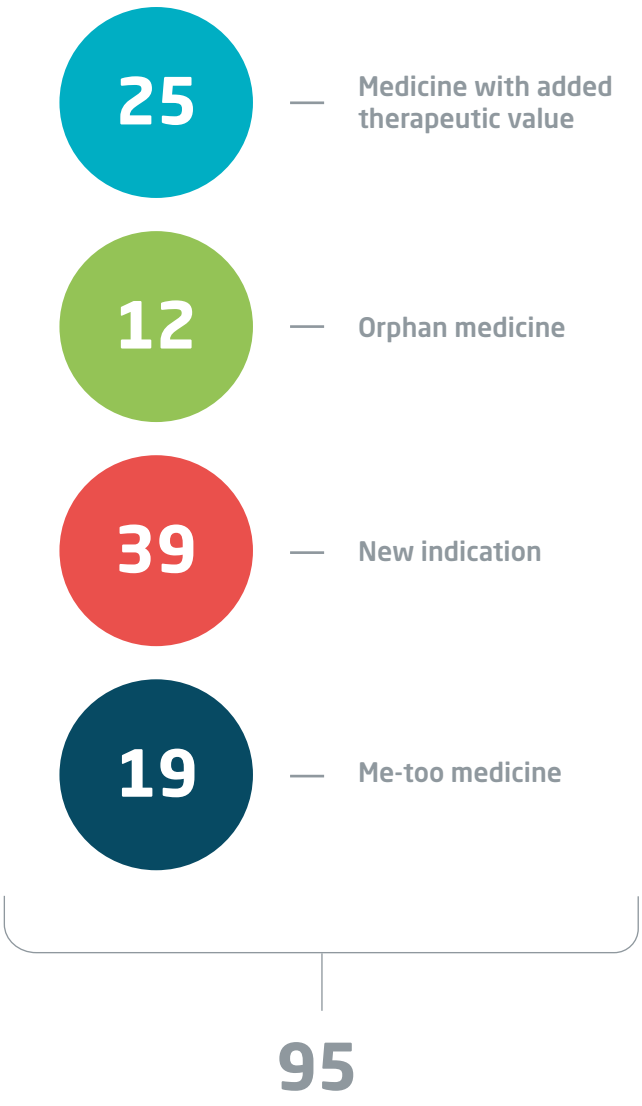
Our member companies' R&D activities and clinical trials in Belgium and abroad result in the development of new medicines. To make these available to patients in Belgium, companies apply for reimbursement with the National Institute for Health and Disability Insurance (NIHDI) so that patients do not have to pay the full cost. Below we provide information on the number of newly reimbursed medicines in Belgium in 2022. The added value of some of these medicines is discussed in chapter 3.

2.4.1 According to type

In 2022, **95 new medicines** were reimbursed (see figure for distribution by type).

Notes:

- A medicine with **added therapeutic value** offers higher therapeutic value than an accepted standard treatment, according to the pharmaceutical company concerned. This means the disease is better treated with this medicine.
- **An orphan medicine** is a medicine for the treatment of a rare disease and therefore often provides a solution to an unmet medical need.
- A **new indication** refers to a medicine that is already reimbursed for a particular indication/condition and for which the company applies for additional reimbursement for another indication/condition. For example, this could be a medicine that is already reimbursed for the treatment of lung cancer but is now also reimbursed for the treatment of colon cancer.
- A **me-too medicine** does not offer a higher therapeutic value than existing medicines for the same indication/disease but may add value to the patient because of improvements in dosage, administration schedule, comfort or ease of use. An additional advantage of these medicines is the greater guarantee that a treatment can be continued in the case of unavailability of the existing 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 2022. More than half of these were new cancer medicines or immunomodulatory agents (ATC L). In addition, relatively newer medicines also became available to combat cardiovascular diseases (ATC C), and those of the respiratory system (ATC R).

ATC code	Number of newly reimbursed medicines in 2022	ATC main group	Examples of pathology
A	3	Alimentary tract and metabolism	Diabetes, hepatic porphyria, hereditary tyrosinemia
B	5	Blood and blood-forming organs	Haemophilia A, thrombocytopenia, beta-thalassaemia
C	6	Cardiovascular system	Heart failure
D	1	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	6	Anti-infectives for systemic use	HIV infections, bacterial infections, hepatitis B
L	44	Antineoplastic and immunomodulating agents	Solid and haematological tumours, multiple sclerosis, haemorrhagic colitis, psoriasis, a.o.
M	4	Musculoskeletal system	Spinal muscular atrophy, osteoporosis, a.o.
N	6	Nervous system	Migraine, epilepsy, severe depression, amyloidosis, a.o.
P	0	Antiparasitic products, insecticides and repellents	Anthelmintics
R	14	Respiratory system	Cystic fibrosis, asthma, obstructive airway disease
S	1	Sensory organs	Hereditary retinal dystrophy, diabetic macular oedema
V	3	Miscellaneous	Hyperkalemia, contrast medium

2.5 Rare diseases: challenges and solutions

Rare diseases, in a sense, are not rare at all: **more than 500,000 Belgians have a rare disease**. In addition, despite huge scientific, medical and biopharmaceutical advances in recent decades, there are still many thousands of rare diseases for which there is no adequate treatment or even no treatment at all.

Rare diseases

A rare disease is defined as a condition affecting no more than 1 in 2,000 people in the European Union. But there are wide variations: only 4 % of rare diseases occur in between 1 to 5 people in 10,000, while 84 % affect less than 1 in 1,000,000 people. In other words: 84 % of all currently known rare diseases occur in less than 1 in a million people. Rare diseases are also called **orphan diseases**, this is because, for example, hardly anything is known about them medically, sometimes even very small numbers of patients are affected by them worldwide, and there is no proper treatment or even any treatment for them. On top of that, orphan diseases are often life threatening or chronically debilitating. A major problem is also that rare diseases are usually diagnosed too late: on average, it takes 4.9 years to get a correct diagnosis.

Many rare diseases, thus numerous patients

Some **7,000 rare diseases are currently known to** affect people around the world. Even if certain diseases are rare or even ultra rare, that does not mean that rare diseases affect only a few patients and families. Even though there are sometimes only a few patients per rare disease in Belgium, the large number of rare diseases means that there are more than half a million Belgians with a rare disease. An estimated 30 million people in Europe and 300 million worldwide have a rare disease.

Many new treatments have become available …

Fortunately, significant progress has been made in developing treatments for rare diseases over the past 20 years. The European Medicines Agency (EMA) has now approved more than 200 new orphan medicines[6], meeting the needs of 6.3 million rare disease patients[7]. Moreover, more than 700 medicines for rare diseases are in development[8].

… but many thousands of rare diseases still await solutions

No approved therapy exists for 95 % of the approximately 7,000 rare diseases identified[9]. In fact, for most of these diseases, no research even exists. However, the search for new treatments for the many even rarer diseases is very difficult and hampered by large scientific unknowns and huge scientific challenges. At the current rate, it would take more than 100 years to develop treatments for all rare conditions.

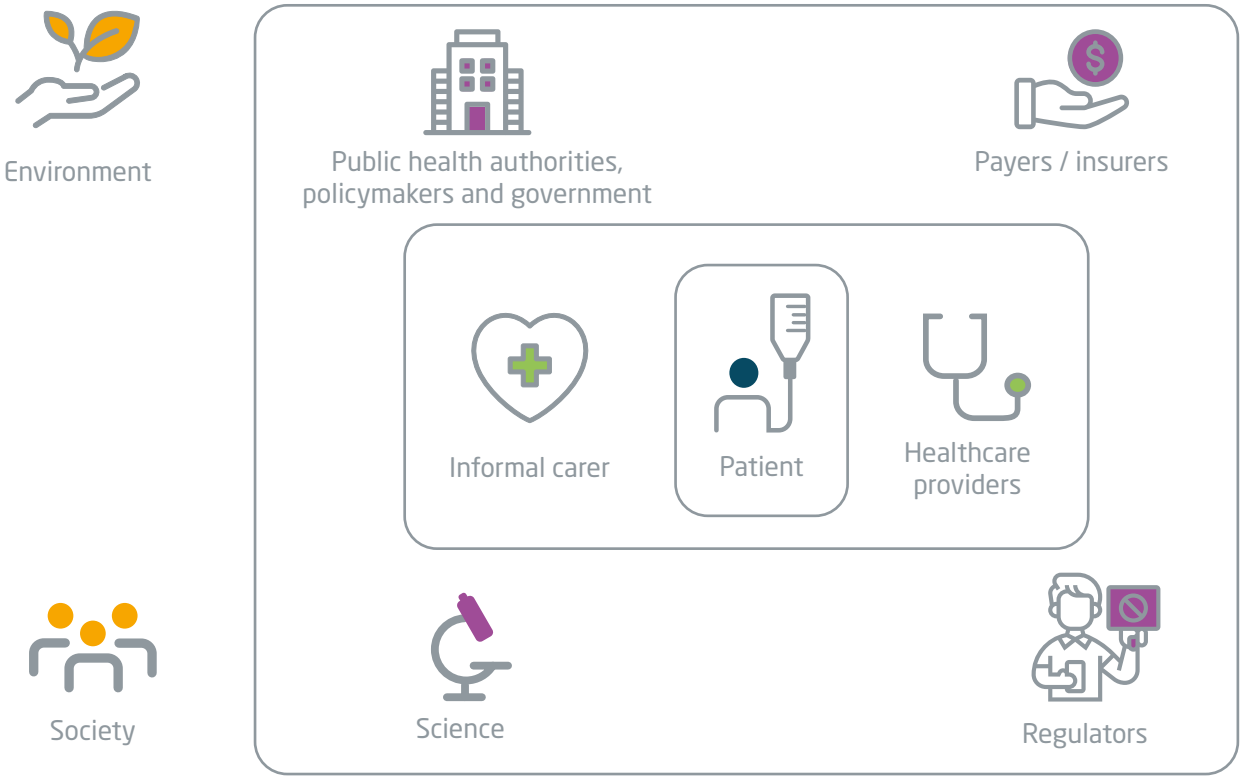
The "RD Moonshot" initiative

Therefore, 7 international parties (industry, governments, patient organisations and research organisations)[10] launched the **"Rare and Paediatric Disease Moonshot"** initiative at the end of 2022, known as the **"RD Moonshot"** initiative for short[11] [12]. The aim is to improve patients' quality of life and accelerate and support the development of innovative medicines and technologies for rare diseases and diseases in children that are currently untreatable across the European Union.

3

For whom we create added value

The biopharmaceutical innovation offered by pharma.be members can improve patient outcomes, optimise healthcare, reduce costs and drive economic growth. To better understand its potential impact, we listed the key stakeholders, outside of the biopharmaceutical industry, for whom biopharmaceutical innovation can bring value (see figure and box).



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 some examples of medicines newly reimbursed in 2022 and also take a brief look ahead to promising (r)evolutions in the biopharmaceutical sector. We also provide figures regarding the huge health gains that more recent cancer medicines have brought to patients. And we present the results of a study by Prof. Lichtenberg who investigated whether the advent of new medicines led to fewer deaths and fewer hospital admissions in Belgium. However, the story does not stop there. Our sector is also an important driver of our knowledge economy. The numbers in terms of employment and export were already impressive and have only continued to grow in 2022. This is reflected in the positive cost-benefit analysis of our sector for the Belgian government.

Added value for whom?

In total, we defined nine major stakeholder groups that can directly or indirectly benefit from biopharmaceutical innovation. Medicines are, of course, first and foremost for **patients**. They value biopharmaceutical innovation because it can directly improve their health. The development of new or improved treatments can lead to better disease management, increased longevity and improved quality of life. Biopharmaceutical innovation can also reduce the treatment burden, for example through treatments that have fewer side effects or are easier to administer. Looking at it slightly more broadly, the availability of good medicines is also very important for informal carers and caregivers.

- Biopharmaceutical innovation can have an indirect effect on the well-being of the **informal carer**. Reducing the burden of treatment and improving the patient's quality of life can lead to an increase in the well-being of the informal carer.

- For **healthcare providers** such as doctors, nurses and pharmacists, biopharmaceutical innovation can offer new tools to improve patient care. This can lead to better treatment outcomes, more efficient patient management and greater job satisfaction. Healthcare providers can also benefit from innovations that simplify or improve their work process, such as medicines that require less follow-up. Looking at it even more broadly, there are a number of other stakeholders for whom medicines create added value.

- **Payers and insurers** such as the NIHDI value biopharmaceutical innovations that are cost-effective and improve patient outcomes, as healthier patients require less medical intervention. Medicines can also prevent or detect diseases at an early stage, reduce the need for hospitalisation or shorten the duration of expensive treatments, which can lead to significant cost savings.

- **Regulators**, such as the European Medicines Agency (EMA) in the EU or the Federal Agency for Medicines and Health Products (FAMHP) in Belgium, are tasked with ensuring the safety and efficacy of medicines. They value biopharmaceutical innovation that provides clear evidence of safety and efficacy, addresses unmet medical needs and/or improves existing treatments. They also value innovation in areas such as medicine manufacturing that can improve medicine quality and safety.

- **Public health authorities, policymakers and government** may value pharmaceutical innovation for its potential to improve public health and reduce healthcare costs. These could be innovations such as new vaccines that reduce disease transmission or treatments for widespread diseases. Public health authorities also value innovation that reduces health inequalities and improves health equity. Policymakers and government can additionally consider the broader economic benefits, such as new jobs in the pharmaceutical sector, higher productivity through a healthier population and the potential for international leadership in the biopharmaceutical sector.

- For the **scientific community**, new biopharmaceutical innovations can open up new areas of study, increase understanding of disease mechanisms and stimulate further innovation. Finally, the environment and society at large also benefit from biopharmaceutical innovation.

- Biopharmaceutical innovation can reduce **environmental impact**, such as green chemistry approaches that reduce chemical waste in medicine production, or designs that minimise environmental pollution after use.

- **Society** as a whole benefits from biopharmaceutical innovation in numerous ways. Better public health and less disease transmission lead to societal benefits, as do the economic consequences of a healthier, more productive population. Society also benefits from advances in scientific knowledge, environmental management and health equity.

3.1 A positive impact for patients, healthcare sector and society

3.1.1 Added value of newly reimbursed medicines

In 2022, many new medicines received approval for reimbursement (see 2.4). These provide significant added value for patients. We provide below some **examples** from the group of medicines whose therapeutic added value was recognised by the Commission of Reimbursement of Medicines (CRM), as well as orphan medicines.

Hereditary angioedema

About one in 50,000 people worldwide have hereditary angioedema (HAE). It is a rare genetic disorder that makes patients suffer from frequent swelling. These appear mainly on the face, hands, feet and genitals. The attacks can be painful and cause deformities, and if they reach the respiratory tract, they can even lead to death. Underlying these attacks is bradykinin, a molecule of which too much is produced due to a lack of C1 esterase inhibitors.

To treat HAE, there are traditionally two choices: 1. Treating the acute attacks with intravenous injections of C1 esterase inhibitors or subcutaneous injections of a bradykinin receptor antagonist. 2. Seizure prevention via intravenous injections of C1 esterase inhibitors two to three times a week.

Recently, a new therapeutic treatment has now been reimbursed to prevent HAE attacks in patients older than 12 years: subcutaneous injections of a monoclonal antibody against plasma kallikrein. Indeed, this protein is partly responsible for the production of bradykinin. Clinical studies have shown that this molecule works particularly well to reduce the regularity and severity of HAE attacks. In patients treated with this new molecule in a phase 3 study, the average number of seizures was reduced by as much as 87 % after six months versus those who received a placebo. The treatment is also well tolerated; there are no reports of serious side effects.

Not only does this new treatment provide a significantly better preventive effect, but it is also much more user-friendly: the frequency can be reduced from 52 to 104 administrations a year with a C1 esterase inhibitor to only 52 or even 26 administrations a year with this new molecule. Subcutaneous injection is also more convenient and comfortable than intravenous injection.

Thanks to this new molecule, HAE patients can now count on a practical and above all effective preventive treatment that increases their quality of life and reduces the impact of this debilitating disease. This innovative treatment thus also makes an important social contribution.

Spinal muscular atrophy

In 2022, Belgium reimbursed a new treatment for spinal muscular atrophy (SMA) for the first time. This genetic neuromuscular disease causes muscles to weaken and die. The disease affects about one in 10,000 babies worldwide every year, making it the most common genetic cause of death in young children. Fortunately, more and more countries, such as Belgium, are implementing newborn screening. This radically changes the prognosis of SMA. Thanks to oral administration, it can be treated at home. This also allows treatment of patients who cannot tolerate medicine administration in the cerebrospinal fluid or in whom this is technically difficult or even impossible due to complications of the disease. This new treatment is the result of close collaboration with the patient community from start to finish. Because collaboration across the healthcare ecosystem drives innovation and is key to improving our healthcare system. Only by working together can we build a better world for our patients.

Cholangiocarcinoma

Cholangiocarcinoma is a rare form of cancer that originates in the bile ducts[13]. People with bile duct cancer are often only diagnosed at a late or advanced stage. As a result, the prognosis is poor[14 15] and possible treatments are limited[16]. However, a new oral medicine has been available in Belgium since July 2022. The active substance belongs to the class of protein kinase inhibitors and blocks the action of fibroblast growth factor receptors (FGFRs). These play an important role in the rapid multiplication and survival of cancer cells and in the migration and formation of new blood vessels in specific cancers[17].

This is the first new treatment option in Europe for more than a decade for adult patients with locally advanced or metastatic bile duct cancer with FGFR2 fusion or rearrangement after at least one previous systemic line of treatment. This group comprises 10 % to 16 % of patients with bile duct cancer in the liver[18 19 20]. No effective standard treatment has existed for them yet. A large study showed that in 37 % of patients, the tumour was effectively reduced in size; life span was extended by an average of 9.1 months[21].

Mantle cell lymphoma

Mantle cell lymphoma (MCL) is an aggressive form of lymphoma diagnosed in over 100 Belgian patients each year[22]. Standard care in the first line of treatment typically consists of chemo-immunotherapy and a Bruton's tyrosine kinase (BTK) inhibitor. However, the risk of relapse is high. In all cases, the health condition worsens at an accelerated rate and the prognosis becomes more unfavourable[23]. The disease is therefore considered incurable with conventional treatment options. Recently, a new form of immunotherapy is being reimbursed in Belgium that does offer MCL patients the prospect of longer survival and even a chance of a cure. This new form of therapy, CAR-T cell therapy, has long been used for other aggressive lymphomas and has already proven its clinical benefit and cure rate there. In CAR-T cell therapy, T cells are isolated from the patient's blood. These are then given a special antenna or CAR (Chimeric Antigen Receptor) and administered back to the patient. CAR recognises lymphoma cells and attacks them in a targeted manner. In this way, the patient's own immune system is modified to target the cancer cells. Clinical studies show that this newly reimbursed indication represents a significant improvement in the treatment of patients with mantle cell lymphoma who do not respond to treatment or have relapsed after at least two lines of treatment: if the prognosis after two previous lines of treatment was previously very unfavourable, with a median survival of less than one and a half years[24], it is almost four years with CAR-T cell therapy. In doing so, over a third of patients still showed no signs of cancer after three years[25]. On this basis, CAR-T cell therapy has rapidly become the new standard treatment for these patients. Efficacy and safety for other types of lymphoma and blood cancer are under further investigation.

Human immunodeficiency virus (HIV)

Every year, more than 700 people in Belgium are told they are infected with human immunodeficiency virus (HIV)[26]. Fortunately, antiretroviral treatment has since been fine-tuned such that people living with HIV today have a near-normal life expectancy. This is provided that the virus is kept under control with a suppressive treatment[27]. A new medicine for HIV has been reimbursed in Belgium since 2022. It should be taken twice daily in combination with other antiretroviral medicines[28]. This represents another step forward as it is the first medicine in a new class that can be used in adults infected with type 1 HIV that is resistant to multiple medicines[29]. Thanks to the new medicine, suppressive antiretroviral treatment can still be initiated in these patients. In the phase 3 study, patients who received the new treatment saw a significantly greater reduction in viral load after eight days than those who received a placebo[30]. An open-label follow-up study found that the medicine was still effective even up to week 96. The medicine also causes few serious side effects.

Currently, antiretroviral treatment is not the main problem for the vast majority of our patients with HIV: one pill a day, good tolerance, undetectable viral load, etc. Most of the problems we face are incidental to the viral problem, although they are equally important: psychosocial malaise, stigma, co-morbidities, ageing, sexual health. Yet we still regularly treat patients where the viral problem remains the main problem: because of multiple medicine resistance, intolerances and medicine interactions. For these patients, the recent arrival of this new medicine has really made a difference: it is a new class of medicine that is also well tolerated. For these patients, there was a "before" and an "after".

Charlotte Martin *MD, PhD, Head of Department, Infectious Diseases, CHU Saint-Pierre*

3.1.2 Promising (r)evolutions in the biopharmaceutical sector

Precision medicine puts the patient first

Precision medicine represents a radical shift in the approach to treating patients. This involves using precision medicine and biomarker testing to give **the right patient the right treatment** at the right time. Sciensano is currently conducting a forward-looking study on the implementation of precision medicine in Belgium in which pharma.be is participating as a key stakeholder. For patients in our country, further investing and building the precision medicine ecosystem is crucial to enjoy all the benefits of this rapid innovation, in which our industry has been investing tremendously in recent years.

What is precision medicine?

With precision medicine, patients' treatment is tailored to their individual characteristics and needs. The goal is to give the right treatment to the right patient at the right time. Testing patient characteristics, called biomarkers, allows doctors to identify patients who would benefit most from a precision medicine. These biomarkers are objective biological traits that can be measured genetically or chemically. Measuring biomarkers is done using modern diagnostic instruments.

How does a biomarker test work?

A biomarker test analyses specific characteristics in the patient's body (e.g. in blood or tumour tissue), to determine whether the precision medicine is suitable for the patient and whether it will have the desired therapeutic effects. Using biomarker testing significantly increases the chances of successful treatments and reduces the likelihood of unwanted side effects. By giving patients a medicine specifically designed to address their unique biological characteristics and disease profile, precision medicine has the potential to increase successful treatments and improve patients' health outcomes. More and more knowledge on biomarkers is being gained which encourages broader testing, enabling accurate treatment decisions and monitoring.

In which therapeutic areas are precision medicines used?

Precision medicines already account for more than a quarter of newly approved medicines. Precision medicine has become a mainstay in healthcare for various diseases, in particular for the treatment of oncological and genetic diseases but also infectious diseases, cardiovascular diseases and diabetes. The diagnosis of type 1 diabetes, for example, is based on glucose measurements, namely fasting glucose, a glucose tolerance test (only for gestational diabetes or scientific purposes) or an HbA1C determination. The medicines developed from them are more accurate, effective and safer than traditional treatments, allowing patients to achieve better health outcomes and experience a better quality of life. We expect major breakthroughs in precision medicine in the future thanks to further research and continuous development. Its full potential is yet to be tapped.

Why are precision medicines important?

Precision medicine puts the patient first. Indeed, when applying precision medicines and biomarker testing, precious patient time is not wasted on ineffective treatments. This results in lower overall healthcare costs and doctors can make more informed decisions for the right treatment. This is positive for patients' confidence in their treatment. Continuing to measure the effects of treatments in daily practice will ensure that we will be able to use the most optimal (cost-effective) therapy per patient, thus creating a healthcare system that can prevent, diagnose and treat diseases efficiently and sustainably. Moreover, by collecting all relevant real health data (results of diagnostic tests, therapies administered and treatment results) in a centralised platform, patient health can be improved by making better treatment decisions for current and future patients. During the COVID-19 pandemic, for example, scientists developed new biomarkers and advanced diagnostic technologies, which led to greater public health benefits in Belgium, both for individual patients and for our society as a whole.

Combination therapies offer additional hope

A combination therapy combines two or more separate medicines in one treatment regimen. These individual medicines often come from different companies. In recent years, combination therapies have become increasingly prominent in the treatment of various conditions. Practical experience with complex diseases has convincingly demonstrated it: **combining treatments can provide significant clinical benefits for patients**.

Combination therapies can have distinct **advantages** over monotherapies:

- Several biological signalling pathways responsible for disease development can be addressed simultaneously;
- The risk of resistance is reduced because - for example, in cancer treatment - cells are fought in different ways;
- The medicines work together, enhancing the effectiveness of each medicine individually. So, 1+1 is 3.

These benefits translate into better clinical outcomes and therefore additional hope for patients. In recent years, therefore, combination therapies are increasingly coming to the fore in the treatment of complex diseases such as cancer, HIV, rheumatoid arthritis and hepatitis C. This trend will only intensify in the near future, as the biopharmaceutical industry intensifies its commitment to research and development of combination therapies. Combination medicines **already** represent **more than 1 in 5 of current medicines in development** today, and even up to 1 in 2 for cancer treatment.

3.1.3 The health benefits of recent cancer medicines

Unfortunately, cancer is still the leading cause of death in our country. But many clinical trials in Belgium involve cancer medicines, and the vast majority of newly reimbursed medicines in 2022 are also for cancer. Fortunately, these new cancer medicines bring hope because of the **impressive health gains** they bring:

- Since the advent of immunotherapies, the 5-year survival rate for patients with **metastatic melanoma** has increased to 50 %. In 2010, the 5-year survival rate was only 5 %. More specifically, this means that in 2010, 1 in 20 patients were alive 5 years after diagnosis while in 2019, 1 in 2 patients are still alive after 5 years[31].

- The 5-year survival of patients with **HER2+ breast cancer** increased from 63 %, before entry of anti-HER2 therapy, to 88 %, after the advent of anti-HER2 therapy. The prognosis of this highly aggressive form of breast cancer has thus increased significantly thanks to the targeted, effective and well-tolerated treatments these therapies bring[32].

- The 3-year survival of patients with **chronic myeloid leukaemia** increased from 75.2 % in 2004 to 88.7 % in 2017. During this period, tyrosine kinase inhibitors entered the Belgian guidelines for the treatment of chronic myeloid leukaemia[33].

- The 3-year survival of patients with **multiple myeloma** increased from 56.4 % in 2004 to 67.4 % in 2017. During this period, proteasome inhibitors entered the Belgian guidelines for the treatment of multiple myeloma[34].

- The 3-year survival of patients with non-small-cell lung cancer increased from 6.3 % in 2013 to 15.5 % in 2017. During this period, for the treatment of **non-small-cell lung cancer**, EGFR & ALK inhibitors as well as immunotherapy entered the Belgian guidelines[35].

- The 3-year survival of patients with prostate cancer increased from 56.2 % in 2004 to 66.2 % in 2017. During this period, non-steroidal antiandrogens (NHA) for the treatment of **prostate cancer** entered the Belgian guidelines[36].

- The 3-year survival of patients with **renal cell cancer** increased from 22.7 % in 2004 to 34.3 % in 2014. During this period, tyrosine kinase inhibitors for the treatment of renal cell cancer entered the Belgian guidelines[37].

These developments clearly show the added value of many of the new innovative oncology medicines for the survival of Belgian patients. Besides being more effective, these targeted therapies are also better tolerated compared to conventional chemotherapy. Hopeful evolutions, then, that will ensure not only a higher life expectancy but also a better quality of life.

3.1.4 Impact of new medicines on mortality and hospital admissions in Belgium

Does the advent of new medicines lead to fewer deaths and fewer hospital admissions? The answer is abundantly clear: Yes! Year after year, new innovative medicines enter the market, making medicine use change significantly over the years. But what exactly does the arrival of these new medicines mean for both patients and society? Prof. Frank R. Lichtenberg, commissioned by pharma.be, examined the impact of this evolution on mortality rates and hospital use in Belgium[38].

The figures paint a very clear picture. The number of medicines prescribed rose from 1,212 in 1989 to 1,450 in 2019. Moreover, 51 % of medicines that were on the market in 1989 were no longer sold in 2019. Conversely, 60 % of prescription medicines in 2019 were not yet on the market in 1989. Medicines have thus evolved significantly over the past 30 years. This should not come as a surprise, as the biopharmaceutical sector is one of the most research-intensive sectors. The stakes are therefore particularly high: the health of people and, by extension, that of society.

Are all those newly developed and reimbursed medicines indeed having a positive impact? To answer this crucial question, Lichtenberg analyses the correlation, for about 100 diseases, between changes in medicines used for the disease and changes in mortality rates and hospital admissions due to the disease during the period between 1999 and 2019. He uses a "difference-in-differences" model for this purpose (see box).

Lichtenberg tests the effect of the change in medicine use using **two hypotheses**:

1. Diseases for which more new medicines were reimbursed had a lower increase (or a sharper decrease) in deaths and hospital admissions.
2. Diseases for which newer medicines are used on average (i.e. medicines with a later introduction date) have a lower increase (or sharper decrease) in deaths and hospital admissions.

Does the research confirm these hypotheses? Lichtenberg concludes that the mortality rate across all diseases is significantly inversely related to both the increase in the number of medicines used for treatment and the average year of introduction in which medicines to treat a disease entered the market. The same applies, in an even more pronounced manner, to the impact on hospital admissions. In other words, **the advent of new medicines has reduced both the mortality rate and hospital admissions**.

Specifically, it was calculated that the increase in the number of medicines in Belgium over the period from 1998 to 2018 reduced the number of deaths in 2018 by 31 % (48,379). Over the same period, the increase in the average year of introduction reduced the number of deaths in 2018 by 42 % (80,235). For the same variables, a decrease in the number of days spent in hospital of 26 % (3.75 million) and 30 % (4.71 million) respectively is also observed. The availability of new medicines is therefore good news for patients, both in terms of mortality and the number and duration of hospital stays. **But the added value for society is also clear**: the financial impact in terms of hospital spending alone is impressive. Lichtenberg concludes that even his most conservative estimate in 2019 regarding the reduction in hospital costs due to the introduction of new medicines over time (i.e. 5,004 million euros) is greater than the total public expenditure on prescription medicines in Belgium in the same year (i.e. 4,894 million euros).

A word on methodology

A "difference-in-differences" model is a combination of, on the one hand, a time period difference, comparing outcomes by disease over the period before and after treatment, and, on the other hand, a cross-sectional difference, comparing outcomes between different diseases. This methodology allows the pure effect of new medicines on mortality and hospital admissions to be measured, and excludes the impact of macroeconomic and demographic trends, which are assumed to occur across all diseases.

The change in medicines used is measured using two different variables. The first variable concerns the evolution of the number of medicines available on the market used to treat a particular disease. The second variable looks at the evolution of the average year of introduction in which medicines to treat a particular disease entered the market. A higher value for the average year of introduction indicates the use of newer medicines. Both variables give an indication of the amount of new innovative medicines that have entered the market over time.

3.2 A positive impact on the economy[39]

Belgium's unique biopharma valley has world-class players and is a leader in the development of revolutionary medicines and vaccines. **Besides added value for patients, the healthcare sector and society, our strong biopharmaceutical sector also provides a direct economic return and even a positive impact on public finances.**

In terms of employment, as many as almost 137,000 jobs are linked to the biopharmaceutical industry (direct, indirect and induced employment). The sector also occupies an important place in terms of exports, contributing significantly to Belgium's positive trade balance. In addition, the huge investments in R&D and clinical studies (see above) make an important contribution to the Belgian knowledge economy, which is the basis of our welfare state.

3.2.1 The economic value of the biopharmaceutical sector

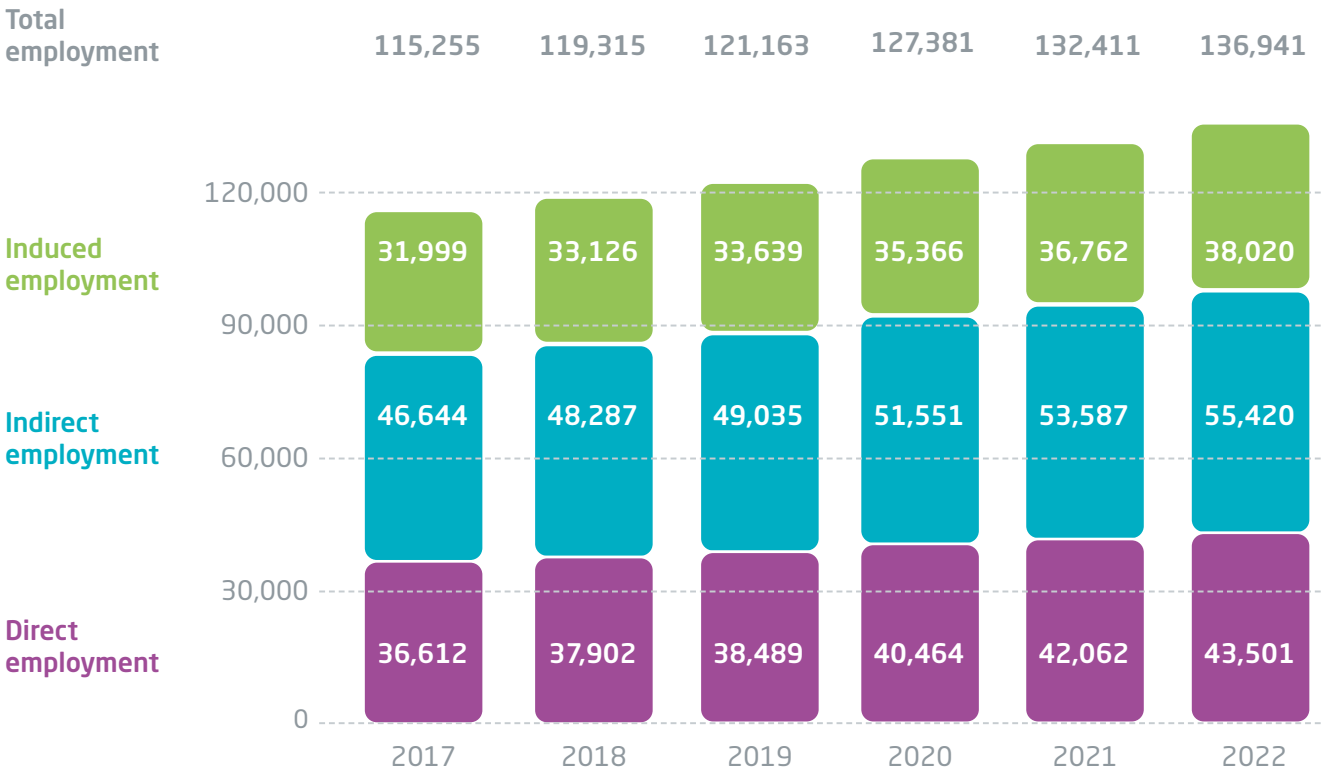
EMPLOYMENT

In Belgium

The biopharmaceutical sector manages to create **more jobs** in Belgium **time and time again**. Employment increased by about 19 % in five years to 43,501 employees. Growth in jobs was significantly higher than in the manufacturing industry overall, which recorded growth of less than 4 % in the same period. As a result, biopharmaceuticals accounted for some 9 % of manufacturing jobs in 2022. The biopharmaceutical sector's growth rates exceed those of not only the manufacturing sector but also the private sector and the Belgian economy as a whole.

However, it does not stop there - the sector **also has a positive impact on other sectors**, such as transport and logistics. This indirect employment accounts for another 55,420 jobs. If you take into account employment resulting from the spending of direct and indirect jobs, the sector accounts for 38,020 induced jobs. **This means that for every job created in the Belgian biopharmaceutical industry, two other jobs are created**. The sector therefore provides nearly 137,000 jobs in Belgium.

Evolution of direct, indirect, and induced employment in the Belgian biopharmaceutical sector



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

In Europe

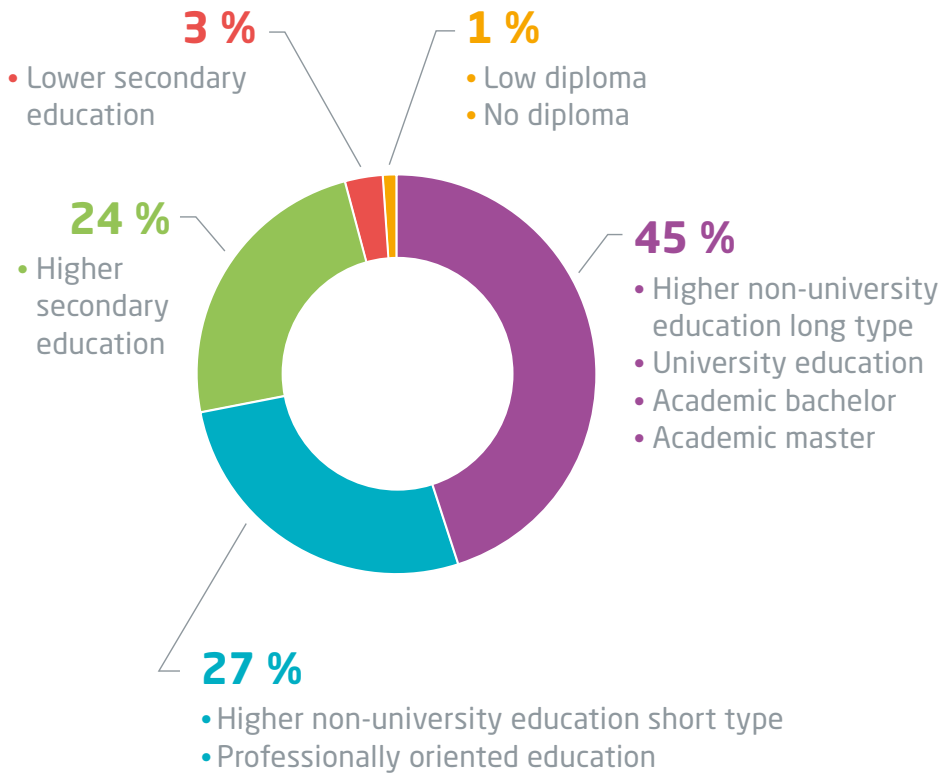
The importance of these figures becomes even clearer when you put them in a European context. Belgium ranks third, both in terms of the share of total employment and of employment in the manufacturing industry.

A diverse sector – role model for our economy

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 through 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 employees. In this knowledge-intensive sector, there are already considerably more highly educated employees than in other sectors, with around 72 % of employees holding a higher education degree. In terms of the total working population, this is about half. Specifically for the manufacturing industry overall, this comes out at just 40 %, and for the chemical industry at around 57 %.

Distribution of profiles in the biopharmaceutical sector in 2022



Source: STATBEL labourforce survey 2022

In terms of gender diversity, the biopharmaceutical sector is fairly gender-balanced. In 2022, the proportion of female employees reached 49 %. Female researchers are in the majority, with 74 % in 2022. Compared to a few years ago, we can see a particularly striking increase in the number of women on corporate boards, as this was about 45 % in 2022 and just 29 % in 2018. The board of pharma.be also has a good gender balance with 7 out of 15 members being women.

The sector is **also diverse in terms of the number of non-Belgian employees employed**. Between 2018 and 2022, the proportion of these employees rose from 8 % to 14 %. They have an even stronger presence in the management of biopharmaceutical companies, with a share that has risen from 15 % to 29 %. In 2022, 22 % of board members were non-Belgian employees, but this figure fluctuates fairly sharply from year to year. This is also the case for the proportion of non-Belgian employees active in research, which represented 17 % in 2022.

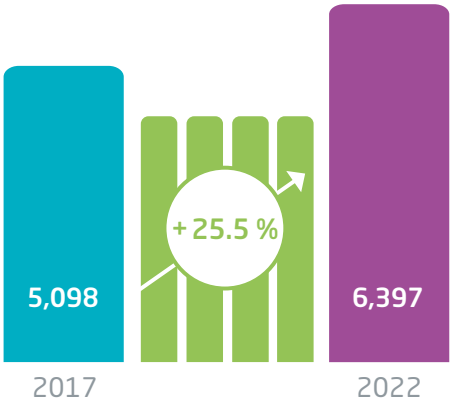
Number of women				
%	total	in management	On board of directors	In research
2018	49	46	29	57
2019	49	47	35	57
2020	48	47	38	60
2021	51	48	46	63
2022	49	49	45	74

Number of non-Belgian workers				
%	total	in management	On board of directors	In research
2018	8	15	21	10
2019	11	21	19	13
2020	14	28	25	16
2021	13	29	17	23
2022	14	29	22	17

A strong foundation

The sector has an extensive pool of skilled employees to draw from in Belgium thanks to the presence of 12 universities which provide a strong educational basis and a stable influx of highly qualified and productive employees. Some of these highly skilled employees are employed as researchers in R&D. In five years, a quarter more researchers have been employed in the sector and **in 2022, 6,397 researchers were working in the biopharmaceutical sector in Belgium**. That is an increase of almost 25.5 % in five years. This growth rate again underlines the highly innovative nature of the sector. These employees are the cornerstone of the biopharmaceutical industry and contribute substantially to its success.

Increase in the number of researchers in 5 years



Source: phrama.be member companies conducting fundamental research in Belgium

Behind the numbers: who are the young talents in the biopharma sector?

On 25 October, Prime Minister of Belgium Alexander De Croo interacted with a number of young talents who recently started working in the biopharmaceutical sector. This follows an event looking back at the initiative set up by the government two years ago to ensure the competitiveness of Belgium's unique biopharmaceutical sector in the longer term. We would like to introduce you to them: who they are, what they do and, above all, why they chose to work in the biopharmaceutical sector.

My choice of career in pharmaceuticals stems from my personal background. My father is a surgeon and that influenced me to pursue a career that allows me to explore my interest in science, but also to make a significant contribution to patients' health. I oversee two key therapeutic areas: fertility and infections. My main goal is to facilitate the care process. It gives me great satisfaction because I actively contribute to the well-being of patients during their treatment.

Elise Steuve, *Product Manager, Marketing, Gedeon Richter*

I graduated in 2022 with a background in Business Engineering and have a great passion for Data Science and Technology. At the same time, I wanted to work in an environment where I can see the direct impact of my contributions. The pharmaceutical sector offers the perfect opportunity to see the positive effects I can have on people's lives, while also developing my passion further.

Safira Nur Allya Ramadhant, *MTO Global Business Excellence Engineer/Analyst, GOLD Associate, Janssen Pharmaceutical Companies of Johnson & Johnson*

I started working at UCB in 2022, which also led to my moving from Romania to Belgium. With my educational background in psychology, I help my colleagues to be more impactful in their jobs. Knowing that my work at UCB ultimately supports people living with serious diseases, I feel very grateful to be able to align my human and scientific aspirations. Overall, I believe that working in the pharmaceutical industry keeps me close to my core values, which are integrated into my daily work. Jumping from statistics to understanding human nature is my way of caring!

Ecaterina Sauta, *Graduate (GDP) Learning Ops Specialist, UCB*

As Brand Manager, I specialise in hormonal therapy in prostate and breast cancer. I deliberately chose the pharmaceutical sector because I believe in the power of scientific innovation to improve patients' lives. My work contributes to the accessibility of innovative medicines for prostate cancer patients. This means that not only can we improve quality of life, but also offer hope for a healthier future.

Arthur Demolder, *Brand Manager, Ipsen*

Human diseases and their treatments have always intrigued me. This passion led me to study pharmaceutical sciences. I wanted to work in the pharmaceutical industry so I could stay in a scientific environment, closely involved in the latest developments. But most importantly, I wanted to contribute to the well-being of patients. My position as Medical Information Manager aligns perfectly with my interests. And the realisation that I am contributing to better patient care through my work energises me every day.

Chloë Crespinet, *Medical Information Manager, Medical Affairs BeLux, Novo Nordisk*

I have a great passion for the sciences. My education has enabled me to combine STEM expertise with business knowledge. This is how I discovered my preference for a career in which science and operational management play a crucial role, but which aligns with my vision of how science should be used to positively impact the health of people around the world at the same time. In the process, the pharmaceutical industry emerged as the perfect candidate. I am currently starting a new chapter at GSK, where I can continue my professional development. It is really exciting to be part of this constantly evolving and impactful pharmaceutical industry.

Antoine Termote, *Global industrial operations Future Leader Program, GSK*

When I graduated, my decision to work in the pharmaceutical industry was driven by a number of compelling factors. First and foremost, I was attracted by the opportunity to participate in the production of something tangible that contributes to public health. Equally important was the industry's reputation for valuing and prioritising employee development. In addition, the pharmaceutical sector is a very dynamic and forward-thinking environment. Working in an environment like this means being under a lot of pressure, but it also means learning quickly and being challenged for the better. And last but not least, I very much wanted to contribute to one of the cornerstones of the Belgian economy.

Claire Schmitz, *Manufacturing Operations & Quality Future Leader Program Graduate, GSK*

I have been working at Johnson & Johnson for about a year at the site in Geel where we produce active pharmaceutical ingredients. My current role is that of process engineer, designing and improving our processes to produce the active ingredient for life-changing medicines. I have always been very passionate about science and my current role allows me to contribute to bringing innovative medicines onto the market while learning and understanding different perspectives. Working in the pharmaceutical sector allows you to really experience the impact you have by helping patients who are waiting.

Filip Voorspoels, *Supply Chain Young Graduate, Janssen Pharmaceutical Companies of Johnson & Johnson*

Growing up near my family's pharmacy, I witnessed the direct impact of prevention and treatment on people's lives, which fuelled my interest and enthusiasm to contribute to the health of individuals and their families. Moreover, the dynamic pharmaceutical industry provides a challenging working environment characterised by constant innovation. The opportunity to be part of a community with the same goal of improving healthcare is both motivating and enriching. I am proud to be able to contribute to bringing innovation to patients; it is the driving force behind my daily work.

Paulien Demyttenaere, *Market Access Manager, AstraZeneca BeLux*

However, the biopharmaceutical sector is not just an attractive employer for these young people. An annual survey by Randstad shows that the biopharmaceutical sector has been ranked as the number 1 most attractive employer for no less than the 22nd time.

The pharmaceutical sector has been the most attractive employer for 22 years

Every year, Randstad conducts research on the quality of the employer image of Belgium's largest companies and also gauges the most attractive sector to work in. In spring 2023, Randstad published the results of the 23rd edition of this Employer Brand Research.

The pharmaceutical sector was ranked as the number 1 most attractive employer for no less than the 22nd time. A strong brand as an employer makes it easier for your company not only to attract people – crucial in today's war for talent – but also to retain them for longer. Employees feel more committed and are more willing to go the extra mile. However, a good reputation as an employer is not acquired overnight. It is about much more than a communication campaign; it is a process of years of sustained effort in very different areas.

For 23 years now, Randstad has been asking students, employees, jobseekers, etc. between the ages of 18 and 65 for their opinions on the attractiveness of Belgium's largest employers. At the same time, Randstad also gauges the most attractive sector to work in based on 10 criteria.

The overall score shows that the biopharmaceutical sector ranks number 1 for the 22nd time, followed by the aviation sector and media.

Looking at the scores per criterion, the pharmaceutical sector scores best for work atmosphere, job security, remuneration, financial health, job content and reputation. Thus, unlike the other sectors, the pharmaceutical sector can present a consistently high score across the board.

Pharmaceuticals is not just the most attractive sector. If you look at the different criteria we examined, the sector scored in the top 3 in 8 out of 10 criteria. By comparison, aviation, the second most attractive sector, scores in the top 3 in only one of those 10 criteria, and media, the third most attractive sector, in just 2 criteria. These are very attractive sectors, but the pharmaceutical sector is far better established in terms of all these different criteria. It holds a lot of cards.

***Jan Denys**, Director Public Affairs & Labour Market Expert, Randstad*

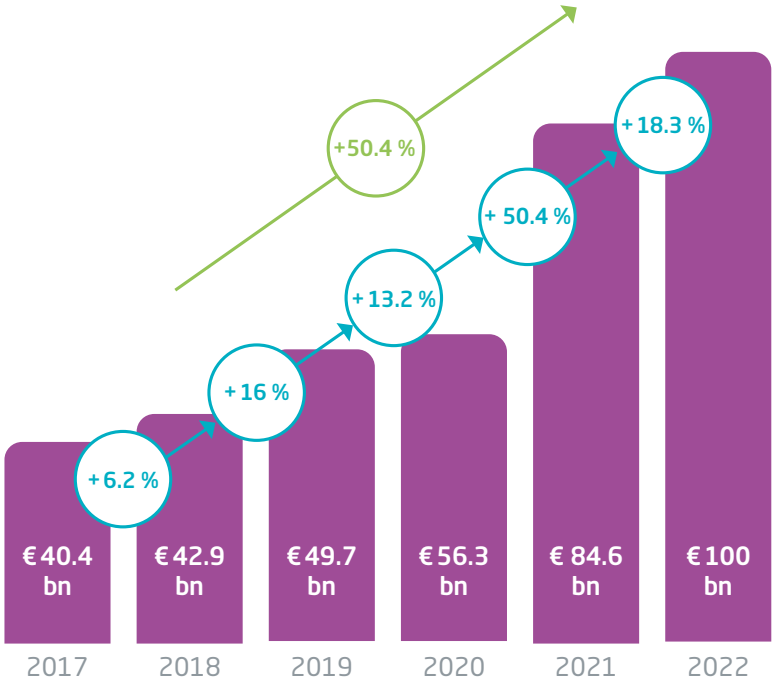
GLOBAL EXPORT

In Belgium

The year 2021 was already a record-breaking year, but exports saw a sharp increase in 2022 too. For the first time, more than 100 billion euros' worth of medicines and vaccines were exported. Belgium thus confirms its unique position as an international medicine hub. By 2021, exports were up 18 % – if you look at the past five years, we are talking about an increase of more than 150 %. Unlike 2021, the increase is not solely due to exports of COVID-19 vaccines. Their share remains stable, accounting for about a third of Belgium's total biopharmaceutical exports. Quite a few Belgian sectors experienced an increase in exports in 2022. These growing export figures were mostly driven by high inflation. This effect plays a much less significant role in the biopharmaceutical sector, partly due to regulated prices. This is also confirmed by the considerable growth in terms of volume exported.

The biopharmaceutical sector can therefore call itself a role model in terms of exports. By 2022, the sector accounted for around 17 % of total Belgian exports, confirming the sector's position as an export champion. Thanks to the sharp increase in recent years, biopharmaceutical products with a value up to 275 million euros were exported from Belgium every day in 2022. Belgium's overall trade balance shows a surplus of 11.8 billion euros. The biopharmaceutical sector has the largest surplus, with a contribution of 19.4 billion euros. Without the sector Belgium would have to present a negative trade balance for 2022, proving that it is one of the pillars of the Belgian economy even during and after the difficult COVID-19 period.

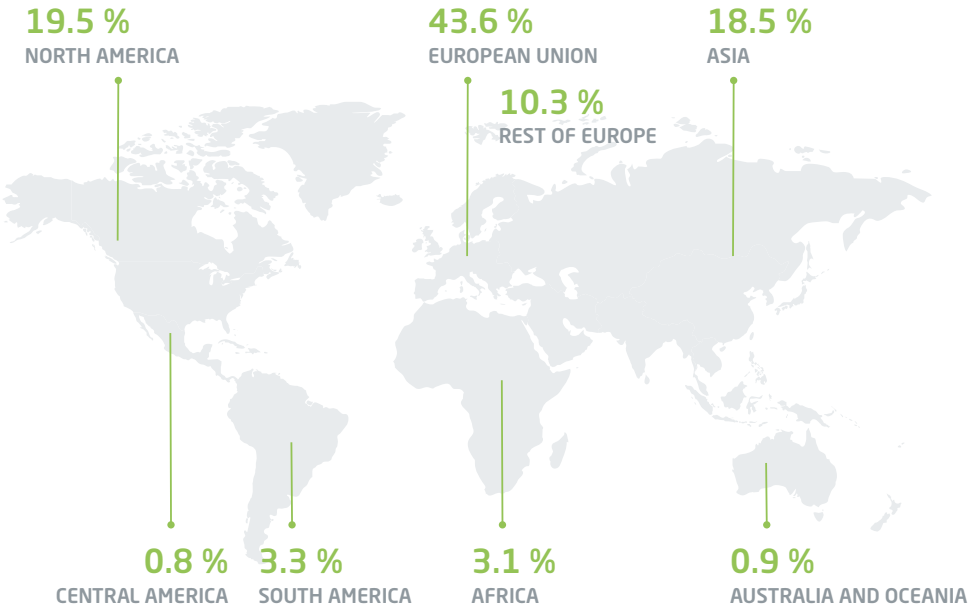
Evolution of biopharmaceutical exports (billion euros)



Source: NBB

Comparison with Europe and the world

Belgium is also doing very well from a global perspective. In terms of total biopharmaceutical exports, Belgium is only ahead of Germany within the EU. Taking population into account, Belgium is also second only to Ireland. **In total, almost a fifth of total EU pharmaceutical exports are shipped from Belgium.** More than half of exports from the biopharmaceutical sector come out of the European Union. In total Belgian exports, this is less than a third. The US is the main trading partner, accounting for almost 18 % of biopharmaceutical exports. This is followed by Germany and Japan, accounting for 15 % and 8 % respectively.



Port of Antwerp-Bruges: global role model in maritime transport of medicines

Belgium remains a major leader in biopharmaceutical exports even after the pandemic. To achieve those exports, logistics partners are needed. Previous editions covered airports and road freight, but another key partner in getting all those products to patients worldwide is Port of Antwerp-Bruges.

Key figures

Port of Antwerp-Bruges is the second largest port in Europe. The port houses 1,400 companies and accounts for 164,000 direct and indirect jobs, with almost 4 % of Belgians employed thanks to the port. Port of Antwerp-Bruges creates added value of almost 21 billion euros, or some 4.5 % of GDP, making it Belgium's biggest economic driver. The port has connections to more than 800 destinations and handles some 290 million tonnes of international maritime cargo annually.

World's first GDP seaport

Biopharmaceuticals make up some of these 290 million tonnes. To distribute these products safely, Europe has set strict conditions in the form of the Good Distribution Practice (GDP) guidelines. These are meant to ensure that the quality of medicines and vaccines, for example, is maintained throughout the distribution chain. That is no mean feat, as just the slightest difference in temperature can be harmful.

In 2022, Port of Antwerp-Bruges was the very first seaport in the world to translate the GDP guidelines into the maritime sphere so that all links in the port's logistics chain, including container terminals, can now operate under GDP guidelines. This is a crucial step forward in the safe transport of biopharmaceuticals.

Additional transport options for the biopharmaceutical sector

With this move, the biopharmaceutical sector has already added an important option in terms of transport. Maritime shipping, like air transport and freight, can now guarantee the safe transport of biopharmaceuticals. Maritime shipping is also catching up in terms of digital technology, which means that maritime transport can now be monitored in great detail, just like air transport, for example. Air transport does offer the advantage of speed and flexibility; transport by sea requires significantly more planning and is obviously slower. Maritime transport is therefore not the most appropriate choice for all biopharmaceuticals. Then again, an important advantage is that the carbon footprint of maritime shipping is a lot lower. Or, as Port of Antwerp-Bruges puts it in a way you can visualise, one container ship is equivalent to 4,000 aircraft. In any case, thanks to the GDP recognition of Port of Antwerp-Bruges, the biopharmaceutical sector in our country can now boast strong, quality logistics actors by land, air and sea. Together, they ensure that medicines can travel all over the world, to the patients who need them.

Discover the GDP-flow

3.2.2 Cost-benefit analysis for the Belgian government

The direct economic impact of a strong biopharmaceutical sector in Belgium is clear. The presence of the sector also has a positive impact on public finances, as shown in the following calculation based on 2022 statistics.

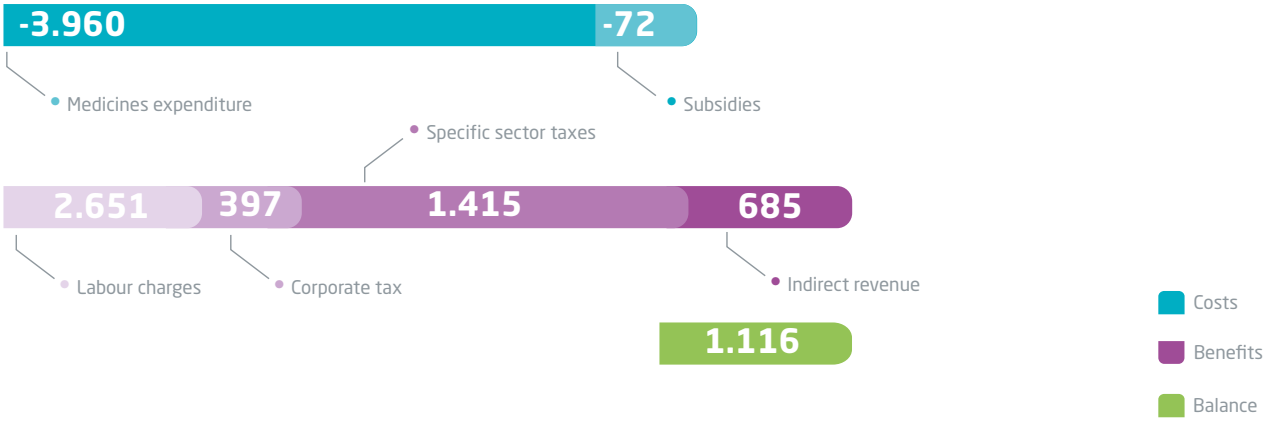
To create this cost-benefit analysis (see also Appendix 1), we first take into account the costs incurred by the government for medicines. These costs are reimbursed by the NIHDI and include expenditures on all reimbursed medicines. Government subsidies for the biopharmaceutical industry are also included here. In total, these expenditures amount to **4.0 billion euros**.

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

1. Taxes on labour, amounting to almost **2.6 billion euros**
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 come to **5.1 billion euros**.

Public finance costs and benefits of the biopharmaceutical sector (million euros)



Source: pharma.be

This comparison between expenditure and revenue for the government shows that the biopharmaceutical sector's contribution to our country's revenue is substantially higher than Belgium's expenditure on the sector.

The surplus amounts to 1.1 billion euros. A comparison with other countries shows that this position is unique, and the envy of many countries.

4 Our approach

4.1 We take responsibility

4.1.1 Following strict ethical standards

Although the biopharmaceutical sector is one of the most regulated sectors, the various rules applicable to it are often unknown to the general public. **Both legal and deontological rules** apply to activities specific to the sector, as well as to interactions with other healthcare stakeholders, such as healthcare practitioners, patients and healthcare organisations. The law defines the minimum standards applicable to the sector. Moreover, since 1976, pharma.be has a deontological code with strict ethical principles that go one step further than legislation. Our association was therefore **the first Belgian business federation** to introduce such a code of conduct.

Since then, pharma.be has strived to continuously re-evaluate this code of conduct so that it continues to meet the expectations of a society on the move. The pharma.be deontological code defines **the essential values of care, integrity, respect and honesty** that underpin the activities of pharma.be member companies. These values are particularly important for cooperation with different stakeholders. They ensure that cooperation is done in the best interests of the patient, and that it is transparent, free from any influence and of high quality. For instance, biopharmaceutical companies work closely with doctors and the health sector during the R&D process, but also later when a medicine enters the market. These interactions are not only **legitimate, but they are also necessary**. As the first point of contact with patients, healthcare providers have invaluable expertise. This expertise is crucial for the biopharmaceutical sector to develop increasingly effective treatments for patients.

Conversely, biopharmaceutical companies have a responsibility to inform healthcare providers 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, data protection legislation and anti-corruption regulations. Our member companies also voluntarily commit to **additional, binding standards in the pharma.be's Code of Deontology**. This Code of Deontology provides a framework for developing sustainable relationships with healthcare partners. The Code defines the requirements to be met by the industry and supports member companies' commitment to operating in a professional, ethical and transparent manner.

The Code of Deontology applies to various activities of pharmaceutical companies:

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

pharma.be's
Code of Deontology

Procedure when the provisions of the Code are breached

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

These deontological bodies are independent of pharma.be. They are comprised of:

- a chairman, legal expert, 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 tendency 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. 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 disputed 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 a 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 contrast to previous years, no new complaints proceedings were brought before the DEP Committee in 2022, nor were any appeals lodged on a previous DEP Committee ruling. However, in March 2022, the Board of Appeal did rule on a case that had arisen in late December 2021. Interested parties may request an excerpt of these decisions at deonto@pharma.be. However, communication regarding an excerpt 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) specifically aims to monitor communications from our member companies to healthcare providers about medicines they place on the 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 this information and check that it is in line with pharma.be's Code of Deontology and with the laws and regulations. This self-regulation project is unique in the world.

Why do pharmaceutical companies share information with healthcare providers?

Biopharmaceutical companies invest on average 10 to 12 years in the R&D of a new innovative medicine. During this process, they build up a great deal of expertise and gather a wealth of scientific information, which they make available to healthcare providers, so that they have sufficient prior knowledge to guide their patients and encourage the appropriate use of medicines.

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 medicines, 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 pharmaceutical 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.

What happens 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. Through this initiative, our member companies recognise and take responsibility for sharing scientific information and the quality of the medicines they place on the 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 correct use. Advertising is ethical, accurate, balanced and must not be misleading."

Some excerpts from the 2022 BCWC annual report

Between 1 January and 31 December 2022, the BCWC re-examined written communications concerning 50 medicines and reached conclusions on them. The following is a summary of the observations made by the BCWC in its conclusions from 2022. As was the case in previous years, these can be grouped into a number of categories according to the item they refer to. Thus, conclusions were formulated in relation to:

1. The rules on advertising of medicines in general;
2. The procedure and/or its practical aspects;
3. The key information in communications;
4. References in communications;
5. The clarity, completeness or accuracy of the information;
6. Various topics.

Sixty per cent of the companies that received conclusions from the BCWC in 2022 commented on these conclusions. The relatively high number of companies responding to the BCWC's initial conclusions indicates the importance companies attach to sharing information and advertising that complies with legal and deontological requirements in this area.

You can request a digital version of the 2022 report at deonto@pharma.be.

The deontological platform Mdeon

Deontology and self-regulation go far beyond the workings of our association. The pharmaceutical industry (including pharma.be) and the medical and dental technology sector are all members of the Mdeon deontology platform, 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 also manages the betransparent.be platform.

Mdeon
Code of Ethics

Betransparent guarantees 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 answers to 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 via the platform www.betransparent.be.

An overview of the Transparency Register in 2023

The figures published in 2023 refer to the 2022 operating year:

- A total of 268.8 million euros' worth of cooperation with healthcare actors was published. This is a 5 % increase compared to 2021.
- **Most of the collaborations refer to scientific research:** 169.8 million euros or 63 % of the total amount. These are mainly collaborations in the context of clinical studies. This is because Belgium is a leader in clinical studies in Europe.

- The other forms of cooperation include:
  - Participation in scientific events (39.9 million euros), which must be pre-approved by Mdeon through a visa procedure
  - Donations and grants to support healthcare (20.2 million euros)
  - Fees from service contracts (24.2 million euros)
  - Contributions to patient organisations (14.6 million euros). This mainly concerns European patient organisations that are based in Belgium because of the presence of the European institutions.

	2022
Scientific research	€ 169,823,132
Scientific events	€ 39,903,534
Donations and grants to support healthcare	€ 20,220,422
Fees from service contracts	€ 24,196,13
Other funding (PO)	€ 14,625,699
	€ 268,768,800

Source: www.betransparent.be

An improved search engine for the transparency register

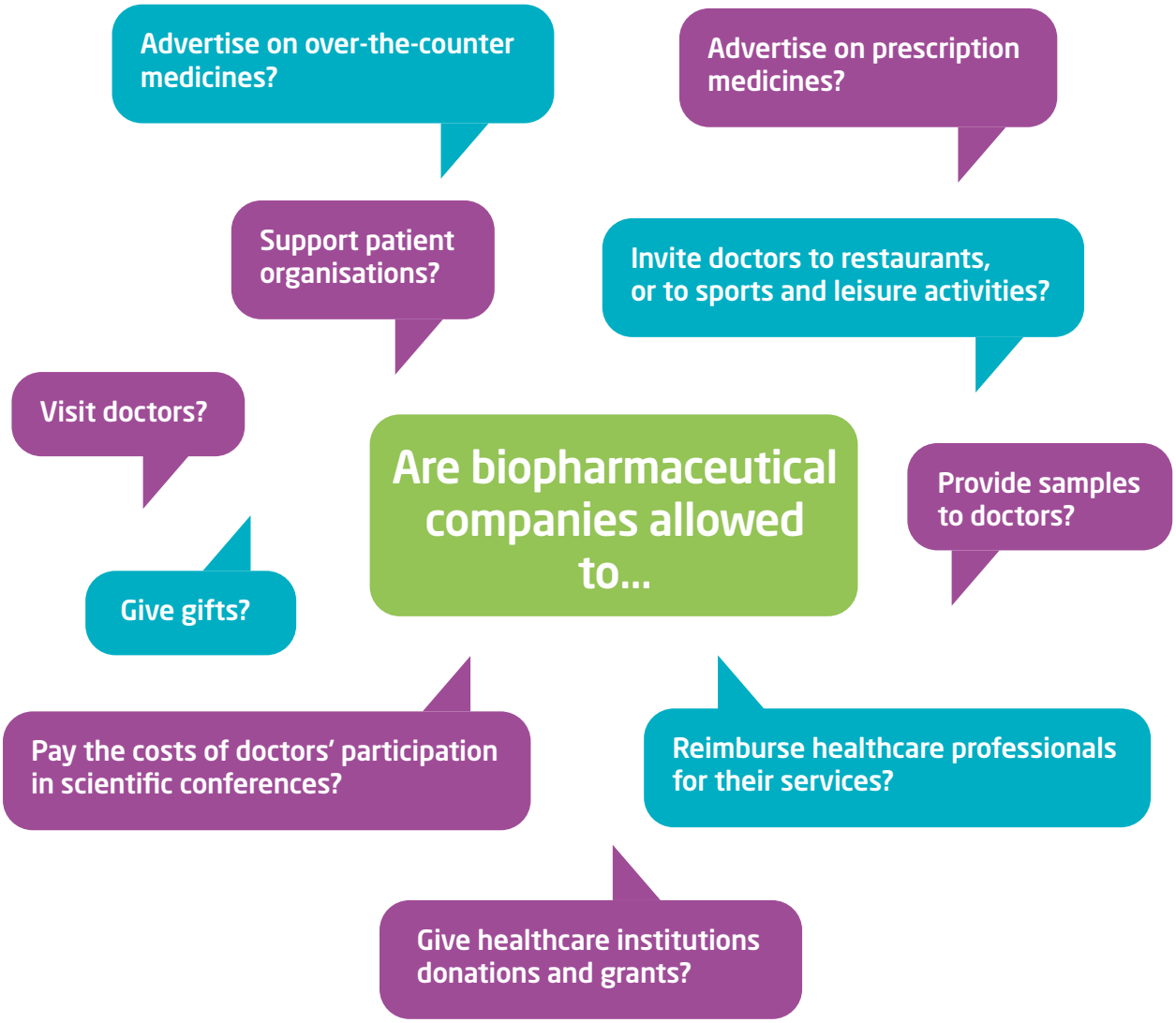
In 2022, the transparency register was criticised for being too unclear and not user-friendly. Spurred by pharma.be, it looked at how to improve the system in line with the Sunshine Act's objective. This led to the launch of a more user-friendly search engine for the transparency register in mid-2023. The new search engine allows you to perform cross-sectional searches. The last three calendar years are now immediately visible, and you can switch between reported years. You can also retrieve the financial fees received per beneficiary and download the search results. Thanks to these improvements, the register is easily accessible, and you can easily view interactions. pharma.be is also still exploring what content improvements can be made to achieve even better transparency, working closely with the FAMHP and the cabinet of the Minister of Social Affairs and Public Health to this end.

"Health Ethics" brochure - aimed at the general public

For more information on the ethical and deontological rules applicable to the biopharmaceutical sector, anyone can consult the brochure "Health Ethics - Ethical cooperation between the health sector and pharmaceutical companies in Belgium".

This brochure provides an overview of the broad spectrum of legal and ethical rules applicable to the relationship between the pharmaceutical sector and its stakeholders. These rules are essential elements in its mission to improve the health of the population.

Discover our brochure



4.1.2 Addressing urgent patient needs

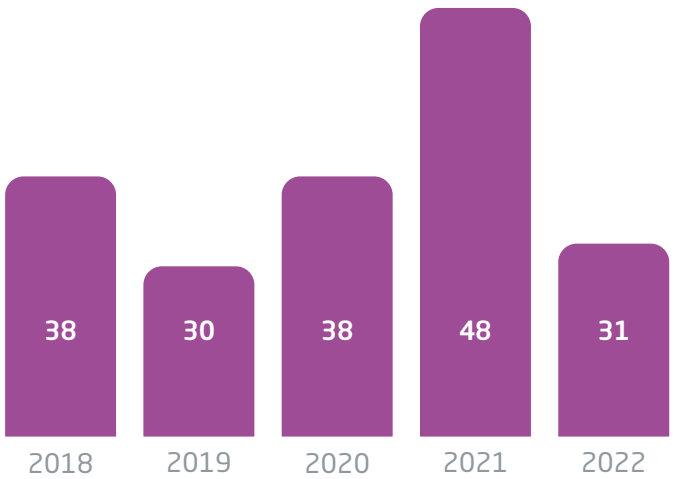
The **compassionate** use and **medical need** programmes permit, in exceptional cases, the administration of a medicine that is under review but not yet approved by the EMA, to patients suffering from a chronic or serious disease who cannot be treated with a medicine that is already available on the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

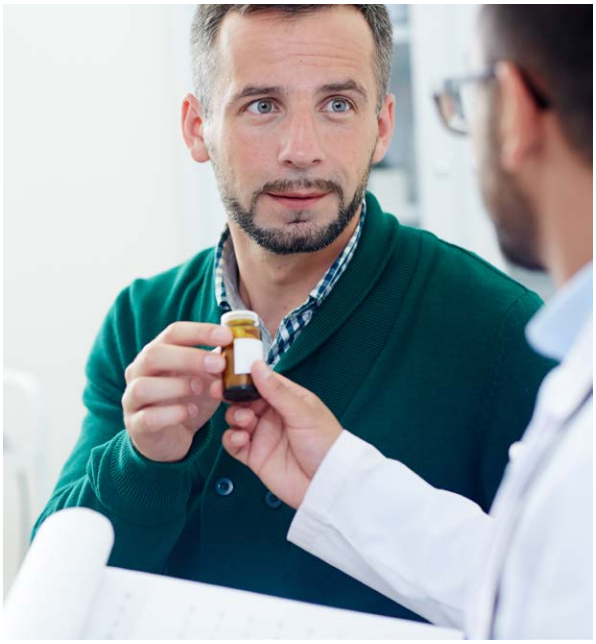
With new legislation in 2014, Belgium implemented European Regulation 726/2004 (Article 83) and introduced the concept of compassionate use. At the same time, our country took the opportunity to create a broader legal framework by also allowing Medical Need Programmes. The main difference between these two programmes has to do with marketing authorisation:

- Compassionate use programmes (CUP) cover medicines that have not yet received marketing authorisation.
- Medical Need Programmes (MNP) involve medicines 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 medicine. If the application is approved, the company gives the new medicine free of charge to patients who are included in the programme at the request of their treating doctor. The programmes last until the medicine 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[40]. Patients and healthcare providers can consult them there. By the end of August 2023, more than 55 programmes were ongoing.

Number of Compassionate Use and Medical Need programmes submitted to the FAMHP





4.1.3 Through education and dialogue

pharma.be launched an educational information campaign on Monday 25 September. Topics currently on many people's minds are answered through short questions. Indeed, many topics related to our health and medicines in particular are quite complex. For example, what is being done to address a temporary shortage of medicines? When will there be a cure for serious diseases? Or why is a new medicine reimbursed in neighbouring countries but not in Belgium?

pharma.be aims to give even clearer answers to clear questions with information on why certain problems can only be solved through cooperation and, above all, what the sector itself is doing, for the health of everyone in Belgium. For the questions and answers, see pharma.be also reached out again this year to many stakeholders in Belgium. By listening to each other and not shying away from critical discussions, we can make progress. Publications in the media, sometimes heavily critical of the pharmaceutical industry, posed a challenge in terms of discussions with journalists, providing interpretation and explaining the complexity of the existing systems and regulations. pharma.be also did not shy away from discussions with other stakeholders such as, for example, the sick funds. Our CEO and advisors participated in several events covering specific issues and discussion programmes on various topics such as (temporary) unavailability of medicines, transparency in conventions with the government and the value of medicines.

Questions and Answers

4.1.4 Caring for the environment and climate

The ultimate goal of pharma.be members is to ensure that patients have medicines that make them healthy and keep them healthy. Because a healthy environment contributes to healthy people and animals, it is important to the biopharmaceutical industry that the world we live in is also as healthy as possible. **Our members therefore make a lot of efforts to reduce their impact on the environment**. Here are some **examples** below.

Reduction of CO2 emissions

One of the key elements in the fight against climate change is reducing CO2 emissions. Over time, we need to move towards complete climate neutrality. Our members therefore invest not only in energy sources such as **solar panels and wind turbines**, but also in more innovative technologies such as **geothermal and heat networks**. In addition, our members are committed to **raising awareness** among their employees. This is done, for example, through campaigns around rational energy use and by encouraging the use of alternative means of transport such as (electric) bicycles. Where alternative transport is not easy to use and you still have to travel by car, hybrid and/or 100 % electric cars are increasingly being used. **Green transport** is also chosen wherever possible for the transport of medicines: transport by sea or rail, for example, as an alternative to air travel.

Making production processes more sustainable

Making a medicine is complex and involves a lot of different raw materials and products. There are still many opportunities to improve sustainability here too. For example, the industry is considering how to reduce the amount of water used during medicine production. Discharging it into other bodies is not an option, nor is simply reusing it. Our members therefore invest in **innovative water treatment technologies** so that water can still be reused and no residues from medicines or other products end up in streams and rivers. In addition, our members are extremely committed to making **materials** used in medicine production **more sustainable**. One example is reducing and even avoiding single-use plastic packaging altogether. Or also separating waste streams as much as possible so they can be recycled.

New campaign to inform the public

A new version of the brochure around unused and expired medicines was launched in 2023. This version contains the latest guidelines on how to dispose of medicines and other products in the safest way possible. Together with all partners within the multistakeholder consultation, an extensive campaign was also launched to raise awareness on the new brochure and to once again inform the public about the importance of returning old medicines to pharmacies.

Brochure

A greener working environment

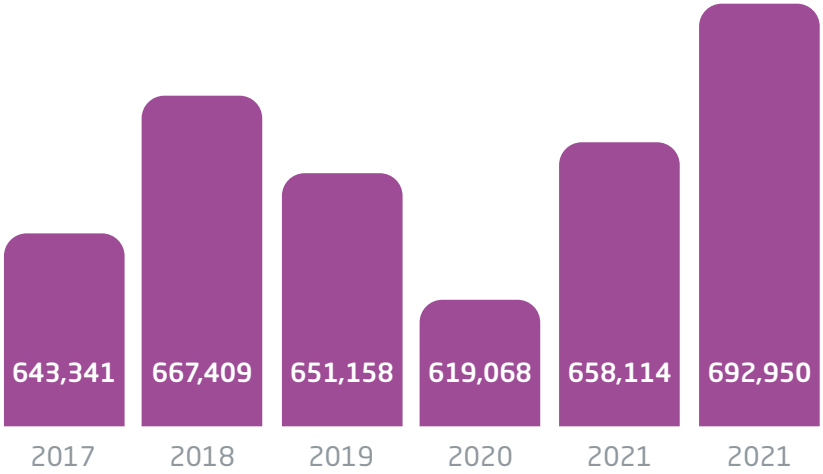
Our members, especially those companies with a large campus, are also increasingly investing in a **green, stimulating working environment**. This includes ensuring biodiversity on the site, right down to partnering with beekeepers so that employees can enjoy honey from their 'own' production. There are also several collaborations with Natuurpunt (governing body of protected sites) to purchase nature reserves and to plant trees.

Multistakeholder collection of expired and unused medicines

Another example of pharma.be members' efforts to reduce their impact on the environment concerns the collection of expired and unused medicines. You can't just flush those down the toilet or dispose of them in the rubbish bin. 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 carelessly (children playing could find them, 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 zero-cost solution to the patient. Thanks to this **multistakeholder 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 692,950 kg of unused and expired medicines were collected in Belgium in 2022.** The table below shows that after a dip due to the pandemic, the volume collected has been rising again since 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.

Total amount of expired or unused medicine in kg



Source: pharma.be

e-PIL: Electronic Patient Information Leaflet

A final example concerns the package leaflet for medicines. 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 packs are dispensed each year for reimbursed medicines. The environmental impact of the leaflet is therefore huge. This is why the biopharmaceutical industry launched a pilot project in 2018 around a safe and more sustainable digital alternative, the e-PIL or Electronic Patient Information Leaflet. The e-PIL pilot project focuses on a selection of medicines on the market in Belgium and Luxembourg whose administration is limited to the controlled environment of a hospital. 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. Digital access means users always have access to the latest information. The ease of reading is also greater because you can, for example, choose the language or font size yourself. **Four years after the pilot project started, the interim results were extremely positive.** For 95 % of the hospital pharmacists surveyed in 2022, a paper package leaflet would no longer be needed in the future for medicines administered in hospital.

The European Commission therefore extended the project's approval until 1 August 2025 and allowed it to be expanded to include even more medicines.

A new call to pharmaceutical companies was therefore launched in late 2022. These sent in a large number of candidate medicines to be included in the e-PIL project. The competent authorities in Belgium and Luxembourg evaluated them closely. This resulted in a new list of validated medicines in June 2023:

- **9 additional pharmaceutical companies** stepped into the project, including **6 members** of pharma.be.
- **88 additional medicines** were validated.
- A total of **27 pharmaceutical companies** are now participating, including **20** pharma.be members.
- A total of **129 different medicines** can now be delivered to hospital pharmacies without a paper package insert.

Follow this project on our website

The future of electronic leaflets

On 12 September 2023, pharma.be organised **an info session on electronic leaflets**. In a first session, European initiatives and legislation were discussed in more detail. The e-PIL pilot project was then explained afterwards. Finally, in a panel debate, representatives of the various stakeholders – patient, pharmacist, doctor, authorities and biopharmaceutical industry – discussed the benefits and challenges of electronic leaflets.

There are already many benefits:

- Faster information updates
- Access to tailored information
- Positive impact on the environment
- Improving the medicine supply chain

However, these benefits should be widely available: no single patient should be forgotten. It is therefore crucial to ensure that electronic product information is accessible and understandable to all. Doctors and pharmacists play a central role in this.

In any case, a majority of the attendees agreed that electronic inserts should be possible outside the hospital environment in the future. However, the rollout should be well thought out and take place at different speeds depending on the context.

We need to start the discussion, in consultation with all partners (primary care providers, industry, patients, reimbursement institute, etc). We have an interesting ecosystem here in Belgium with the electronic prescription; there must be opportunities to find solutions. We are happy to take the lead and start a consultation.

Erik Everaert, *Head ad interim DG-Post, FAMHP*

Sustainability in practice: not a walk in the park

That significant challenges still remain in the biopharmaceutical sector's drive towards greater sustainability was evident at a CESPE conference. There, collaboration with academia in addressing those challenges was also on the agenda.

How do we ensure that sustainability is more than just a buzzword?

And how can the pharmaceutical industry and the academic research community join forces to achieve this? The business world is not exactly sitting still, as the CESPE conference on 21 September 2023 in Ghent showed, but the challenges are as big as they are diverse.

"Globally, the healthcare sector accounts for 5 % of global greenhouse gas emissions. So, it would be difficult to maintain that we are already truly sustainable today."

Bert Heirman, Program Manager Strategic Sustainability Initiatives at Janssen Pharmaceutica in Geel, immediately put both feet firmly on the ground in Ghent. Janssen Pharmaceutica itself aims to use only green electricity as early as 2025 and hopes to emerge with a completely climate-neutral value chain by 2045. That this is not exactly a simple task for a company of that size and with such an impressive portfolio of medication might be evident from the figures that Head of Operations, Bie Lambert, presented to the audience.

"Every year we produce some 250 tonnes of chemical end-molecules at our site in Geel. That production process involves more than 1,800 different liquid waste streams. Often those production processes are very specific, which means we have to develop very specific tools each time. But if we want to improve patients' health with our medicines, we owe it to ourselves to produce those medicines in a sustainable manner. A challenge, as more sustainable production sometimes risks coming at the expense of the absolutely essential quality of medicines."

To make production more sustainable locally, the Geel-based company is already betting on circular water management systems and cold-heat storage, among other things. At the same time, Bert Heirman left little doubt: it is particularly the global sustainability programmes that will have the biggest impact over time. One example is the Energize programme, which also aims to help suppliers make their production processes and waste streams more sustainable.

Green and social revolution

Simon Gilleman, Sustainability Manager at Takeda, was on the same wavelength but also added some striking touches of his own. The Japanese company, which develops plasma-based therapies and employs 1,200 people at its Lessen site, is betting heavily on water recycling and biomass, among other things, to eventually replace gas. *"Today we already recycle 60 % of the water used, in time this should become 90 %,"* was the statement. *"To accelerate the achievement of those targets, we partnered with a specialist Ghent-based company. At the same time, we try to make maximum use of the opportunities that arise around our site. For example, water will be recovered from a nearby quarry and thermal energy will be generated from the wood waste of a wood processing plant also located nearby."* Takeda's focus on caring leadership is noticeable. *"The green revolution must eventually also become a social revolution. That is why we want to actively help our employees switch to more sustainable production, for example by helping them to acquire new skills themselves."*

Measurable processes

David Vertongen, Sr. Technical Design Lead at Pfizer, in his presentation, drew sharp attention to the gigantic energy challenges facing the company, including in Puurs. Pfizer has long been focusing on energy-saving and more efficient processes and on better management of its 20,000 m^2 of cleanrooms, but Vertongen did not mince his words either: switching from gas to electricity is a particularly difficult task for a site of that size. After all, this requires doubling the capacity of the network while saving on energy consumption.

"There is still a huge amount of work to be done," also concluded Jan-Sebastiaan Uyttersprot, PAT Principal Scientist at UCB Pharma. "And we have to be honest: other sectors are already doing a lot better than the pharmaceutical industry when it comes to sustainability." He particularly stressed the importance of green thinking in the entire R&D process of pharmaceutical companies. This is not only a sustained effort every day, but it also requires objective quantification and measurability of all processes. Only then can you green it thoroughly. "In view of this, we will often have to dare to completely turn our production around, and it is written in the stars that we will be working on this for quite a few years."

Some impressions from the speakers at the conference:

As a co-founder of CESPE - which, after all, is also heavily committed to research into sustainable production processes - I was surprised to hear that large companies today are already collaborating intensively on sustainability in a pre-competitive phase. This is a particularly good thing: after all, a lot of processes also have great similarities.

Thomas De Beer

I think there are still a lot of opportunities for better collaboration within the pharmaceutical industry. But I have also learned here today that we are not alone in the challenges ahead and that we can count on a lot of scientists willing to work with industry on the road to greater sustainability.

Bert Heirman

I am a big fan of diversity of thinking. Events like this bring together very diverse people and opinions. The enormous challenges we face today make new partnerships essential. This is another reason why this kind of initiative is very valuable.

Bie Lambert

In terms of sustainability, we are actually not competitors. This is precisely why it is particularly valuable to be able to have an open conversation about this now. This confronts us with both inevitable tunnel vision as well as problems and challenges that we experience collectively. That's why conferences like this are particularly inspiring.

David Vertongen

The development of new, sustainable processes by different companies working together can definitely happen within pharma in a pre-competitive phase. That way, you will make faster progress anyway. Large pharmaceutical companies have long operated mainly on their own little islands. I found it particularly interesting to note here that this is now quietly changing anyway.

Jan-Sebastiaan Uyttersprot

CESPE aims to bundle and accelerate innovation

That the biopharmaceutical sector is indeed awake to the huge sustainability challenges is evidenced by, among other things, the ambitious plans of CESPE (Centre of Excellence for Sustainable and Pharmaceutical Engineering). This research and innovation platform of Ghent University was established in 2020. pharma.be supported its establishment with a letter of support. Meanwhile, CESPE already brings together over 170 researchers from different faculties. Besides technological innovation, it is resolutely committed to rapidly making the pharmaceutical industry more sustainable. By 2026, a brand-new innovation accelerator and incubator is planned to open in the Zwijnaarde science park for this purpose. Which, besides state-of-the-art lab facilities and clean rooms, will provide space for offices and warehouses. Christophe Portier, general director of CESPE, sees the new CESPE business card as a meeting place where industry people and scientists can exchange ideas. *"If we want to make the sector sustainable, we need to bring together people with complementary expertise. It is crucial that some kind of ecosystem is created."*

4.1.5 Caring for people and animals

Limiting animal testing[41]

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 of 6.9 % compared to 2020. 55 % of the experimental animals are mice; 13.1 % are rabbits. Dogs and cats were used to a much lesser extent (0.32 % for both species).

In 2021, the majority of laboratory animals were used for fundamental 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 as a proportion (29.1 %).

Number of animals used in research

Source: EU Statistical Data of all users of animals

More rational use of antibiotics in animals

Ensuring that medicines are used properly is an important objective for pharma.be and its members. One of the initiatives taken by the pharmaceutical industry around this in 2011 was the establishment of **AMCRA**, the knowledge centre on antibiotic use and resistance in animals (see box). Within AMCRA, pharma.be works together with the faculties of veterinary medicine of the Universities of Ghent and Liège, farming organisations, veterinarians and animal feed manufacturers to promote the rational use of antibiotics in animals based on the principle: **"as much as necessary, as little as possible."** By creating guidelines, benchmark reports for veterinarians and information campaigns for farmers and the general public, we have thus succeeded in significantly reducing the use of antibiotics in animals without negatively impacting the health and welfare of agricultural and domestic animals.

To make this reduction specific, we work with some **very clear objectives**. For example, by 2024, total antibiotic use should be 65 % lower than in 2011, and over the same period we want to see at least a 75 % reduction in the use in veterinary medicine of critical antibiotics that are also important for treating humans such as 3rd- and 4th-generation cephalosporins, fluoroquinolones and colistin. **The figures on antibiotic use in 2022 show that we are clearly on the right track** with a total use of 61.3 mg of antibiotics per kilogram of biomass[42]. This is a decrease of 24.5 % compared to 2021, but more importantly an overall decrease of 58.2 % if we compare it with 2011. Among critical antibiotics, we have also seen a decrease of more than 80% since the start of our efforts.

However, these good-looking figures do not include the full use of antibiotics in animals. Currently, only pigs, chickens and veal calves are monitored for what is effectively administered to the animals. For other farm animals, horses and pets, the method of collecting usage data has yet to be worked out and until then, it is sales data that provides insight into the overall use of antibiotics in animals. And again, the figures are very positive and clear. In 2022, 122 tonnes of antibiotics were sold, down by as much as 28.8 % compared to 2021 and almost 60 % less than in 2011 when just under 300 tonnes were sold. All these encouraging results show that the choice pharma.be made in 2011 was the right one and that supporting farmers and veterinarians and promoting measures around hygiene and prevention is the right way to achieve proper use of antibiotics in animals. pharma.be and its members will therefore remain a loyal partner within AMCRA in the future. We will continue to work with all relevant stakeholders to ensure that both animals and humans can continue relying on high-performing antibiotics when they need them.

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 this 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.

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 an absolutely necessary condition for health and innovation. pharma.be is therefore continuously working on sustainable, high-quality collaborations. The previous chapters have already covered a number of examples, such as in the creation of the portal clinicaltrial.be, within the deontology platform Mdeon, in the collection of expired medicines, in the E-PIL project or within AMCRA.

In this chapter, we elaborate on our collaboration with patient organisations, when collecting health data or ensuring the availability of medicines.

4.2.1 Working together with patient organisations

High-quality collaboration is a must, especially in a fragmented healthcare system. By building bridges, we can make better use of each other's expertise and thus improve healthcare. pharma.be puts cooperation with patient organisations (PO) first. After all, who better than the patient himself to indicate his experiences, needs, challenges and expectations?

pharma.be therefore established the Patient Engagement Working Group in April 2021. It is composed of patient ambassadors and those responsible for "Patient Engagement" within our member organisations. **Four specific work items** were on the agenda for 2023:

- Developing a clear framework for cooperation with POs
- Continuing the dialogue to even better include the patient perspective
- Establishing a patient advisory board
- Continued support to POs in terms of professionalisation, financial autonomy and independence

A clear framework

To ensure an ethical, transparent and productive collaboration, the Patient Engagement Working Group developed two manuals:

- **A Q&A**: there were many questions among POs about pharma.be's Code of Deontology describing collaboration with patients. 28 questions were answered in detail. This Q&A clarifies the complex regulations and clearly states what can or cannot be done and why.

- **A 10-point checklist:** capitalising on feedback from our survey and a roundtable discussion in 2022, we created a guide for our members on interacting with POs. This is summarised in a simple 10-point checklist. Our members can use this checklist as a yardstick to check whether they are truly patient-centred.

An ongoing dialogue

A **panel discussion** took place on 22 March 2023 following pharma.be's General Assembly: Why is the patient voice important? Patients there gave good examples of collaboration. In doing so, they stressed the importance of systematically incorporating the patient perspective into the broader health ecosystem, at both medical and policy levels. They also expressed concern over the lack of financial resources and capacity, which threatens the sustainability of POs.

A further dialogue took place at a **second round-table** on 28 November 2023, where representatives from more than 50 POs discussed topics such as collaboration, partnership and supporting the patient voice. The plenary session included an update on recent changes and novelties in favour of POs:

- The new Patients Act, which was due for an update after 20 years
- Including the patient voice in the new medicine reimbursement system
- New platforms with information on clinical trials

One of the things pharma.be also learned from a survey of patient organisations in 2021 was that it is difficult for patient organisations to find the right contacts within our companies. To respond to this need, pharma.be members have compiled a contact list indicating for each company (i) for which therapeutic area(s) the company is open to cooperation with patient organisations and (ii) indicating the e-mail address of the contact point for patients. Patient organisations can further engage with the innovative biopharmaceutical companies through this contact list.

Consult
our contact list

A patient advisory board

To help the Patient Engagement working group prioritise and evaluate its projects, pharma.be relies on a patient advisory board.

The advisory board has 9 members:

- Inge Van de Velde (MS)
- Veerle De Pourcq (ReumaNet)
- Elke Stienissen (Lymphoma cancer)
- Axel Vanderperre (HIV)
- Eva Schoeters (RadiOrg)
- Stefan Joris (Muco)
- Gay Charles (MyMu)
- Veronique Van Assche (SMA)
- Katleen Franc (Crohn's & Colitis)

At the Patient Advisory Board, we not only discuss current needs, but also look ahead to future needs. Together, we determine the actions through which we can create the greatest impact. Thus, we want more pre-competitive collaboration between companies so that the result for POs becomes even higher in quality and the work for POs becomes easier at the same time.

As a patient expert with multiple sclerosis, I am honoured to be part of the new Patient Advisory Board established by pharma.be. It is absolutely useful and necessary that patients' perspectives are heard in the work that the innovative biopharmaceutical industry does for us. As patients, we can bring our expertise, questions and critical comments to the debate on current work and future needs. Thank you for this opportunity!

Inge Van de Velde, *Adult Education Teacher and Patient Expert, MS League Flanders*

Continued support for POs

Structural funding and capacity building are the pain points most often cited by POs. **pharma.be wants to work with the government, industry and academia to find solutions** so that the added value of POs is guaranteed in the future. For instance, in our memorandum for the upcoming elections, we call for strengthening the patient voice in health policy "by supporting disease-specific patient organisations in their professionalisation, financial autonomy and independence".

In terms of professionalisation, we already see many opportunities in designing the care pathway (from diagnosis to treatment to aftercare), supporting awareness campaigns, producing educational material, scaling up clinical studies with patient-relevant criteria, to name but a few examples where our partnership needs to grow to create even more added value.

In conclusion: from co-creation to co-impact

pharma.be will make further efforts to simplify interaction with POs so that they have to use their limited capacity as little as possible for administrative work and practical organisation. Together with the Patient Expert Centre (PEC), which trains patients to become experts in Belgium, pharma.be will contribute as a board member to the development of **standardised operating frameworks** for more efficient interaction between industry and POs. One of the concrete actions included is better coordination between companies for pre-competitive collaboration such as in awareness campaigns or in creating disease-specific content. This way, we avoid a multitude of similar initiatives from different companies. Besides these concrete actions, pharma.be generally wants to continue to ensure **that listening to the patient's voice becomes a reflex in prevention, development, treatment and aftercare.** The Patient Engagement Working Group and our other task forces will ensure that we effectively deliver on these good intentions and create an impact that makes sure all patients get the best care they deserve.

A 10-point checklist for good cooperation with POs

This 10-point checklist was developed by the pharma.be's Patient Engagement working group together with POs. With this, pharma.be wants to provide companies with a guide to setting up efficient and fruitful collaborations with POs.

1. **Be transparent**
   Make clear which stakeholders will be involved during which phase. Be transparent about the timing of your engagement.

2. **Work together from the start**
   Test ideas first at POs even before starting a project. Don't fully work out an idea internally only to present the results at the end.

3. **Give sufficient time**
   Build in sufficient time for drawing up contracts. Give patient representatives a chance to read everything thoroughly.

4. **Collaborate on pre-competitive initiatives**
   Resources are limited. So, avoid fragmentation or duplication by better cooperation between companies around non-competitive issues. If necessary, also lay this down in a charter.

5. **Designate a single point of contact (SPOC)**
   Appoint a permanent contact person responsible for cooperation with POs. pharma.be compiles these contact details on its website.

6. **Promote patient-centred communication**
   Make documents available to patients in Dutch, French and German. Avoid jargon. Use clear and direct language. Always ensure that the information is tailored to the specific Belgian or regional context.

7. **Use patient-friendly collaboration agreements**
   Ensure collaboration agreements are drafted clearly and, in a patient-friendly way. Use templates from POs or other stakeholders to make the process more streamlined.

8. **Guide patients through your operating procedures**
   Provide guidance to POs on complex internal procedures such as billing terms. Use local language and procedures and ensure local follow-up if possible.

9. **Pay a market-based fee and recognise expertise**
   Ensure fair compensation for work according to the principles of Fair Market Value. Work with POs, regardless of their size or structure. Acknowledge their expertise and differentiate the fees provided.

10. **Support the independence of patient organisations**
    POs must be able to make their voices heard independently. By spreading grants, donations or sponsorships, they avoid becoming dependent on one company. Therefore, discuss the overall project together.

A detailed version of this checklist

4.2.2 Working together for relevant health data

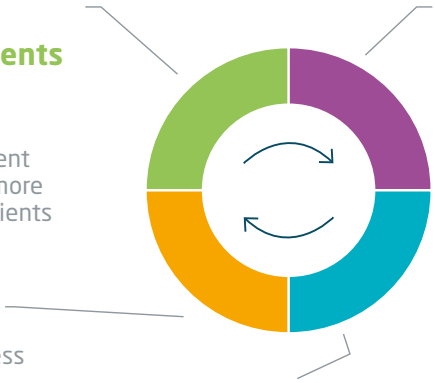
What are Real World Data and Real World Evidence?

Real World Data (RWD) is an umbrella term for data on the effects of health interventions (such as safety or effectiveness) that is not collected in the context of highly controlled randomised clinical trials (Randomised Controlled Trial, RCT)[43]. These may include, for example, clinical and economic outcomes, administrative data, patient-reported outcomes (PROs) and health-related quality of life (HRQoL). RWD comes from very diverse sources, such as patient registries, electronic medical records or health insurance company 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 enable validation in daily clinical practice.

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. **Indeed, this secondary use of data has the objective of reusing data originally collected for a healthcare purpose (primary use) for research**. For example, recorded data on a treatment with the primary goal of patient care, if brought together, can be analysed to discover new insights about the disease state or treatment for future patients. 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, which also provides important societal benefits (see figure), complementing data from clinical trials.

Societal benefits of the secondary use of RWD by the pharmaceutical industry



2. Medicine development development with patients

- Testing study feasibility and optimising trial design
- Optimisation of the recruitment process through better and more efficient identification of patients

3. Acces to the medicine patiënts

- Epidemiological and clinical insights for reimbursement dossier
- Better understanding of resource utilisation, costs and cost-effectiveness
- Segmentation of patient population for optimal therapeutic response in personalised medicine
- Evidence for indication expansion

1. Discovery

- Better understanding of illness origins and progression
- Better characterisation of patient groups and better understanding of current needs;
- Data-driven identification and prioritisation of indications and target molecules

4. Monitoring of the medicine used

- Improved pharmacovigilance
- Information on medicine use in practice
- Creation of clinical decision support systems
- Identification of subpopulations that benefit most
- Promotion of "evidence-based" medicine

Source: HDA law, Annemans study for the NIHDI

A health data ecosystem

FAIR data is 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

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

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 therefore very much welcomed the creation of the Belgian **Health Data Agency (HDA)** as a long-awaited first step in an ambitious Belgian data policy. The bill for its establishment was passed on 9 March 2023 and the management committee met for the first time on 11 October 2023. The HDA's user committee was established in late 2023. pharma.be will continue to work with the Health Data Agency and all user committee partners to ensure that the secure and ethical reuse of health data can be used to bring new treatments to Belgian patients faster.

It goes without saying that the Health Data Agency also supports academic research in this regard, as well as research from the pharmaceutical industry. As you know, we face new challenges in organising Clinical Trials. We need to re-enforce our leadership role, and we can only do that through the smooth and accurate availability of data for product development. Especially in these times of ever-increasing genetic research, and artificial intelligence, that is particularly important.

Frank Vandenbroucke, *Minister of Social Affairs and Public Health*

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. An example is an analysis of Belgian privacy legislation and GDPR with task force members and their legal advisers. Indeed, the secondary use of health data raises many questions in practice because of the complexity and varying interpretations of the application of the GDPR. Therefore, pharma.be set up an expert group among its members to draft guidelines and develop a methodology to assess projects involving secondary use of data for scientific research under the GDPR and the Belgian law on the protection of natural persons with regard to the processing of personal data. **These guidelines aim to clarify in a harmonised way the rights and obligations of pharmaceutical companies involved in secondary use data projects.**

This methodology, illustrated with several use cases, will help companies answer the following questions and do so using a roadmap:

- When do GDPR guidelines apply to specific RWD projects?
- Which parties are involved?
- Who is responsible for GDPR compliance?
- How to comply with GDPR transparency obligations?
- What precautions should be taken to ensure adequate GDPR compliance?
- What contractual obligations are required?

By facilitating the harmonisation of the management of RWD projects under current Belgian and European data protection legislation, the guidelines create a trusting environment among patients and healthcare providers when sharing health data with pharmaceutical companies for the development of and access to new medicines. The guidelines will be reviewed regularly to reflect developments in legislation and practice. Work is also taking place on **a model contract** between the various parties so that appropriate roles, safeguards and transparency are defined. Members want to work with these guidelines and the model contract to raise awareness and support stakeholders, where necessary, to correctly apply Belgium's privacy legislation.

As a biopharma industry, we think it is very important that the data ecosystem handles sensitive health (care) data according to the current GDPR rules to create the necessary trust while allowing research.

pharma.be's annual Health Data & Digitalisation forum on 26 October 2023 brought concrete insights into new and old databases and initiatives. During the event for members, partners and stakeholders, we also engaged in a dialogue on the next steps to prepare Belgium for the *European Health Data Space* (EHDS).

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 can be problematic for patients but, of course, pharmaceutical companies also want their medicines to always be available when patients need them. However, fighting medicine shortages requires more than just the good will of stakeholders on the ground.

Situation in Belgium

Many initiatives are already being taken in Belgium to supply wholesale distributors and pharmacists in time for patients to have their medicine, in consultation with the Federal Agency for Medicines and Health Products (FAMHP). It was the first in Europe to set up a reporting system, **"PharmaStatus"**, which ensures thorough transparency around the causes and duration of unavailabilities for the benefit of healthcare professionals and patients (see box). Companies also prudently stockpile medicines to supply pharmacists directly to ensure availability for Belgian patients. Unavailability is a complex issue with many causes at different levels.

Complex production process

First, pharma companies do not take any risk in terms of safety and quality of products. Controls are also particularly strict in Europe. **Medicine and vaccine manufacturing processes are very time-consuming, extremely complex and fragile.** Most vaccines, for example, have a manufacturing process that takes more than 18 months. The same applies to other biological medicines developed from living cells. An unexpected event in a single step in this process, can sometimes not be taken care of immediately or in a simple way, which can cause major delays in the delivery of the next batch. With direct consequences, including stock-outs, often not only for the Belgian market but also for other European or even non-European countries. After all, medicines are rarely produced for one country, but for an entire region or even the world. Scaling up in the face of increased demand cannot be done overnight. Raw materials are also often scarce and these need to be handled very carefully. Holding large reserve stocks is therefore not justified and could lead to major upward price pressure or even scarcity of other medicines that require the same raw materials.

Price pressure

Second, we note that maintaining local production in Europe is a major challenge for all industrial sectors. **Higher wage and energy costs mean that production at low prices is not competitive, and those activities are shifting to other parts of the world.** The biopharma sector cannot escape that dynamic. Only high-value-added activities that require a lot of specialised knowledge are able to escape the dance for now. But the lack of local production is not just an economic reality. Also, to ensure access to low-cost medicines to developing countries, there is a lot of pressure to shift production facilities to those regions. Consider the political pressure to facilitate local production of COVID-19 vaccines in Africa, for example. Moreover, due to the frequent price cuts of medicines in the off-patent segment imposed by the Belgian government, companies are sometimes no longer able to keep the medicine available and it disappears permanently in Belgium, which can sometimes be very disadvantageous for the Belgian patient.

Free movement of goods

Finally, medicines must be able to circulate in Belgium according to the free movement of goods in the European Union. Since the price of a medicine is determined by governments on a country-by-country basis, we see flows from countries where prices are low to countries where they are sold at a higher price. We call this **parallel export**. The quota system tries to find a way around this, but it is often impossible for pharma companies to provide adequate supplies sufficiently quickly in the event of an export leak. Scaling up production is no easy matter.

Our commitment

The issue of unavailability is being discussed with the health minister as part of the reform plans. To make and keep medicines available to Belgian patients in the future, we will have to make the necessary long-term adjustments to make our distribution system less susceptible to all kinds of external factors. Encouraging a healthy competitive economic environment that allows multiple stakeholders into the Belgian market is one of the necessary adjustments to put a sustainable distribution system in place.

That is our commitment to society, a role we take very seriously as an industry. **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.**

What does PharmaStatus teach us?

Along with the other actors, the biopharmaceutical sector should be transparent and provide clear information on medicines that are not available. 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 work together to find solutions if a medicine is unavailable in a pharmacy or at a wholesale distributor. Looking at the actual figures, we see that 662 medicines were temporarily unavailable in November 2023. 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 426 cases there was at least one alternative available, and in 362 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.

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

Cost for the government (2022)	4,032,148
1.1 State expenditure on medicines (industry costs, excluding VAT) - NIHDI	3,960,377
1.2. Subsidies	71,771

State expenditure on medicines is based on the NIHDI figures of expenditure on specialty biopharmaceuticals. 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 subsidies paid by the government to the biopharmaceutical industry comes from the annual accounts of companies operating in Belgium. These are headings 740 (operating subsidies and compensatory amounts received on behalf of the government), 9125 (capital subsidies granted by the government) and 9126 (interest subsidies granted by the government).

Detailed income statement (in thousands of euros)

Income for the government (2022)	5,148,288
2.1. Labour charges	2,650,893
2.1.1. Employer's social security contribution	925,692
2.1.2. Employee's social security contribution	498,328
2.1.3. Retained amounts charged to third parties as tax on wages and salaries	1,226,872
2.2. Corporate tax	397,186
2.3. Taxes	1,415,421
2.3.1. VAT on turnover (6 % ex-factory price non-reimbursed medicines)	180,505
2.3.2. NIHDI taxes on turnover	383,918
2.3.3. Amounts retained on behalf of third parties for tax on income from investments	85,153
2.3.4. Corporate taxes and levies	765,845
2.4. Indirect revenues from third party transactions and investments	684,787
2.4.1. Purchase of raw materials and merchandise, miscellaneous goods and services	615,474
2.4.2. Investments	69,313

The income from labour charges is based on the yearly financial statements of companies operating in Belgium. These are headings 621 (employer's social security contribution), 620 (remuneration and direct social benefits, NSSO part) and 9147 (withholding tax). The same holds for corporate taxation. This relates to heading 670 (taxes).

The taxes are divided into four elements:

1. VAT on non-reimbursed medicines
   For the calculation, we use the turnover figure for non-reimbursed medicines as indicated by IQVIA. We do not take into account VAT on reimbursed medicines because the NIHDI pays it to the government, so it does not affect the comparison.

2. the taxes paid by companies to the NIHDI based on their turnover figure
   This figure comes from the NIHDI.

3. the balance sheet item 9148 (tax on income from investments)

4. balance sheet item 640 (corporate taxes and levies)

Besides direct revenue, there are also indirect revenues for the government:

1. revenues resulting from domestic purchases of raw materials, merchandise, miscellaneous goods and services by the biopharmaceutical industry
   The calculation is based on information from input-output tables (Federal Planning Bureau), which reflect the domestic demand of the biopharmaceutical 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 assessment rate (42.02 %, OECD).

2. revenues resulting from investments by the biopharmaceutical industry
   To the amount of investment, based on Statbel data, we apply the ratio of value added to turnover of the manufacturing industry. Then the average (para)tax assessment rate is applied (42.02 %, 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
- CRM: Commission of Reimbursement of Medicines
- CUP: Compassionate Use Programme
- DALY: Disability Adjusted Life Years
- DEP Committee: Comittee 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 Program
- NIHDI: National Institute for Health and Disability Insurance
- OECD: Organisation for Economic Co-operation and Development
- PEC: Patient Expert Center
- PO: Patient Organisation
- PRO: Patient-Reported Outcomes
- QALY: Quality-Adjusted Life Year
- RCT: Randomized Controlled Trial
- R&D: Research and Development
- RWD: Real World Data
- RWE: Real World Evidence
- SmPC: Summary of Product Characteristics
- Statbel: the Belgian statistical office
- STEM: Science, Technology, Engineering & Mathematics

References

1 European Commission, European Innovation Scoreboard (EIS) 2023
2 Eurostat, Gross domestic expenditure on R&D
3 Eurostat, Gross domestic expenditure on R&D by the business sector
4 Belspo, Total domestic R&D expenditure
5 European Commission, European Innovation Scoreboard (EIS) 2023 Methodology Report
6 Source: : https://health.ec.europa.eu/non-communicable-diseases/expert-group-public-health/rare-diseases_en#orphan-medicinal-products
7 Source: : https://efpia.eu/news-events/the-efpia-view/blog-articles/moonshot-mindset-can-make-the-impossible-possible/
8 Source: https://www.phrma.org/Scientific-Innovation/Progress-in-Fighting-Rare-Diseases
9 Source: : https://efpia.eu/news-events/the-efpia-view/statements-press-releases/rare-disease-moonshot-scaling-up-public-private-partnerships-to-accelerate-research-into-world-s-rarest-diseases/
10 Critical Path Institute (C-Path), European Infrastructure for Translational Medicine (EATRIS), European Clinical Research Infrastructure Network (ECRIN), European Federation of Pharmaceutical Industries and Associations (EFPIA), European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), EuropaBio, and EURORDIS - Rare Diseases Europe
11 Source: : https://efpia.eu/news-events/the-efpia-view/statements-press-releases/rare-disease-moonshot-scaling-up-public-private-partnerships-to-accelerate-research-into-world-s-rarest-diseases/
12 A moonshot initiative is a large-scale, ambitious project with a high risk of failure but which, if successful, can lead to a major breakthrough or ground-breaking innovation. The term originated by analogy with the Apollo 11 mission that sent humans to the moon for the first time
13 Source: www.cancer.org/cancer/bile-duct-cancer/about/what-is-bile-duct-cancer
14 Banales JM, et al. Nat Rev Gastroenterol Hepatol. 2016;13:261-280
15 Uhlig J, et al. Ann Surg Oncol. 2019;26:1993-2000
16 Blechacz B, et al. Nat Rev Gastroenterol Hepatol. 2011;8:512-22. 11
17 A. Vogel, et al. Annals of Oncology, Volume 33, Supplement 4, 2022, Page S379, ISSN 0923-7534, https://doi.org/10.1016/j.annonc.2022.04.443
18 Summary of Product Characteristics, 24 February 2023, (the link to the SmPC can be accessed at info@pharma.be)
19 Graham RP, et al. Hum Pathol. 2014;45:1630-1638
20 Ang C. J. Gastroenterol Hepatol. 2015;30:1116-1122
21 Ross JS et al. The Oncologist. 2014;19:235-242
22 Belgian Cancer Registry 2021. Haematological Malignancies Belgium, 2004-2018
23 Smith et al. Br J Cancer. 2015 Apr 28;112(9):1575-84. Epub 24 March 2015
24 Hess et al. Br J Haematol. 18 October 2022
25 Wang et al. J Clin Oncol. 2023 Jan 20;41(3):555-567. doi: 10.1200/JCO.21.02370. Epub 4 juni 2022
26 Deblonde J. et al (SCIENSANO). November 2022
27 Marcus JL et al. JAMA Network Open 2020
28 Summary of product characteristics, August 2022
29 Idem
30 Kozal M et al. N Engl J Med 2020; 382:1232-1243.
31 Source: https://www.esmo.org/newsroom/press-releases/esmo-congress-melanoma-immunotherapy-checkmate067-larkin
32 Overall survival for HER2-positive Breast Cancer Patients in the HER2-Targeted Era: Evidence from a population-based study. Marczyk et al. Clinical Breast Cancer July 2022
33 KCE report 343, p 76
34 KCE report 343, p 158
35 KCE-rapport 343, p209
36 KCE-rapport 343, p238
37 KCE-rapport 343, p259
38 Lichtenberg, F. (2023), "The long-run impact of changes in prescription medicine sales on mortality and hospital utilization in Belgium, 1998-2019"
39 Methodology: see Appendix 1
40 Source: https://www.fagg.be/nl/MENSELIJK_gebruik/geneesmiddelen/geneesmiddelen/onderzoek_ontwikkeling/gebruik_in_schrijnende_gevallen_medische_noodprogrammas
41 Source: https://assets.vlaanderen.be/image/upload/v1636361168/EU_statistieken_Belgie_2020_u9lq5r.pdf
New data for 2022 are not available yet
42 To avoid a change in the number of animals giving a false picture of antibiotic use, this is expressed in mg per kilogram of biomass.
43 Makady et al., 2017

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