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

Belgium, a European leader in clinical trials

An attractive country for clinical trials to test innovative medicines

In Europe it is nearly impossible to find other countries with as many clinical trials running as in Belgium. With **507 new applications** for clinical trials in 2016 and a total of **1,399 trials that year,** Belgium is one of the leaders in Europe. Based on the number of inhabitants, **Belgium is in 2nd place in Europe.**

The fact that Belgium is an attractive country for starting up clinical trials offers **many benefits for patients** here. As well as providing **rapid access to innovative medications,** the trials can also generate valuable insights into treatments for other conditions. All actors involved in health care make every effort to keep Belgium's strong position as an attractive country for carrying out clinical trials.

Belgium is 2nd in place in Europe

1,399 clinical trials in Belgium in 2016

507 new applications in 2016

Source: clinicaltrials.gov

Optimal preparation in 2017 for the new European framework in 2018

At the end of 2018 a new **European Regulation (536/2014)** will be coming into force to harmonise the application and approval procedures for clinical trials within the European Union (EU). Prior to this date, **several initiatives** are taking place in Belgium to maintain its strong position in the area of clinical trials.

In July 2015 the Federal Government in Belgium signed a **'Pact of the Future'** with the pharmaceutical sector, which runs until 2019. This pact underlines the strong ambition to create a stable framework for companies investing in pharmaceutical Research & Development (R&D) in Belgium. One of the objectives was to create "a strategic plan in order to hold on to our **'yellow jersey' in clinical trials within Europe".**

A concrete result of the Pact is the **new Belgian Law on Clinical trials,** voted on 20 April 2017, which will further strengthen Belgium's competitive advantages in the area of clinical trials.

"The new Belgian law testifies the high level of commitment among all the stakeholders in health care to continue to attract clinical research. The intense cooperation between pharmaceutical companies, universities, hospitals, the agency for the evaluation of medicinal products and the ethics committees is a huge asset, meaning that clinical trials can be started up quickly and under the best possible conditions. That expertise and attractiveness also generates major benefits for patients in Belgium."

Catherine Rutten, CEO of pharma.be

New Belgian law: coordinated, simple and rapid clinical trial evaluations

15 days approval time for phase 1 trials

The law creates **a new framework for clinical trials in Belgium.**

- Thanks to the new law, Belgium is able to continue to implement **its ultra-fast approval procedures** for clinical trials, particularly for phase 1 trials. With a procedure that takes **barely 15 days,** Belgium is still the **absolute leader in Europe.**
- A **national College** will ensure **the harmonised assessment** of new study applications. The College will also monitor compliance with procedures to ensure high quality studies.
- The **evaluation** of applications will be **centrally coordinated** in a **simple and consistent way** by the competent authorities and designated ethics committees.

Belgium is one of 'the best in Europe': why is this?

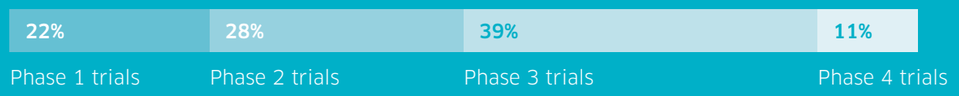
01 Strong expertise

Belgium has acquired exceptional expertise over the years in the field of clinical trials involving new medicinal products. This is shown by WHO figures indicating that **more than 10,200 clinical studies** have been carried out in Belgium **since 2000.** In 2016 alone, there were **1,399 studies** taking place in Belgium.

Furthermore, a total of **507 new clinical trial applications** were submitted in Belgium in 2016, representing a proportion of about **12% of the 4,000 new trials started up each year in Europe** according to the European Medicines Agency (EMA). The trials in Belgium are distributed evenly across the various phases of clinical research.

Source: WHO figures (2017): Global Observatory on Health R&D

Fig. 1: Applications for clinical trials in Belgium



Source: famhp (2016)

The majority or **82%** of clinical trials in Belgium are initiated by the pharmaceutical industry. The remaining 18% are clinical trials initiated by universities or academic centres.

Fig. 2: Distribution Industry-sponsored clinical trials vs. Academic clinical trials

Source: famhp (2016)

02 Wide range of therapeutic domains

The clinical trials carried out in Belgium cover nearly all therapeutic areas. Belgium's specific expertise in oncology is notable: approximately **30 percent of the applications for clinical trials are intended to test new cancer treatments.** Other trials address central nervous system disorders, digestive diseases, cardiovascular conditions etc.

Fig. 3: Clinical trials in Belgium address a broad range of therapeutic areas – top 15 (2014-2016)

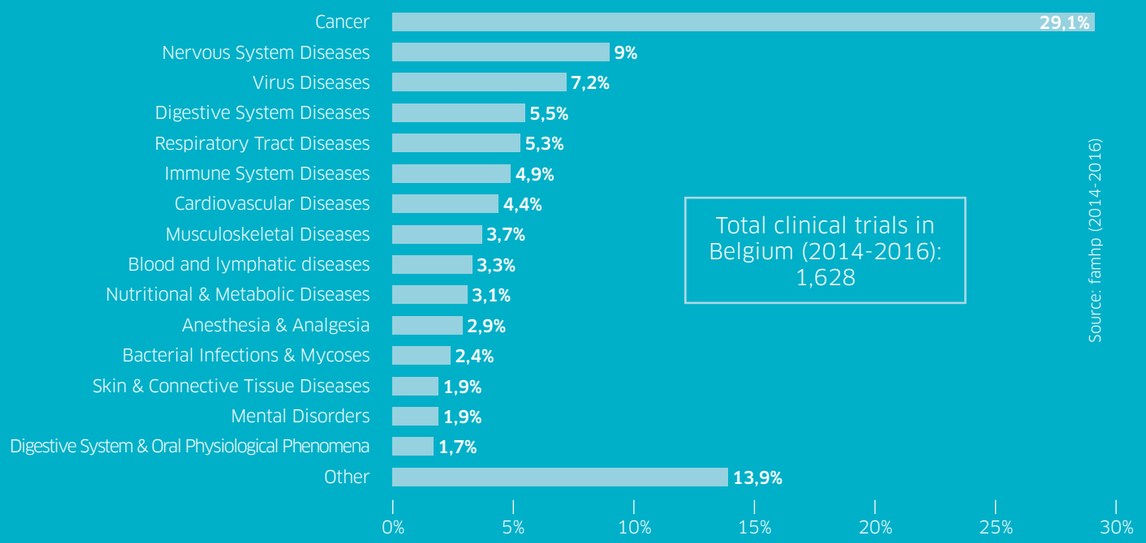


Fig. 4: Belgium's remarkable position in the EU

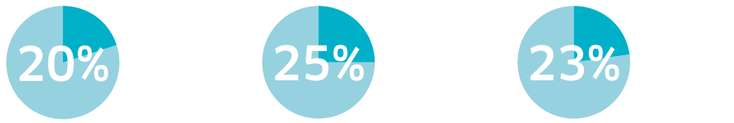


Fig. 5: Belgium at the forefront of novel medical techniques

Source: famhp (2014-2016)

03 Advantage of speed

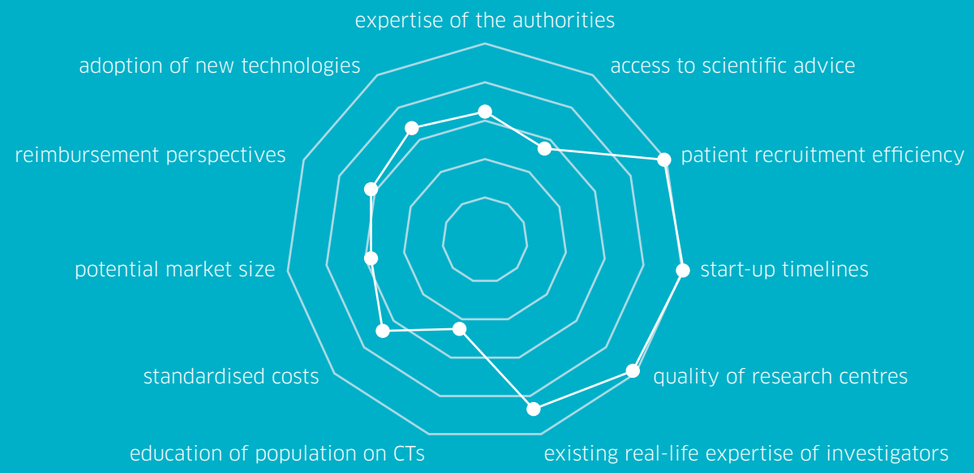
Thanks to the new law, Belgium will continue to be a champion in the rapid evaluation of applications to set up clinical trials. The **15 day approval time for phase 1 trials** will remain in place. This rapid evaluation process is very important for pharmaceutical companies, as was shown by a survey of pharmaceutical companies carrying out clinical research in Belgium.

Key drivers to choose a country to conduct a clinical trial

pharma.be survey among 45 company members conducting clinical trials

In March 2017, pharma.be questioned 45 innovative pharmaceutical companies that are conducting clinical research in Belgium. The survey aimed at **defining the industry's main influencing criteria to select countries for conducting phase 2 or phase 3 clinical trials** with innovative medicines. The second objective of the survey was a scoring of **Belgium's performance** for these different criteria.

Fig. 6a: What are the decisive key drivers to choose a country to conduct a clinical trial?



* relative score of each indicator. N = 45 (participation N = 31), April 2017

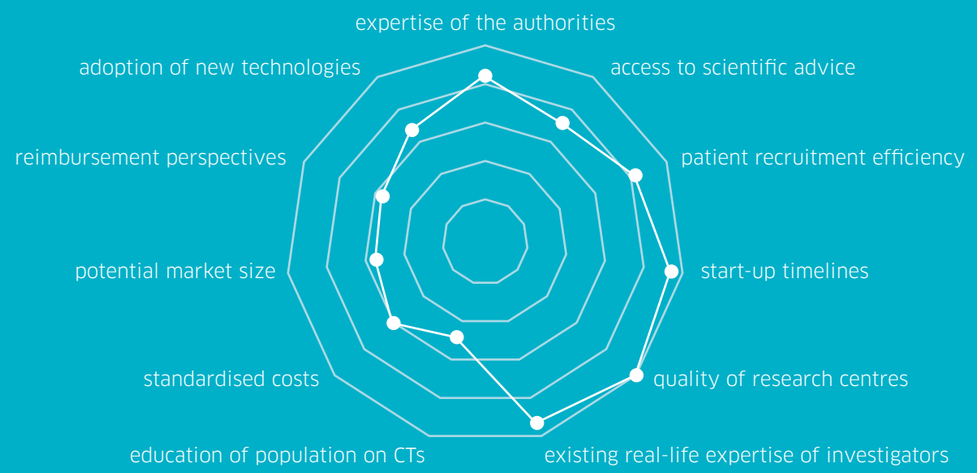
Conclusions: The results illustrate that **companies attach high importance to the following key drivers:**

I **Rapid start-up timelines:** the study approval by the authorities and the ethics committee, as well as the study initiation timelines.

II **Patient recruitment efficiency** (e.g. volume or speed).

III **Quality of research centres** and dense medical infrastructure.

Fig. 6 b: How does Belgium perform for the defined key drivers?



* relative score of each indicator. N = 45 (participation N = 31), April 2017

Conclusions for Belgium:
The results show that **Belgium has excellent assets in:**

I **Quality of research centres** and dense medical infrastructure.

II **Rapid start-up timelines of clinical trials:** the study approval by the authorities and the ethics committee, as well as the study initiation timelines.

III **Existing real-life expertise of investigators** with innovative medicines and access to state-of-the-art medical infrastructure in the investigated medical domain.

04 State-of-the-art infrastructure

Pharmaceutical companies in Belgium have access to an extensive infra-structure comprising **more than 70 hospitals** with top quality clinical services clinical services and well trained staff. The **quality of the research centres,** the **'real life' expertise of scientists** and a **strong willingness to collaborate** are all highly valued. Through intensive collaboration, the pharmaceutical sector, hospitals, universities and research centres are continuing to build Belgium's strong reputation as a destination for clinical research.

05 Pilot projects: optimum preparation for European harmonisation

The new Belgian law has given the starting signal for **pilot projects** in April 2017 in preparation for the implementation of the European Regulation in 2018. Belgium is one of the first countries in Europe to initiate pilot projects. This multi-stakeholder initiative demonstrates the high level of willingness among all the stakeholders in health care to preserve and even reinforce the existing favourable climate for clinical research.

06 National Innovation Office within famhp

One of the examples illustrating the Belgian support to companies and universities, is the **newly created National Innovation Office** within the famhp, starting in late 2017.

- The *National Innovation office* will provide a **simple, central access point for scientific and technical/regulatory questions.**
- It will encourage both companies and academics to set up **early-phase clinical trials** and will specifically **support SMEs in their R&D activities.**

The famhp also wants the *National Innovation office* in Belgium to play a strong role within the **European network *of Innovation offices,*** to ensure that the responses that are provided can also be placed within a European context. There will be further consideration in the future of ways to develop a more iterative advisory process and possibly to accelerate the procedures for early-phase applications, one of the spearheads of the famhp.

What are the advantages of a strong position in clinical trials?

Belgium's top position in Europe results in **benefits for patients, the doctors treating them, the research community in Belgium and also for the Belgian economy.**

Advantages for patients in Belgium and the doctors treating them
- Patients will have faster access to the latest treatments, which are often not yet available elsewhere.
- Testing new medicinal products that are under development can generate valuable new insights into the treatment, prevention or cure of other or future conditions.

Advantages for Belgian researchers:
- Clinical trials contribute towards the development of scientific knowledge and innovation in Belgium and serve as an important source of inspiration for new fundamental scientific research.
- Thanks to clinical trials, Belgian researchers and research are always at the forefront of innovative treatments.

Benefits for the Belgian economy:
- With a record level of **investment of 2.89 billion euros in 2016** in research into new medicinal products, the pharmaceutical industry in Belgium is one of the most R&D-intensive sectors in the country.
- Clinical trials create **jobs** in research centres, universities, hospitals, Clinical Research Organisations and supporting services.
- There are more than **4,500 researchers** working in the pharmaceutical industry in Belgium.
- Each job in the pharmaceutical sector creates approximately 4.6 additional **jobs** in other sectors.

Source: Pharma figures 2016 www.pharma.be

About clinical trials

The innovative medicinal products, vaccines or other treatments that are now available to patients are the result of many years of clinical research. Clinical trials are complex and strictly regulated and can easily take 10 to 12 years. The studies are very important to test potential innovative medicines for efficacy and safety, including possible interactions with other medicinal products and possible side-effects, as well as the most effective route of administration to patients and the optimum dose.
In addition, clinical trials can shed light on the type of patients who receive the greatest therapeutic benefits from the treatment.

10-12 years of research

- Thousands of drugs and combinations have to be screened in a process that takes several years, before a single promising drug with potential new health benefits is able to reach the patient. Out of this huge number, only the most promising drugs of all are eligible for a clinical study programme.
- The likelihood of success is remarkably low: only **10%** of the medicines will reach the end of a clinical study programme.
- Trials can only be carried out in government-approved clinical centres which follow a clearly-defined protocol in which all the data are thoroughly analysed and documented.

Phase 0: screening

- Research into the chemical and pharmaceutical characteristics of the drug, including preclinical tests on cells and animals, to test the efficacy and safety of the new drug.
- Exploratory micro-dosing research in humans to analyse the uptake of the drug in the human body (expectations based on clinical trials).

Phase 1: a few dozen volunteers

- Research involving a few dozen individuals, who are usually healthy volunteers, to gradually analyse the uptake of the new drug into the body and identify possible side-effects.

Phase 2: a few hundred patients

- Research involving a few hundred patients to determine the optimum dose of the medicinal product.

Phase 3: a few thousand patients

- Large-scale research involving a few thousand patients to confirm the previous test results on a large scale.
- Comparison of the new medicinal product with existing treatments and/or placebo in a double-blind, randomised test.
- After a successful phase 3, the results are evaluated by the EMA, which makes a decision on a marketing authorisation for the new medicinal product.

Phase 4: real-life use after market introduction

- Testing of the new treatment in a very large number of patients to gain insights into its use under real-life conditions and its long-term efficacy.

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