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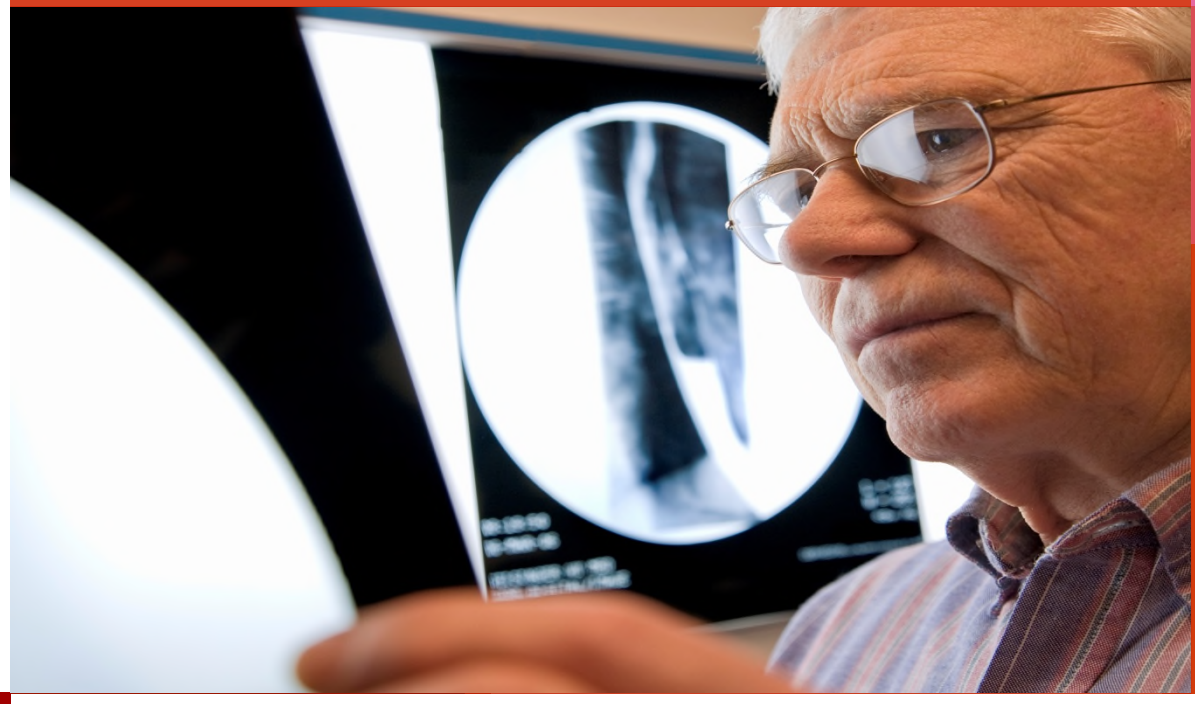
Recent developments on clinical trials in Belgium

March 17th 2011, Brussels



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Outline

1. Trends in clinical trials globally
2. Status and evolution of clinical trials in Belgium
3. Belgium's clinical trial situation within Europe
4. Conclusions and recommendations

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Trends in clinical trials globally

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Trends in clinical trials globally

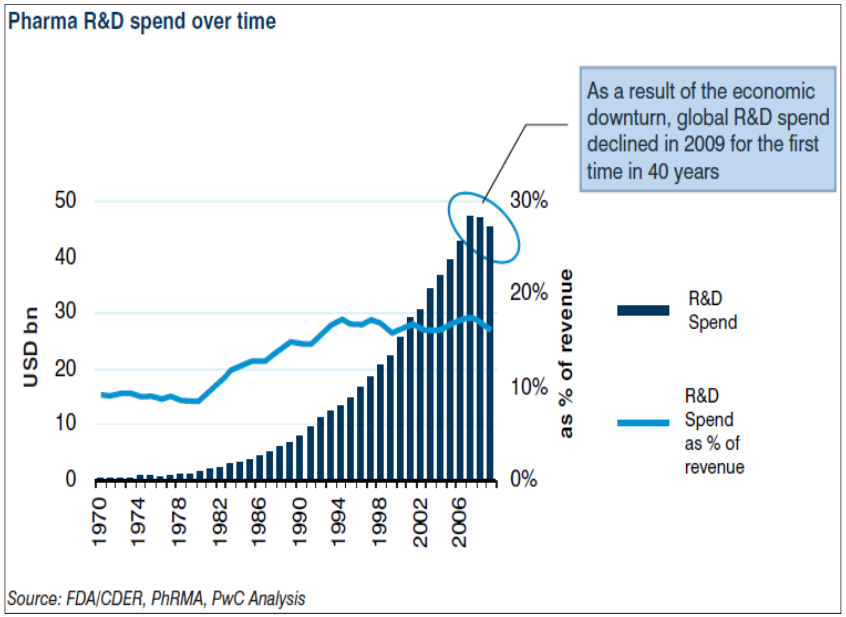
Clinical trials will be highly affected in the coming years

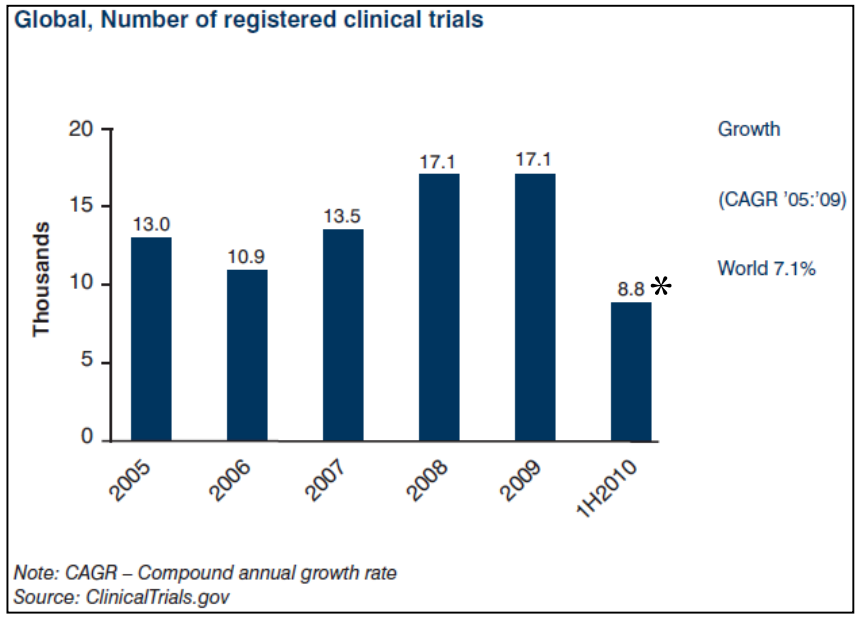
Change drivers	
Pressure on Pharma R&D spend	• R&D spend is directly linked to the **budget allocated to clinical trials**. • R&D spend historically exhibited continuous, long-term growth. However, as from 2009 **R&D productivity declined**.
Increased disease prevalence	• Forecasted trends in disease prevalence and death causes, may indicate **therapeutic areas where demand for drugs**, and thus clinical trials, **will increase**.
Blockbuster patent expiry will reduce clinical trials spending	• The leading pharmaceutical companies will be exposed to **revenue declines** as a result of patent expiries. This will likely have an **impact on new clinical trial launches**.
Patient empowerment will increase	• Patients and patient groups will have **more influence** on recruiting, protocol and **information sharing** through a networked community. • **Ethical pressures** will continue to increase.
Treatment personalization & Pay for performance	• Personalization of treatment requires **specific clinical trial design**. • **Life licensing**: cumulative testing and release of the drug throughout its lifecycle. • **Outcome focussed** clinical trial designs.

Source: Clinical trials – key challenges, November 2010, PwC

Trends in clinical trials globally

Global Pharma R&D spend declined in 2009 for the first time, while the number of registered clinical trials remained stable





* For 2010, data until the end of June 2010 are included.

Source: Federal Trade Commission, PwC analysis

Trends in clinical trials globally

The leading pharmaceutical companies see between 14% and 41% of their existing revenues impacted by patent expiries

Company	2010		2011		2012		Share of Revenues (%)
AstraZeneca	Arimidex	($2.2bn)*	Seroquel	($4.7bn)	Symbicort	($3.7bn)	38**
BMS			US Plavix Avapro	($4.8bn) ($1.3bn)	Abilify	($2.1bn)	30
GSK	Advair	($3.8bn)			Avandia	($2.5bn)	23
Eli Lilly			Zyprexa	($4.8bn)			22
Merck	Cozaar/Hyzaar	($3.2bn)			Singulair	($4.5bn)	22
Novartis	Femara	($1.1bn)			Diovan	($6.0)	14
Pfizer	Aricept	($800m)	Lipitor Xalatan	($12.1bn) ($1.6bn)	Viagra Detrol Geodon	($1.7bn) ($860m) ($1.1bn)	41
sanofi-aventis	Taxotere	($2bn)	US plavix Avapro	($3.8bn) ($2.1bn)	Lovenox	($3.1bn)	34

- Revenue pressure will most likely result in **cost-cutting initiatives** and clinical research expenditure might be negatively impacted.
- Additionally, as the innovative pharmaceutical market consolidation progresses, small R&D oriented companies are acquired by larger players. As a result, **pressure for efficiency and searching for synergies may decrease the overall net R&D spend**.
- However, this might be favourable for low cost CROs, which could benefit from increased outsourcing of clinical research activities – as outsourcing is believed to provide more cost flexibility.

*Estimate of global sales in 12 months prior to patent signing;
**Value of products losing patent protection as a percentage of total company sales over next five years

Source: PwC Analysis, AXA Framlington

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Status and evolution of clinical trials in Belgium

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Status and evolution of clinical trials in Belgium

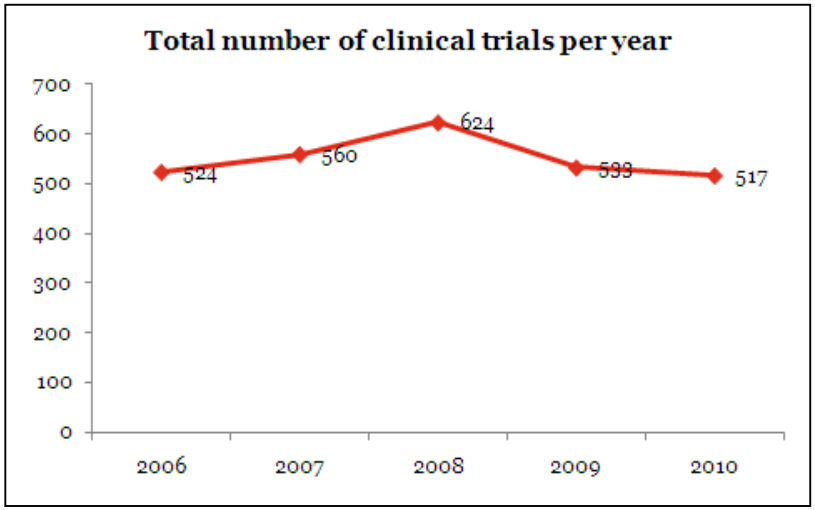
The purpose of this study is to understand if Belgium can maintain its unique position in the clinical trials market

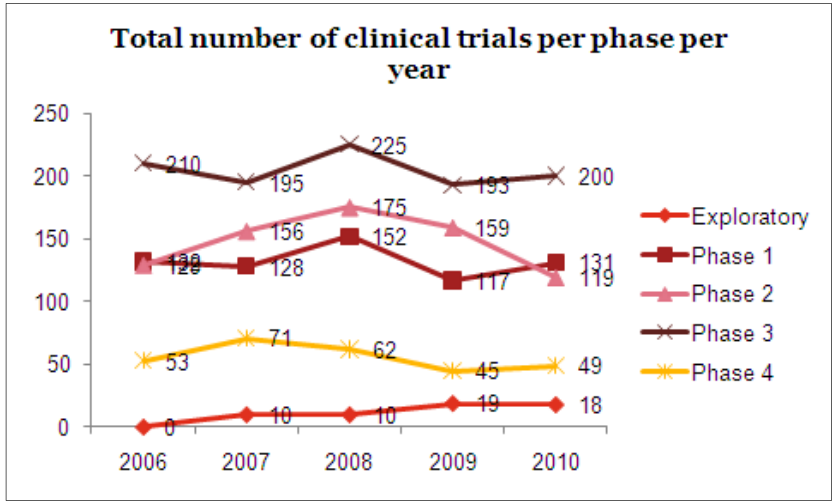
- **Study requested by:**
  - "The initiative to promote clinical trials in Belgium" (www.theinitiative.be)

- **Study goals and scope:**
  - **Understand the market forces** impacting clinical trials
  - Understand **how Belgium performs** in terms of clinical trials and if it is **capable of upholding its unique position** of the last years
  - **Formulate policy recommendations** allowing to strengthen the Belgian clinical trials position where necessary
  - Study time frame: **Jan 2006- Dec 2010**
- **Basis of this study:**
  - CTA FAGG-database
  - Pharma.be input
  - PwC clinical trial reports

Status and evolution of clinical trials in Belgium

In 2009 there is an overall decrease in number of clinical trials, as from 2010 this trend stagnates





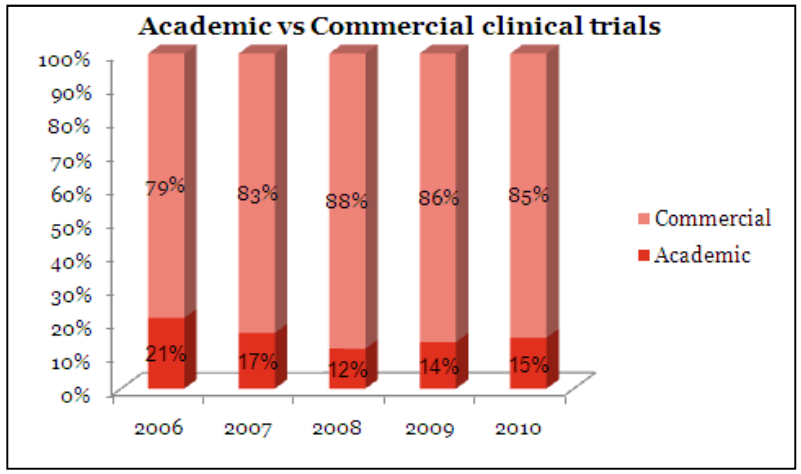
- The number of clinical trials has decreased with 15% in 2009
- There is stagnation in 2010

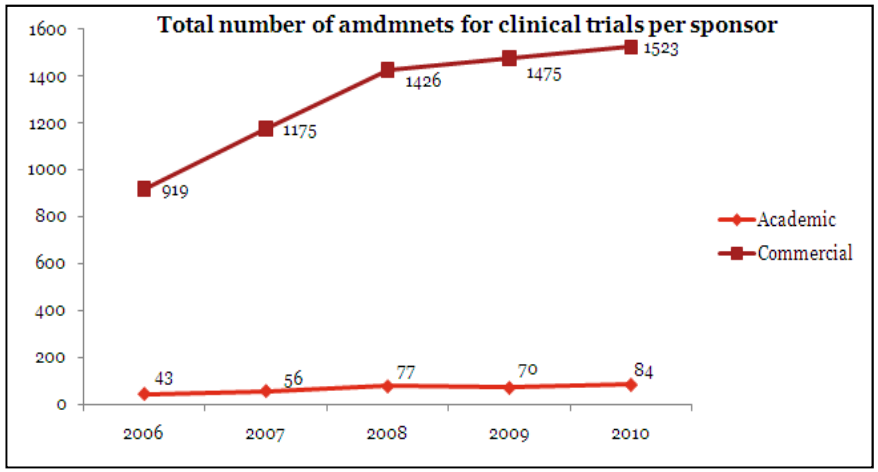
- In 2010, there is a decline in Phase 2 clinical trials (- 25%), but more adaptive trials are applied (Phase 1 & 2 combined)
- Phase 3 stagnates, which is in contrast with the global trend

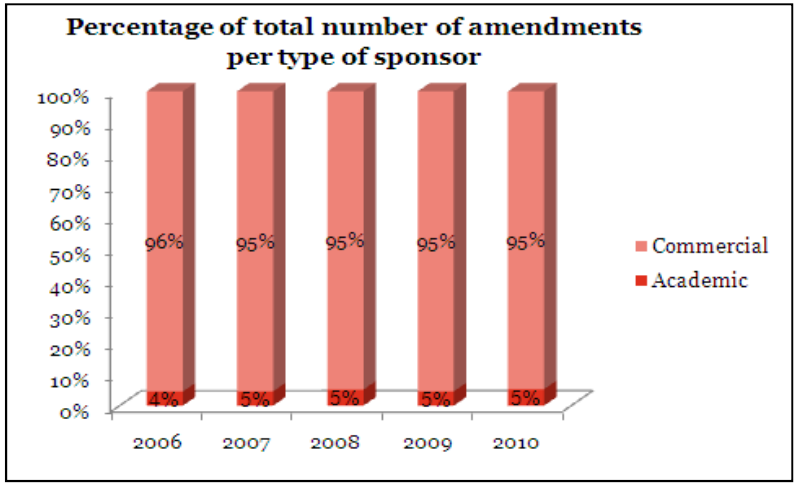
Source: CTA FAGG-database

Status and evolution of clinical trials in Belgium

Although the total number of clinical trials is decreasing, the total number of amendments is increasing





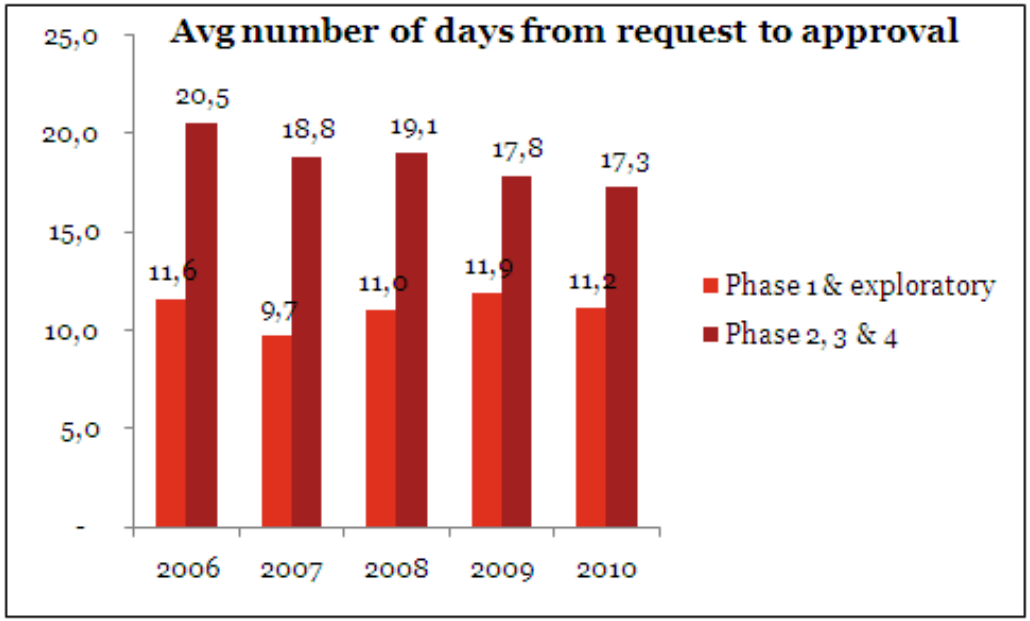


- **Belgium with 15% academic trials is below EU average of 22%.**
- For academic as well as commercial clinical trials, the **number of amendments is increasing**: increase of approx. 7% in the total number of amendments per clinical trial for the period 2009-2010.
- Although the **commercial trials** represent approx. 85% of the total number of clinical trials, they **account for approx. 95% of the total number of amendments.**
- The increase in total number of amendments might **become difficult to manage**.

Source: CTA FAGG-database

Status and evolution of clinical trials in Belgium

Competent authority approval times for Phase 2, 3 & 4 trials continue to decrease, for Phase 1 they remain roughly stable



- The officially stated approval times are:
  - Phase 1: 15 days
  - Phase 2, 3 & 4: 28 days
- The FAGG approval time corresponds to complete file submission until the final approval of the dossier. The time for providing additional information in order to complete the dossier and the time to respond to objections ("clock-stop period"), has been excluded from this calculation.

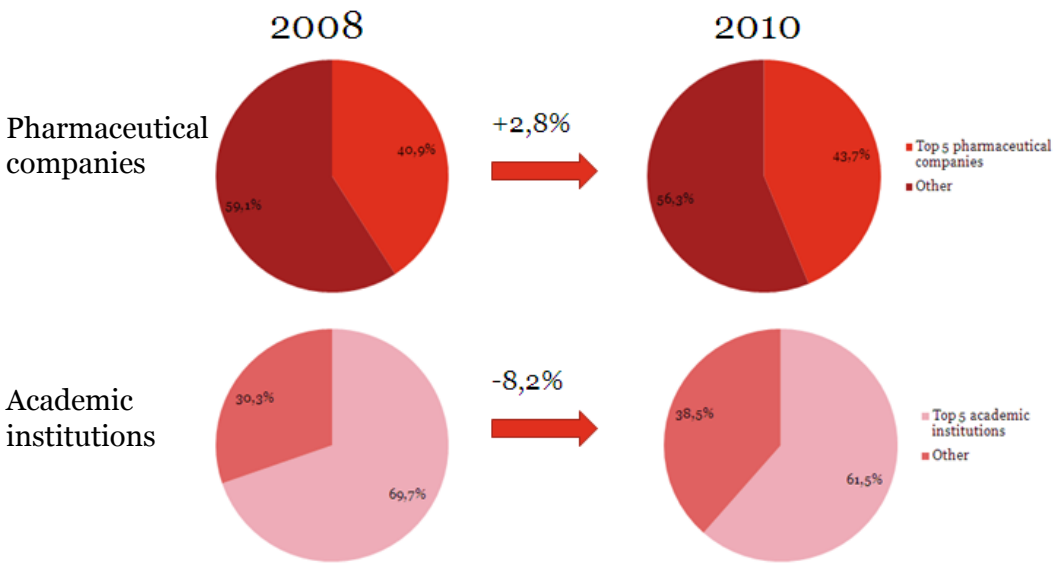
The **approval times are respected** for all phases.

Source: CTA FAGG-database

Status and evolution of clinical trials in Belgium

For the top 5 pharmaceutical companies, there is a slow trend towards concentration, while for the top 5 academic institutions, de-concentration is noticed

Evolution in the top 5 pharmaceutical companies and top 5 academic institutions

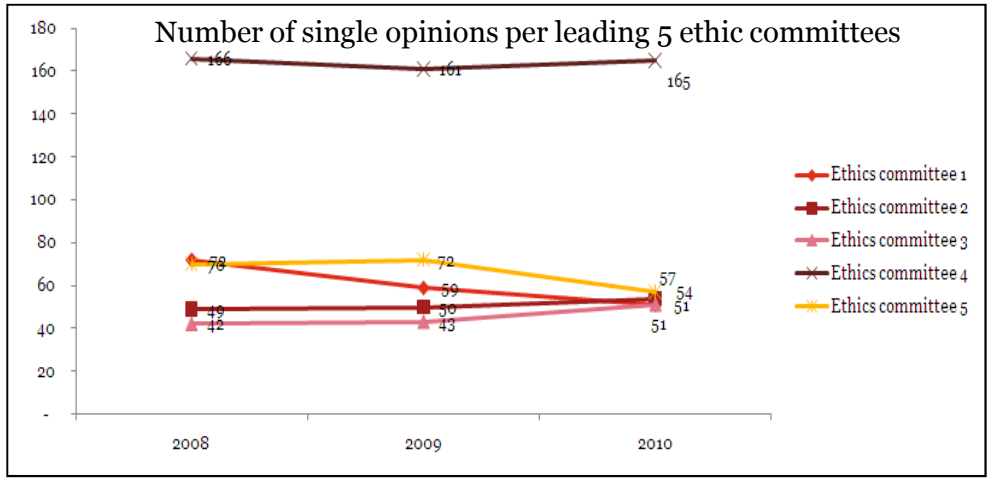


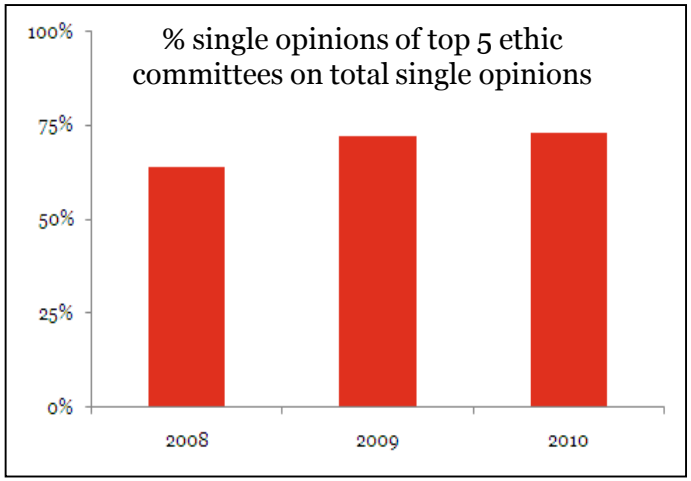
- In 2010, **The top 5 pharmaceutical companies account for** 43,7.9% of initiated industry trials, which is an **increase of 2,8%.**
- In 2010, the **top 5 academic institutions account for** 61,5% of initiated academic trials, which is a **decrease of 8,2%.**

Source: CTA FAGG-database

Status and evolution of clinical trials in Belgium

73% of the studies are evaluated by the top 5 ethic committees





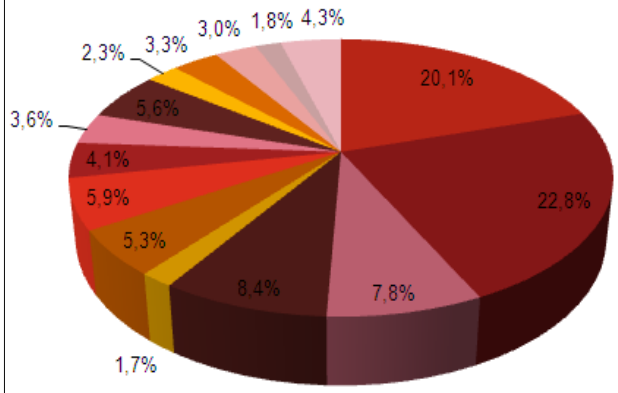
- In 2010, 73% of the studies are evaluated by the top 5 ethic committees
- Certain ethic committees are polyvalent, while others are more specialised (e.g. in phase 1)

Source: CTA FAGG-database

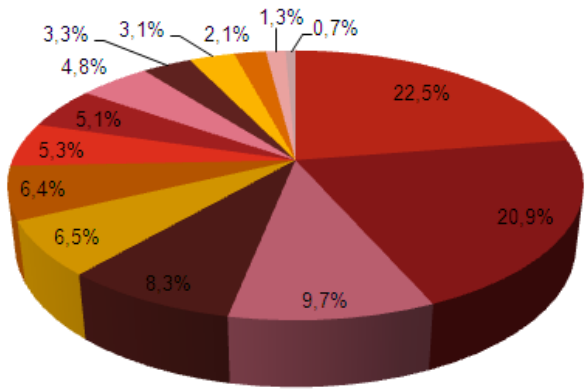
Status and evolution of clinical trials in Belgium

The spread of clinical trials over the different therapeutic areas remains stable

Clinical trials per therapeutic domain **2008**



Clinical trials per therapeutic domain **2010**



*

- Phase 1 (all therapeutic domains)
- Antineoplastic & immunomodulating
- Alimentary tract and metabolism
- Nervous system
- Vaccine
- Blood and blood forming organs
- Cardiovascular
- Anti-infectives
- Musculo-skeletal
- Respiratory
- Genito urinary
- Various
- Sensory organs
- Dermatologicals
- Other

Phase 2, 3 & 4

* Phase I research (all therapeutic domains) is reported separately due to the specificity and importance

There is no significant shift in the spread of clinical trials over the different therapeutic domains

Source: CTA FAGG-database

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Belgium's clinical trial situation within Europe

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Belgium's clinical trial situation within Europe

Clinical trials in Europe are threatened by Emerging Countries and the US

- US
  - The **gap on R&D spending between US & EU is getting wider**:

	2005		2008	
	US	EU	US	EU
R&D spending (million)	30,969 $	21,949 €	38,428 $	27,200 €

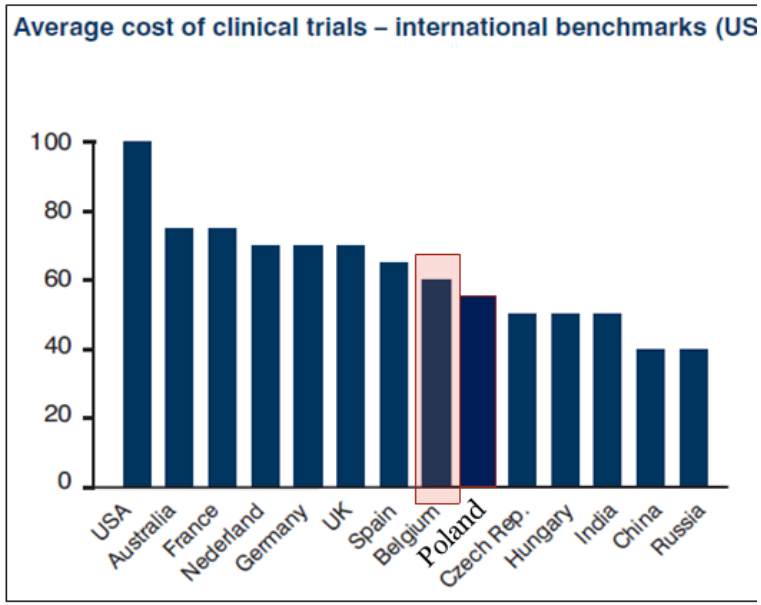
- Emerging Countries
  - Emerging countries are **attracting a growing number of large-scale clinical trials** as they have access to large patient populations required to run these trials.
  - The **costs** of running clinical trials **is lower**.
  - **The shift to the "rest of the world"** has increased markedly in recent years and the trend looks set to continue, ultimately leading to a drop in clinical research activities in EU and US.

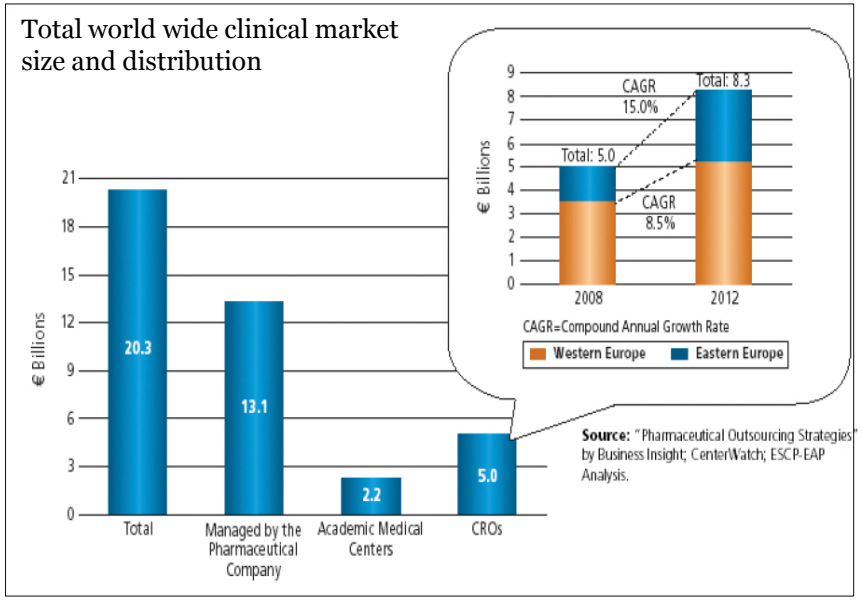
Source: pharma.be

Belgium's clinical trial situation within Europe

Overall, Belgium is scoring well on the average cost of clinical trials, but there is a threat from the Eastern countries

Based on a PwC analysis performed in 2010, **Belgium is scoring well compared to the other EU countries & US**, but the **cost to perform clinical trials is still 10% more compared to Poland and more than 20% compared to China & Russia**.
As a consequence, it can be expected that **by 2012, the clinical trial market for CRO's will increase** by 15% for Eastern Europe, compared to only 8,5% for Western Europe.

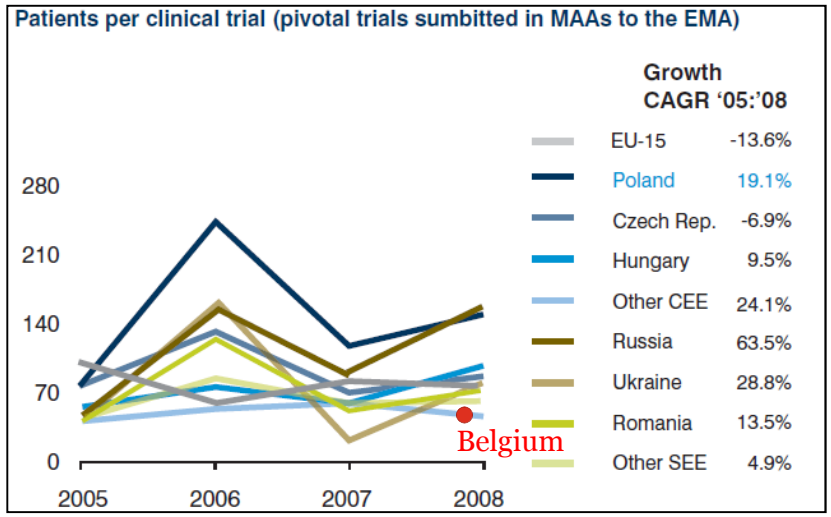


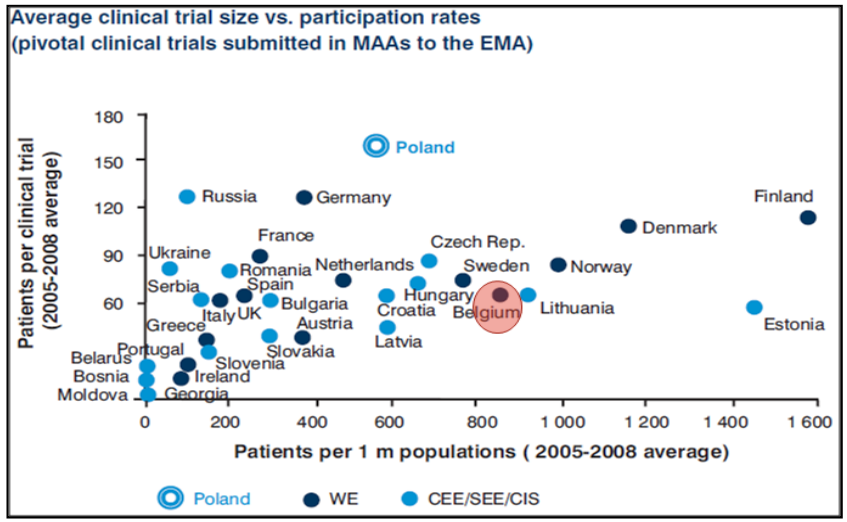


Source: PwC analysis, November 2010
Source: "Pharmaceutical Outsourcing Strategies" by Business Insight; ESCP-EAP Analysis, 2008

Belgium's clinical trial situation within Europe

Belgium is one of the countries with the highest participation rate for clinical trials in Europe





When comparing the **number of patients participating in clinical trials, Belgium ranks lower** (with an average of 54 patients), due to its relatively limited patient population.

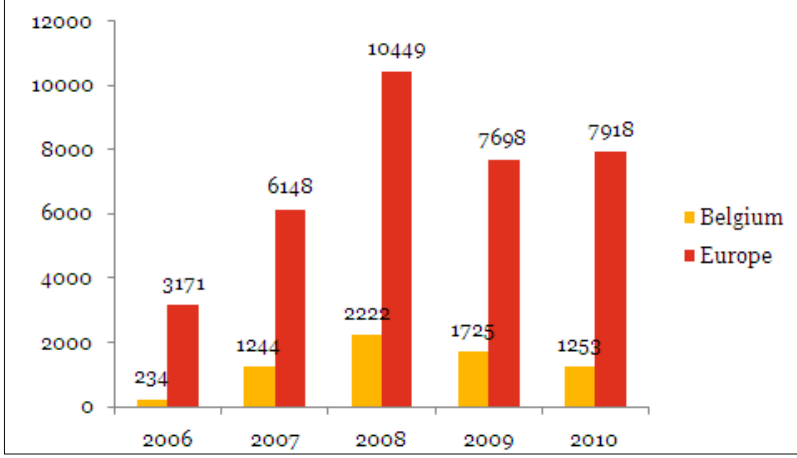
However, when these figures are expressed **in per capita terms, Belgium emerges as one of the countries with the highest participation rate** in Europe.

Source: EMA

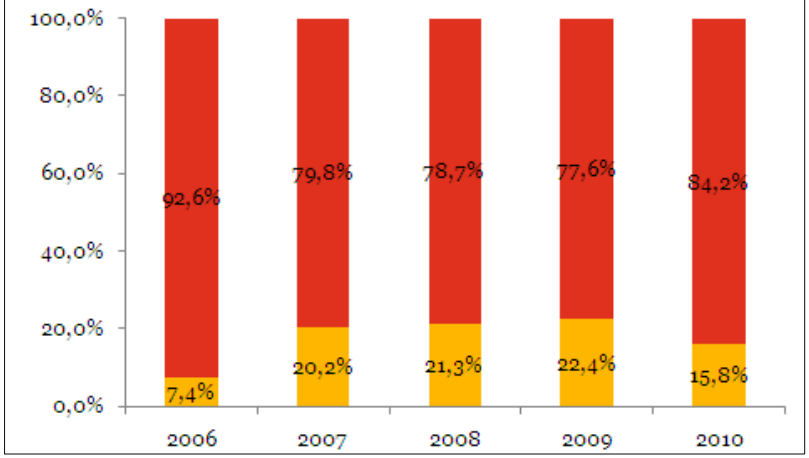
Belgium's clinical trial situation within Europe

For Belgium the total number of planned children & teens participating in clinical trials is declining, while on European level, an upward trend is noticed

Number of planned children & teens participating in clinical trials



Spread of the number of planned children & teens participating in clinical trials between Belgium & EU



- Over the last 2 years, the total number of planned children & teens participating in clinical trials **has decreased by approx. 44% in Belgium.**
- After a drop in the number of planned children & teens participating in clinical trials in 2009, an **upward trend** can be noticed for the year 2010 **on European level**.
- On European level, the participation rate of Belgian children & teens in clinical trials has been decreasing as from 2010.

Source: CTA FAGG-database

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Conclusions and recommendations

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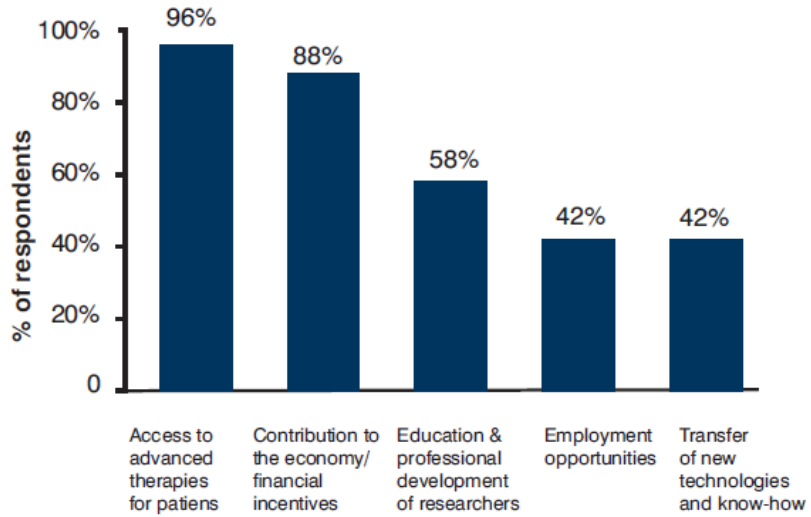
Conclusions and recommendations

The economic impact of clinical trials

- Clinical trials imply a number of **tangible and intangible benefits** to the host economy
- Clinical research market **impacts a number of stakeholders** and many of them benefit from clinical trials as an **additional source of cash flow**
- More than one-fourth of revenue earned on clinical trials by sponsors ends up as a directly paid **tax contribution to the state budget**
- Clinical trials can **provide early access to innovative treatments**

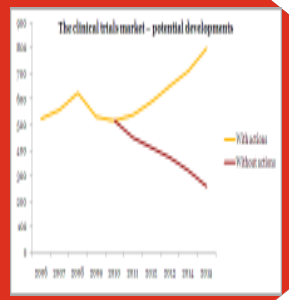


Source: Clinical trials – key challenges, November 2010, PwC

Conclusions and recommendations

Focusing on transparency, structure, cooperation and communication can keep Belgium on the map

- In 2009 there is an overall decrease in number of clinical trials, as from 2010 this trend stagnates.
- The total number of amendments is increasing
- On European level, the participation rate of Belgian children & teens in clinical trials is decreasing
- Belgium is scoring well on the average cost of clinical trials, but there is a threat from the Eastern countries



- Clinical development needs to become more flexible and will require a structure that is more "agile"
- Good communication practices and transparency to patients and health care providers (e.g. information sharing, transparency, developing awareness and positive attitude of general public)
- One-stop-shop idea
- Creating a link between different key-databases (e.g. database of health technology assessment bodies)
- Creating a framework to determine a standard cost for clinical trials

Turning around the market decline and maximizing the potential benefits to the economy is possible providing that a flexible framework is provided, transparency is enhanced, a responsive structure is implemented and that cooperation & communication are encouraged.

Conclusions and recommendations

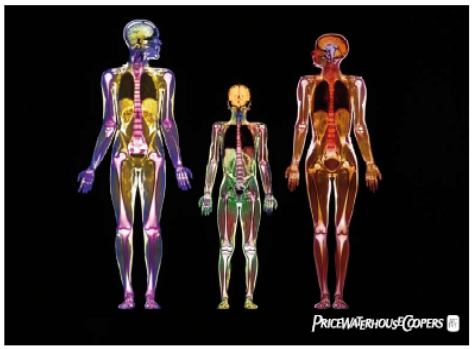
In the light of these market forces, research organizations / companies will need to focus on shorter drug development paths, process efficiency and higher trial flexibility

Change drivers
Pressure on Pharma R&D spend
Increased disease prevalence
Blockbuster patent expiry will reduce clinical trials spending
Patient empowerment will increase
Treatment personalization & Pay for performance

Companies need to focus on strategies that:	
Shorter and more focussed drug development paths (less trial & error)	• The future drug development process is expected to be more refined, as more emphasis will be put on fundamental research (translational research).
Increased focus on process efficiency	• Sponsors seek for increased operational (and cost) efficiency, primarily by outsourcing trials to CROs and considering new locations for research projects.
Higher development flexibility	• Personalized drugs and shorter development paths as well as focus on efficiency will result in requirements for higher trial flexibility. • Adaptive trials and smaller trials with higher complexity will be managed, but recruiting patients that correspond to all criteria and timings will become more challenging. • Life licensing: step-wise approvals.

Source: Clinical trials – key challenges, November 2010, PwC

More info can be found in our reports or on our website



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