A focus on
CLINICAL RESEARCH
in Belgium

2024

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

Giving as many patients as possible opportunities to participate in clinical research

Deloitte's annual study commissioned by pharma.be shows that Belgium accounted for 474 authorized clinical studies in 2022. 20 % of all European clinical studies of cancer drugs take place in Belgium. And companies in our country invest about 15 million euros a day in research and development, of which clinical studies are a big part.

Participating in a clinical study is a patient's first chance to reap the potential benefits of a new, innovative treatment. For some patients, gaining access to a treatment for their disease, where such treatment did not exist before or no alternative is available, can prolong or improve the quality of their lives. It is this human impact that really matters. This is why pharma.be strives to maintain the strong position that Belgium holds today in Europe.

The evolution towards a more inclusive environment for clinical studies in Belgium is an undeniable opportunity, but also brings a number of challenges with it: participant mobility, lack of confidence in medical research due to a lack of knowledge about clinical studies, social and economic barriers, and language and cultural differences that can hinder communication. The implementation of a set of best practices by authorities and companies can ensure long-term progress.

It is important that our country remains at the forefront of clinical studies, particularly by giving more flexibility with the introduction of decentralised clinical studies. Authorities should also be able to guarantee predictable, consistent and efficient approval times for the initiation of clinical studies in our country. Data sharing and intensive dialogue between regulatory authorities, hospitals and the pharmaceutical industry is crucial.

After all, we work together for the good of the patient.

Caroline Ven
CEO pharma.be

The innovative medicinal products, vaccines and other treatments that are now available to patients are the result of many years of clinical research and development

Clinical studies are complex and strictly regulated and can easily take up 10 to 12 years. These studies are very important in testing new potential medicinal products for efficacy, safety and tolerability. They also investigate possible interactions with other medicinal products, as well as the optimum dose and most effective route of administration to patients. Clinical studies can also provide valuable insights into the specific patient populations that benefit the most from the treatment.

Before any potentially helpful medicine can be given to patients, thousands of different molecules and combinations of molecules are screened, and a few hundred enter preclinical testing. From this large number, only ten or so of the most promising molecules will be chosen to be part of a clinical study programme.

Even after this screening, it is important to note that the chance of success for a clinical study is quite low. In fact, only around 10 % of the tested medicines will successfully complete the entire clinical study programme and move forward for marketing registration.

The phases of clinical research

A clinical study can be divided into the following phases:

PRE-CLINICAL

The pre-clinical phase tests the molecule mostly in animals. This is to determine the safe dose for a first-in-man study and to assess the molecule safety and toxicity profile.

PHASE 1

A few dozen volunteers

- Phase 1 involves a few dozen individuals, usually healthy volunteers, to gradually analyse the uptake of the new tested molecule into the body and identify possible side effects. The assessment of safety and tolerability are the main objectives of phase 1 studies.

PHASE 2

A few hundred patients

- Phase 2 involves a few hundred patients. These participants are chosen because they fulfil previously defined criteria to determine the efficacy and the optimum dose of the molecule.

PHASE 3

A few thousand patients

- Phase 3 involves large-scale research into a few thousand patients who fulfil the defined criteria. This phase aims to confirm the previous test results on a large scale, ensuring the medicine candidate is efficacious and safe in a larger group of patients.
- Phase 3 also involves the comparison of the new medicinal product: either to a placebo (an inactive substance) or, if available, to an existing treatment (usually what is called the “standard of care”).
- After a successful phase 3, the results are evaluated by the European Medicines Agency, which decides whether to issue marketing authorisation for the new medicinal product.

PHASE 4

Real-life use after market introduction

- Phase 4 studies are carried out after a medicine has obtained marketing authorisation. Some studies further test the new treatment. Others aim to observe the effects of its use in patients in a real-life treatment setting. In both cases, they aim to find out more about:
  - common and rare side effects
  - long-term risks and benefits
  - risks and benefits in groups of patients not included in the phase 3 study
  - how the medicine compares to alternative treatments

Parties involved in a clinical study

In addition to the patients, several parties are involved in the development and implementation of a clinical study.

- the **sponsor** of the study, i.e. the pharmaceutical company developing the medicinal product
- the **investigator**, i.e. the physician participating in the study
- the **health authorities** and the **ethics committee(s)** in the country or countries where the study is conducted. Each clinical study, whatever the phase, must be reviewed and approved by both regulators before it may start[2, 3, 4]

European Medicines Agency video about clinical studies in the EU:

New ways of designing clinical studies

Nowadays, new and innovative ways of designing clinical study protocols are constantly emerging, aimed at accelerating and increasing the efficiency of all phases of clinical studies, while preserving quality. These new methods have introduced new complexities as they require a high degree of collaboration between sponsors, investigators, and patient organisations.

One example is the use of new technologies to capture patient data in real time during the study, as well as the use of historical data as a comparison. This has decreased the need for a placebo treatment control group.

Ultimately, these new approaches benefit patients, whether they participate in studies or have access to the treatment afterwards.

In clinical studies, diversity, equity and inclusion are of primary importance

These principles ensure that research participants represent a wide range of demographics, including factors like race, ethnicity, gender, age, socio-economic status, and other relevant characteristics. It's essential that study sponsors enrol participants with diverse backgrounds to accurately reflect potential medicine users upon approval. Diversifying study participants also improves access to innovative treatments, particularly benefiting minority groups that may have been historically excluded.

Both within Belgium and throughout Europe, there are various platforms available where anyone can search all ongoing studies. Most often, however, patients will learn about a new study through their doctor or patient organisation. If a patient is interested in participating in a clinical study, the doctor should explain the purpose of the study and its potential benefits. The doctor should also point out that these benefits cannot be guaranteed, and that there may be (unforeseen) side effects due to the investigational stage of the new medicine. The doctor will also check if the patient meets all the inclusion and exclusion criteria outlined in the study protocol for participation in the study.

More information about clinical studies, including an overview of the ongoing clinical studies in Belgium and throughout Europe, can be found on the following platforms:

The Federal Agency of Medicines and Health Products:

The EU Clinical trials Register:

The Clinical Trials Database:

Esperity:

The Federal Public Health Service of Health, Food Chain Safety and Environment has developed a brochure that provides an overview of general information for adult patients who wish to participate in a clinical study of an investigational medicinal product.

Discover the brochure here (in French):

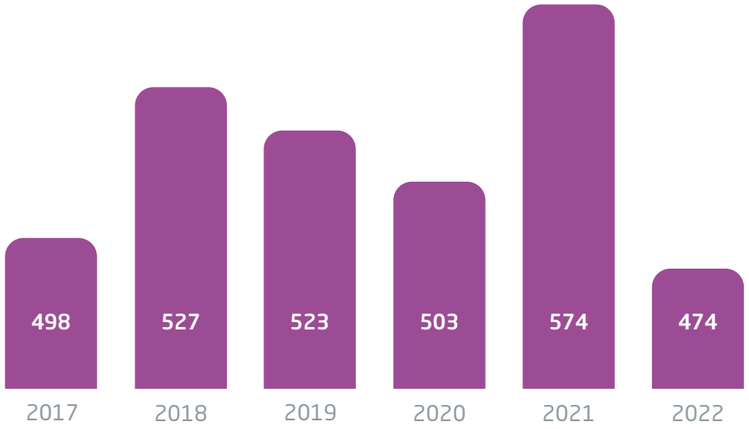
More information on clinical research in general can be found on the website of the European Patients' Academy (EUPATI):

A long history of clinical research

Belgium has a unique health ecosystem in which clinical research can thrive. Thanks to a shared vision and close collaboration between regulators, industry, researchers, investigators and government, Belgium has established itself as a strong location for conducting clinical studies and a best practice reference country in Europe. With 474 new authorisations of clinical studies in 2022, Belgium is one of the top 3 European countries in terms of the number of authorised clinical studies per inhabitant.

Thanks to this leadership, Belgium has played a pivotal role in the development of new medicines and advanced therapies over the years. For instance, Belgium hosted the first clinical study of CAR T-cell therapy to treat cancer in Europe. Belgium also played a primary role in the clinical research of potential COVID-19 vaccines.

Number of approved applications for clinical trials



Source: Federal Agency of Medicines and Health Products data

In Belgium, about 80 % of clinical studies are initiated by pharmaceutical companies. The remaining 20 % are clinical studies that are initiated by universities or academic centres.

Preserving clinical research competitiveness for the future

Preserving Belgium's unique clinical study environment and enhancing its competitiveness are critical for the future of medical research in the country. Belgium's strengths in science, regulation, and testing facilities are well-established. However, with the implementation of standardised regulatory systems for clinical studies across the European Union, there is a chance that Belgium might be less appealing for studies in the future. To maintain its standing, Belgium must differentiate itself by leveraging its strengths. In doing so, the country can continue to attract top researchers and industry partners, staying at the forefront of clinical research and development.

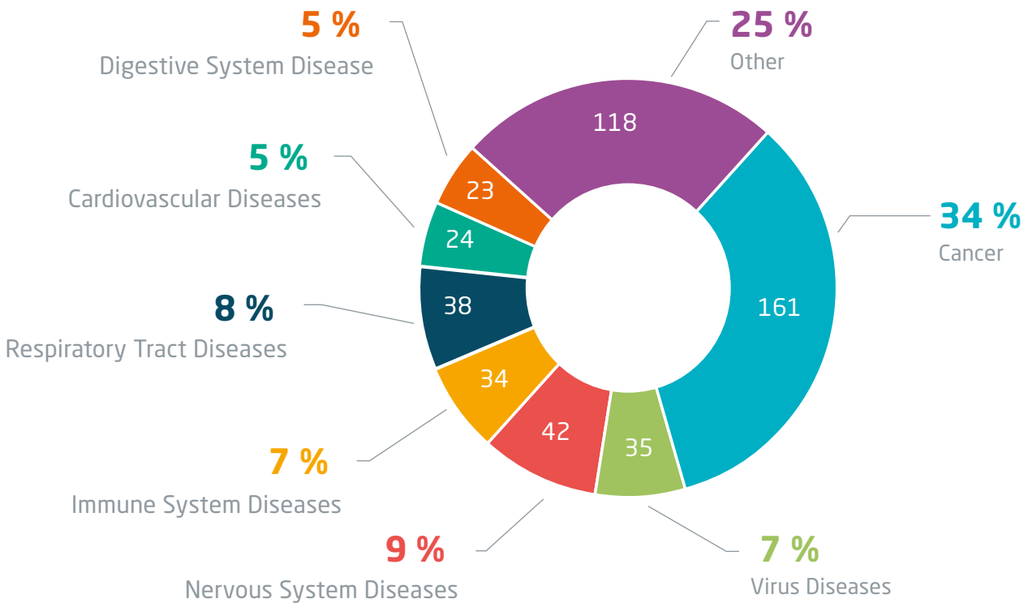
Early phase studies expertise

Belgium has a strong expertise in the early phases of medicine development. In 2022, 22.3 % of the studies authorised in Belgium were phase 1 studies. The proportion of phase 1 studies observed in previous years has been slightly higher than a comparative cohort of nine European countriesi. We owe this world-renowned expertise to a number of different factors. First of all, Belgium enjoys a favourable regulatory framework with specific shorter deadlines for the approval of phase 1 studies conducted solely in Belgium, by the competent authorities and the ethics committee. The Belgian Federal Agency of Medicines and Health Products has also developed an area of excellence in early phase development and can therefore support pharmaceutical companies in their first clinical development programs. And there continues to be a growing number of First-in-Human studies approved in Belgium, i.e. studies that test medicinal products in a human body for the first time. Phase 1 and First-in-Human studies are conducted in specialised units. In Belgium, there are 8 specialised phase 1 units around the country conducting studies in healthy volunteers, along with numerous hospital departments are able to conduct phase 1 studies in patients. A large part of medicine information leaflet content comes from the results of the phase 1 research.

Diverse expertise in almost all therapeutic specialities

The clinical studies conducted in Belgium cover nearly all therapeutic areas, with a notable expertise in oncology. Almost 20 % of European studies in cancer research are conducted in Belgium, in another example of the country's leading role in clinical research in Europe.

Proportion of clinical trial applications for selected disease areas in Belgium (2022)



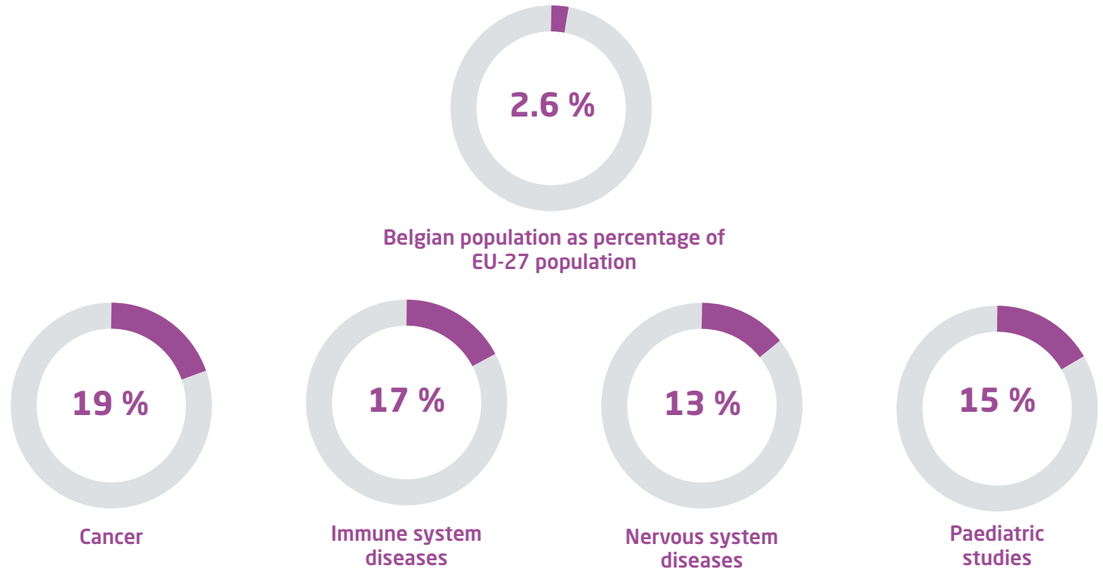
Source: "Belgium as clinical trial location in Europe: Key results 2022", Deloitte report 2023

Cancer research studies in Belgium

Belgium plays an essential role in the global effort to research new treatments in oncology. Many medicinal products and advanced cancer therapies have been developed or tested in Belgium. When participating in clinical studies in oncology, investigators also actively contribute to improving patient prognoses (e.g. see the *CLEOPATRA breast cancer study*, Swain S. et al, ESMO 2014). More than 34 % of newly authorised studies in 2022 were in cancer research, which means almost three new studies were approved per week.

Belgium's remarkable footprint in terms of clinical trials in Europe

Proportion of European clinical trials conducted in Belgium for selected type of studies compared to the proportion of the Belgian population in Europe (2022)



Source: "Belgium as clinical trial location in Europe: Key results 2022", Deloitte report 2023

Rare disease and paediatric studies

A disease is considered rare if fewer than 5 in 10,000 people are affected by it. However, there are a huge number of rare diseases; so much so that around 1 in 17 people suffer from a debilitating rare disease in Europe. This makes the research and development of effective treatments for these rare diseases a considerable challenge. In Belgium in 2022, 24 % of the authorised clinical studies were conducted in the domain of rare diseases, representing 122 new studies.

Children are a unique population with distinct developmental and physiological differences from adults. Therefore, clinical studies in children are essential to develop age-specific therapies and improve upon the best medical treatment available. In 2022, 8 % of newly approved clinical studies were paediatric studies. This is a growing proportion over the last years.

Want to know more about Belgium as a clinical study location? You can consult the latest Deloitte report *"Belgium as a clinical trial location in Europe"* on the pharma.be website:

Belgium is a cluster of excellence at the heart of Europe

The country includes more than 70 hospitals, including 7 university hospitals, 12 universities with internationally renowned bioscience research departments and teams, 14 biotech business incubators and more than 50 pharmaceutical companies active in clinical research[6].

A Federal Agency of Medicines and Health Products with strong expertise

The strong technical expertise and scientific advice provided by the Federal Agency of Medicines and Health Products enables the sponsors of clinical studies to deal with critical questions, even early in the evaluation process. Access to this information increases the predictability of the feasibility of the study for the sponsors, and makes the entire process more transparent and easier to plan. Members of Federal Agency are also well represented in the different working groups at the European Medicines Agency, which benefits Belgium in terms of knowledge generation, steering strategic choices, and leadership opportunities.

The National Innovation Office of the Federal Agency of Medicines and Health Products

The National Innovation Office has been launched within Federal Agency of Medicines and Health Products in order to facilitate and support innovation in pharmaceutical research and development in Belgium, as well as to improve communication with innovators. The National Innovation Office serves as the central access point to the existing scientific and regulatory expertise of Federal Agency of Medicines and Health Products both for human and medicines and therapies. It is accessible for pharmaceutical companies, small and medium-sized enterprises, academic research centres, spin-offs of existing companies/universities, academic hospitals and individuals who are actively involved in pharmaceutical innovation in general and in research and development of new medicines and therapies in particular. The three main pillars of the office's activities are: scientific, technical and regulatory advice, general innovation activities and support for small and medium-sized enterprises and the academic sector.

More information:

Research quality

Pharmaceutical companies in Belgium have access to an extensive hospital network offering top quality clinical services and expert staff. The quality of Belgian research centres, the "real life" expertise of investigators, and our culture of collaboration are all key drivers for sponsors selecting Belgium as a location for clinical studies. Through their exceptional cooperation, the pharmaceutical sector, hospitals, universities and research centres continue to build Belgium's strong reputation as a destination for clinical research and development.

Benefits for patients, physicians and the wider population

Clinical studies may offer people the opportunity to access the latest treatments for free. These treatments may not be available through traditional means, and have the potential to improve their health and quality of life. Clinical studies are a way for patients to actively participate in their health management. They also foster a sense of purpose for participants, who may feel they are helping in developing a better understanding of their condition and contributing to improved treatment options for the future.

Benefits for the Belgian research community

Clinical studies contribute to the development and showcasing of scientific knowledge and innovation in Belgium. This helps Belgian researchers and research centres remain at the forefront of innovative treatments against diseases such as cancer, diabetes and central nervous system conditions.

Benefits for the Belgian economy

The pharmaceutical industry is among the most research and development intensive sectors in Belgium. Our country invested around 5.7 billion euros in pharmaceutical research and development in 2023. Moreover, clinical studies create jobs in research centres, universities and hospitals. In 2023, a total of 6,706 researchers were active in the Belgian pharmaceutical sector.

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 studies, 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 studies 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 clinical studies, data serves as the foundation for evaluating the safety and efficacy of new treatments and making sure patients get the best care. Data is not just needed for getting approval from regulators. Without carefully collecting and studying this information, it is hard to know if a treatment is helpful or has any risks. The availability and collection of data is crucial in every step of the clinical study, from designing the study and recruiting participants, to analysing results and sharing them with regulators.

Primary use of clinical study data

Throughout clinical studies, researchers collect data to understand how individuals respond to treatments, and identify any potential side effects. This is the primary use of the data obtained from a study. By analysing this data, researchers gain valuable insights about the product, leading to the discovery of new treatments. The analysis of the data is reviewed by an independent committee from the sponsor of the study. The committee can decide to stop the study prematurely in the case of severe adverse events or very positive interim results. The data collection process occurs within a highly controlled environment, ensuring accuracy, reliability of the data and the confidentiality of patient information. These elements are key for a credible data generation process to evaluate the efficacy and the safety of the treatment.

Secondary use of clinical study data

The patient data obtained from a study can also be used in connection with other scientific research and development activities that may concern the same medicinal product or similar treatments, the same disease area, or other health problems. This is the secondary use of the data. This use occurs again in a highly controlled environment, in line with the data protection legislation, and with the necessary information provided to study participants in advance.

For more information about health data, you can consult the brochure "Care for your data" by the King Baudouin Foundation (in French or Dutch):

Advanced data collection through new technologies

In recent years, the landscape of clinical studies has evolved through the integration of new technologies, introducing innovative methods for data collection. One such example is the use of smartphone applications and mobile health (mHealth) devices. These tools empower patients to actively participate in their treatment by enabling them to track various health metrics, such as heart rate, physical activity, and medication adherence, from their own devices. This data is a valuable addition to that obtained through standardised questionnaires or easy-to-use scales (e.g. -on pain, tiredness, etc.) These innovative digital tools allow researchers to gather valuable insights into how patients respond to treatments in real time, without the need for frequent visits to the clinical study centre. Importantly, strict privacy measures are in place to safeguard patient data, ensuring confidentiality and trust throughout the clinical study process. This evolution in data collection has not only enhanced the accuracy and reliability of clinical research but also fosters a patient-centric approach to healthcare, where individuals play an active role in advancing clinical research while receiving personalised care.

What is real-world data?

Real-world data is a term encompassing data related to the effects of healthcare interventions (e.g., safety, effectiveness, resource utilisation, etc.) that are not collected within the framework of controlled clinical studies. Unlike data gathered in clinical studies, real-world data is derived from real-world settings and reflects the diverse experiences of patients in everyday healthcare environments. Real-world data can be obtained from many sources, including patient registries, electronic medical records, and administrative databases.

Real-world data can generate new insights, known as real-world evidence, into a treatment or a disease by bringing together anonymised data from thousands or even millions of patients. Rare safety signals that might have escaped the limited setting of a clinical study can then be picked up. The efficacy of a medicinal product in certain subpopulations excluded from the normal clinical studies can be demonstrated. For rare diseases, more information can be discovered about the patient, unmet medical needs, the treatment journey or the frequency of the disease. In certain cases, real-world data can be used as a control to evaluate a tested medicinal product in clinical studies. This limits the number of patients who don't receive the tested new compound or when placebo treatment (i.e. inactive treatment) is not ethical because it would compromise care standards. Real-world data can help to design or plan clinical studies, facilitate patient identification and recruitment in studies.

It is crucial that real-world data is easy to find, accessible, and stored in systems that can operate well together.

The Belgian government recognises the importance of the real-world evidence in healthcare and a dedicated competent authority, the Belgian Heath Data Agency, has been set up to facilitate the further use of health data in scientific research.

The 'Data Saves Lives' initiative

The collection and use of patient data is a key component of clinical research, from providing new insights into tested treatments to supporting the design and planning of studies, to helping with patient recruitment. Data Saves Lives is a multi-stakeholder initiative with the aim of raising wider patient and public awareness about the importance of health data, improving understanding of its use and establishing a trusted environment for dialogue about responsible use and good practice across Europe. Data Saves Lives hosts and maintains a web portal, sharing relevant information and best practices on the use of health data. It also generates easy-to-use educational materials about the basic concepts of data sharing, the data journey and the safeguards in place.

More information about the "Data Saves Lives" initiative:

Notes and References

1. In case of patients with severe diseases, the patient may continue their treatment with the placebo added to this treatment
2. European Regulation 536/2014, which came into force in 2022, governs the evaluation of a clinical studies application, together with the applicable national law
3. https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en
4. In Belgium, this is defined by the law of 7 May 2017 on Clinical Trials.
5. *"Belgium as clinical trial location in Europe: Key results 2022"*, Deloitte report 2023
6. Pharmaceutical companies member of pharma.be

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ASBL/VZW – BE 0407.622.902 – RPR Brussel – Responsible publisher: Caroline Ven
Terhulpsesteenweg 166 Chaussée de La Hulpe , 1170 Brussels, Belgium – www.pharma.be – info@pharma.be