

# Country Profile

A look at the  
Pharmaceutical Industry in

## BELGIUM



Produced in collaboration  
with ISPE Belgium



THE SOCIETY FOR  
LIFE SCIENCE PROFESSIONALS



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Dear ISPE Member,

In the following pages, we have tried to give you a view of the pharmaceutical industry in Belgium, located in the center of Europe and maybe not familiar to each of you. This privileged location, where two different ancient cultures melt and where in educational programs multi-lingualism is strongly promoted as a must, evolves a highly export oriented economy. Around 75% of GNP are exported, mainly within the inner European market, but also an important part into the rest of the world.

A model social welfare system secures a high standard of living with access to all modern pharmaceutical drugs and medical techniques for the whole population.

Educational excellence, ethical management, a stable social environment and a high manpower efficiency on the workforce guarantee a positive climate for new investments in high tech business.

Fundamental research for new pharmaceutical molecules in a close collaboration between different renowned universities or partnership with spin-offs and major pharmaceutical companies creates a well developed operation in the country, in the pharmaceutical as well as in the biological industry.

In this environment, ISPE Belgium was created in 1992 as an Affiliate of the International Society for Pharmaceutical Engineering.

The present committee is staffed with representatives from all major pharmaceutical companies that are active in the country as with members from global engineering contractors and major equipment suppliers.

Through the organization of diversified training seminars, the ISPE Belgium Affiliate grew over the years to a well recognized association with almost 500 Life Science professionals being permanent members.

In line with the strategic objectives of ISPE, the Belgium Affiliate committee continues to organize and provide training in the different disciplines of the Life Science fields in order to make sure that highly educated professionals are available to the industry.

Further information and details on this can be found visiting our Web site at [www.ispe.org/Belgium](http://www.ispe.org/Belgium).

Yours truly,

**Jef De Clercq**  
President, ISPE Belgium

**This new feature in *Pharmaceutical Engineering* is designed so that you can tear it out, three hole drill (if desired), and keep it with other Country Profiles as they are published.**

**Look for the Country Profile on Australia in the November/ December issue of *Pharmaceutical Engineering*.**

# A Look at the Pharmaceutical Industry in Belgium

*"A strong healthcare system, outstanding university hospitals, and a solid scientific and operational knowledge are the Belgian strengths that create a stimulating environment for the pharmaceutical industry."*

## Thriving Sector/ Stimulating Environment

**B**elgium, may be a tiny spot on the world map, but it is globally renown for many things, including its historic cities like Bruges and Ghent; its many varieties of beer and delicious chocolates; for its art nouveau, started by Victor Horta and Henri van de Velde; and for its many famous artists like the Van Eycks, Rubens, and Ensor. Belgium is a country that boasts more history, art, food, and architecture per square centimeter than most of its bigger neighbors. It also boasts a long tradition in healthcare and medical science, witnessed by the fact that there are no less than 150 pharmaceutical companies active in Belgium. And, they're not just small ones. All of the top worldwide players are present, but not merely as a lone sales organization, an R&D department, a manufacturing site, or even a logistics center. They are here with everything they've got. And they are here to stay since they are continuously investing in their Belgian branches, particularly when it comes to research.

Brussels is the lively capital of Belgium. It houses both the European Union and NATO headquarters. With its population of 980,000 added to the many contiguous communities, greater Brussels has a total population of more than one million. With its many nationalities, it is truly at the heart of Europe.

One area where Belgium has been often featured in international headlines is with its Nobel Prize win-

ners, especially in medicine. The latter shouldn't come as a big surprise since this tiny country of some 30,000 sq km and 10.2 million inhabitants, houses no less than 13 major universities.

"Belgium is attractive on many fronts," explains Prof. Dr. Leo Neels, Managing Director of pharma.be, a non-profit society that represents the pharmaceutical industry located in Belgium. "First, there is a general and political impetus for research in Belgium. This has the effect of creating many stimulating projects. Second, academic level and standard of science is very high. Third, the pharmaceutical industry itself is very dynamic in Belgium. The industry has created a very favorable microclimate for research, working closely with university labs of very high standing qualitatively and continuously funding fundamental research."

## Continuous Flow of Investments

There has been a general trend of more and more pharmaceutical companies moving their research to the US, and this has been reinforced by numerous mergers in recent years. "Remarkably, this has had very little effect in Belgium," notes Neels. Research activities in Belgium are still growing. From 1990 to 2001, expenditures in R&D have risen from 183.3 million Euro to 1.18 billion Euro. That is more than a sixfold increase. In 2001, more than 3,150 people were working in R&D. This is approximately 13% of the total workforce in the Belgian pharmaceutical industry. Major companies carrying out very successful research in Belgium include GlaxoSmithKline, Janssen Pharmaceutica, UCB Pharma, and Eli Lilly.

Herman Van Eeckhout, Director at pharma.be adds: "One of the research fields that has shown particularly strong growth in recent years is clinical research. More than 5,000 people work in clinical testing. We are even performing tests on molecules that were developed in the US. Again, this

### Cat. A - Life-saving drugs: cancer drugs, insulin, etc.

100% of the reimbursement base.

### Cat. B - Medicines for treatment of non life-threatening diseases

Ordinary insured parties: 75% of the reimbursement base (maximum of 9.79 Euro)

Insured party with preferential tariff: 85% of the reimbursement base (maximum of 6.57 Euro)

### Cat. C, Cs - Medicines that promote well-being and Cx

Cat. C Ordinary insured parties: 50% of the reimbursable base (maximum of 16.24 Euro)

Insured parties with preferential tariff: 50% of the reimbursable base (maximum of 9.79 Euro)

Cat. Cs 40% of the reimbursable base (no maximum)

Cat. Cx 20% of the reimbursable base (no maximum)

Table A. Reimbursement policy. The Belgian social security system makes healthcare available to all.



## A Look at the Pharmaceutical Industry in Belgium

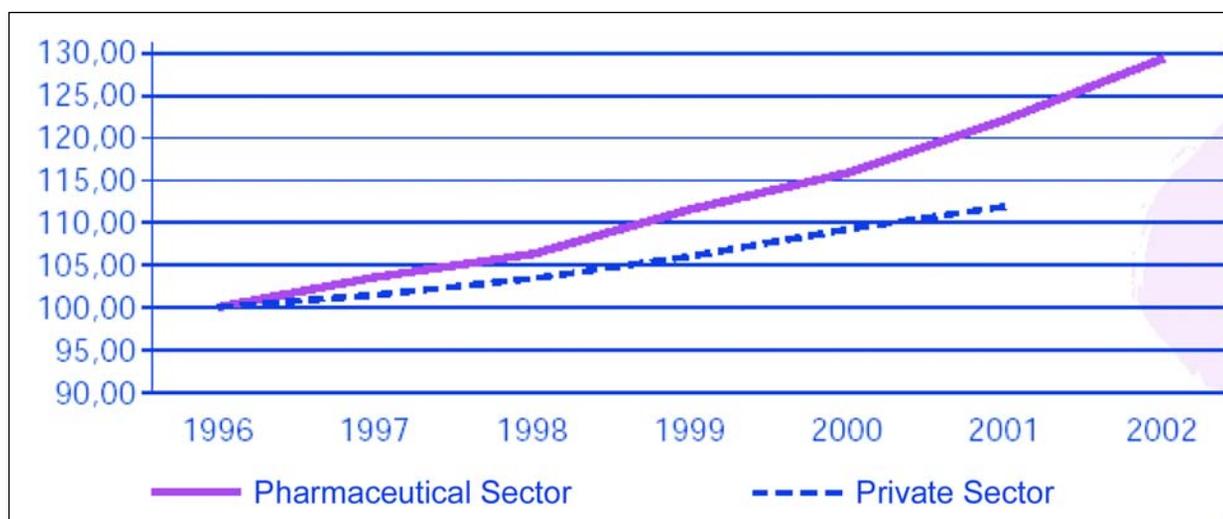


Figure 1. Evolution of the employment rate in the pharmaceutical industry compared to the private sector. The employment level of the pharmaceutical sector is growing significantly faster than the rest of the private sector.

is thanks to not only our high education level and the quality of our scientists, but also to the close interaction between research labs and medical faculties.”

In recent years, there also have been considerable investments in Belgian manufacturing sites. These include, among others, Pharmacia, UCB Pharma, Schering-Plough, and Alcon. Thanks to these investments and others like them, employment has grown steadily. Many companies are growing at the rate of more than a hundred new employees per year.

### Faster Access to Innovative Medicines

Like many European countries, Belgium has a reputation for bureaucracy, slow administration, and everlasting procedures. But this has improved somewhat over

the last few years, asserts Neels. “Remarkable improvements have been made. But let there be no misunderstanding about it. We still have a lot of work to do in that department. We need to continuously remind the government of the importance of research stimulating projects, the need for fast regulation procedures, and a stable and attractive, economic marketplace.

“One important example of progress in this area is the procedure for pricing and reimbursement. This used to take more than 500 days, while the maximum European term is 180 days. Over the last two years, this 180-day target is generally being met. And, this while we continue to foster a consultation climate where the participation of all stakeholders is encouraged. Securing the 180-day limit is an extremely important achieve-

	Million Euros / US\$			
	1999	2000	2001	2002
1. The internal market - Sales of medicines for human use via pharmacies open to the public and via hospital pharmacies, at ex-factory price, exclusive of VAT	2,576.3	2,666.7	2,849.6	3,036.6
2. External trade				
a) Exports: sales of raw materials and medicines at ex-factory price.	6,046.1	7,419.8	10,450.6	23,345.4
b) Imports: acquisition of raw materials and medicines at purchase price.	4,718.0	6,072.0	9,327.1	23,865.0
c) Trade balance: a) - b)	1,328.1	1,347.8	1,123.5	-519.6
3. Employment Number of people employed	21,851	22,732	24,201	25,408
4. Investments	295.7	318.5	380.7	453.2
5. R&D	737.9	762.2	1,178.8	1,279.5

Table B. Basic figures for the Belgian pharmaceutical sector. The pharmaceutical industry is clearly one of the driving forces behind the Belgian economy.

## A Look at the Pharmaceutical Industry in Belgium

1	GLAXOSMITHKLINE	(= no 2 worldwide)	8.33%
2	ASTRAZENECA	(= no 4 worldwide)	7.05%
3	PFIZER	(= no 1 worldwide)	6.42%
4	JANSSEN-CILAG	(= no 7 worldwide)	5.44%
5	AVENTIS PHARMA		4.78%
6	AHP PHARMA		4.67%
7	NOVARTIS PHARMA		4.57%
8	SANOFI-SYNTHELABO		4.57%
9	BRISTOL-MYERS SQUIBB BELGIUM		3.72%
10	ROCHE		3.60%
11	MERCK SHARP & DOHME		3.21%
12	PHARMACIA		2.94%
13	BAXTER		2.93%
14	ABBOTT		2.15%
15	ELI LILLY BENELUX		1.96%

Table C. Top 15 pharmaceutical companies in the Belgian market; Companies/Groups in market share in % of the total pharmaceutical market in Belgium. Most top pharmaceutical companies are active in Belgium. Some of them are still controlled by Belgian capital: UCB Pharma (24), Solvay Pharma (28), and Therabel (18).

ment as innovative medicines can be put on the market much faster, often within a year! Again, this makes Belgium more competitive.”

### Expertise in Manufacturing and Supply Chain Management

When looking at the basic figures outlining the pharmaceutical sector in Belgium (Table B), it's striking that there is a great deal of importing and exporting for such a small country. Herman Van Eeckhout explains this trend: “Belgium has quite an extensive expertise and know-how when it comes to manufacturing and supply chain management. Indeed, we see that many companies have extensive manufacturing sites and distribution facilities in Belgium. Moreover, all major companies must comply with stringent national and international regulations. This means that we can export to virtually every country in the world. In 2002, our export figures grew to more than 23 billion Euro.”

Another definite plus is the fact that the Belgian government has stimulated the distribution sector with fiscal incentives. We've become kind of a tax shelter. This has definitely worked for the benefit of the pharmaceutical sector. We see that several companies import products into Belgium from their production sites all over Europe. They then export these to the rest of the world.” This has led to an exponential growth of 123.39% in exports and 155.93% in imports between 2001 and 2002.

*“There's a strong political awareness of the importance of the pharmaceutical sector, and more importantly, of its research activities.”*

### Employment Rises Faster Than Average

By mid-2002, 25,408 people were working in the pharmaceutical industry in Belgium. Belgium's top 10 pharmaceutical companies in 2001 are listed in Table G. Over the past six years, it can be clearly seen that

### Holistic View on Healthcare

Currently, there is a far reaching project in Belgium to develop a long-term vision of healthcare and related costs. The Added Value Project is an initiative of the LIM, an umbrella organization of research-oriented pharmaceutical companies in Belgium. This renowned medical industry think tank has created a model methodology under the direction of Professor Jan Peers and Deloitte and Touche.

According to Neels, “the thesis is that an innovative medicine or surgery technique can have positive effects on the complete healthcare system including shorter treatments, less surgical intervention, shorter hospitalization times, less absenteeism, etc. So instead of concentrating so much on the cost of a medicine, the government also should take into account the overall healthcare and other social costs that can be saved. Figures show that in countries where the relative share of the cost of medicines in the total healthcare budget is larger, the total healthcare budget is significantly lower. Absenteeism is several times lower and the hospitalizations are less intense and shorter. The Added Value Project takes all this into account. It will help to bring new, innovative medicines, and techniques to patients faster.”

Clearly, this project could be the starting point in a different and better way of looking at healthcare and related costs. Currently, all involved parties are evaluating the model. Now the government needs to be convinced that this is a sound basis for a new policy instrument.

## A Look at the Pharmaceutical Industry in Belgium



Medicines registered for human or veterinarian use <sup>1</sup>	12,354
Medicines registered for human use <sup>1</sup>	11,200
Medicines registered for human use available on the market <sup>2</sup>	5,490
Presentation of registered medicines for human use available on the market (presentations for the public and hospitals and liquid perfusions <sup>2</sup> )	6,502
Portion of the latter that is reimbursable <sup>2</sup>	3,677
Individual medicines for human use available on the market <sup>2</sup>	2,746
Registered active substances used in medicines for human use, available or not <sup>1</sup>	2,292
<sup>1</sup> Source: Ministry for Public Health	
<sup>2</sup> Source: AGIM	

Table D. Registered medicines in Belgium.

	Euros / US\$
<b>1. Costs to the state<sup>2</sup></b>	<b>1,769.4</b>
1.1. INAMI expenditure	1,762.5
1.1.1. Expenditure exclusive of VAT (industry share)	1,662.7
1.1.2. VAT (industry share)	99.8
1.2. Subsidies	6.9
<b>2. State revenue<sup>3</sup></b>	<b>1,789.0</b>
2.1. Taxes on wages	765.0
2.1.1. Employers' social security contributions	320.5
2.1.2. Employees' social security contributions	128.7
2.1.3. Personal income tax deducted at source (from third parties)	315.9
2.2. Corporate taxation	245.3
2.3. Other taxes, deductions and charges	304.8
2.3.1. VAT on turnover (company price) <sup>4</sup>	160.0
2.3.2. Taxes on turnover and charges (INAMI)	126.4
2.3.3. Other taxes on operations <sup>5</sup>	5.0
2.3.4. Movable property income tax deducted at source (from third parties)	13.5
2.4. Indirect revenue from purchases from third parties and investments <sup>6</sup>	473.9
2.4.1. Raw materials and merchandise, miscellaneous goods and services <sup>7</sup>	39.1
2.4.2. Investments	39.1
<b>3. Results (2-1)</b>	<b>19.6</b>

<sup>1</sup> These costs and revenue are limited to companies marketing mainly medicines for human use. Companies involved in the marketing of human medicines and carrying out activities in the area of veterinarian medicines and/or *in vitro* diagnostics as well, were also included in this analysis.

<sup>2</sup> Sources: INAMI, Banque nationale de Belgique (centrale des bilans - annual company accounts); calculations by AGIM.

<sup>3</sup> Sources: Banque nationale de Belgique (centrale des bilans - annual company accounts); ICN: external trade and added value statistics, Ministry for Economic Affairs, INS (statistics on sales and turnover), Fedichem (investments); calculations by AGIM.

<sup>4</sup> VAT calculated on basis of ex-factory price (Ministry for Economic Affairs).

<sup>5</sup> AGIM estimates that these other taxes on operations, exclusive of Inami taxes on the turnover of pharmaceutical companies, amount to a lump sum of around 5 million Euros.

<sup>6</sup> State revenue from purchases and investments was estimated bearing in mind two parameters: the manufacturing industry's share of value-added in the manufacturing industry's turnover and, secondly, the share of total state revenue in the GDP.

<sup>7</sup> The estimate of state revenue from raw materials and merchandise does not include purchases by companies that are mainly involved in importing nor purchases by companies with solely commercial activities and that are part of a group with a production unit in Belgium.

Table E. The pharmaceutical sector in relation to the state in 2000: costs and revenue (in millions of Euros) Contrary to what many people think, the pharmaceutical industry entails a net income to the government.<sup>2</sup>

the employment level in the pharmaceutical sector is growing faster than the average level in the private sector: 23% versus 11.1% (Figure 1). Looking at the evolution of the employment level according to the activities of companies, it is readily apparent that general growth can be ascribed to companies that perform fundamental research in Belgium and that are active in production and export at the same time. This proves that research is still the driving force behind the sector.

### Unique Healthcare System

In addition to an outstanding academic climate, Belgium also has a unique healthcare system. This has been a big factor in the motivation of students to enter medicine. In 1945, Belgium was already a pioneer in social security, strongly believing in the wisdom of mobilizing all available resources. At the moment, all employed citizens contribute part of their wages to social security. In exchange, large parts of the costs for prescribed medicines (Table A) and visits to the doctor, dentist, hospital, etc. are refunded, making affordable healthcare available to all. This has created a positive environment for the healthcare industry, and yet another reason why Belgium is an attractive country for the pharmaceutical industry.

### Expensive Sector?

In Belgium, the total cost for healthcare is constantly under scrutiny. Some feel that the financial pressure on the social security system is due to the fact that the cost of medicines is refunded. Others think that the cost of those medicines is much too high. Some populists are calling on the pharmaceutical industry to make

## A Look at the Pharmaceutical Industry in Belgium

*“All top players have a strong presence here. To name just few: GlaxoSmithKline, Pfizer, AstraZeneca, Pharmacia, and Johnson & Johnson.”*

greater efforts to keep prices down. However, many of these individuals fail to take the realities of the modern pharmaceutical industry into account. It is clear that research has become extremely expensive. The average cost to develop a new drug is 895 million Euro. Only 30% of these are likely to be a commercial success. The survival of companies depends upon a sound pricing policy.

The figures clearly demonstrate that the pharmaceutical industry is not a cost for society. Of course, there are the large sums spent by the Riziv - INAMI, the Belgian institute for health and disability insurance and various other subsidies. But these are, for the most part, covered by deductions from the wages, taxes on company profits, and indirect income due to investments and purchases at third parties. If you look at this total picture objectively, it is clear that the pharmaceutical industry is a profit for the government rather than a cost - *Table E*.

Dr. Neels adds, “it is clear that we need to keep stimulating this sector to keep it investing in Belgian branches and invest in research. This will definitely be in the best interest of our country. The only rational way to accomplish this is to convince the government to initiate stimulating measures. We welcome the plans of our new government to lighten the tax load of

companies with highly educated employees.” This is very important, as one top scientist, for example, leads directly to 10 jobs and indirectly to another 60 within a company.

“We also need to keep working on our registration procedures. The shorter they are, the faster companies can start recovering the costs of their research investments. If we add this to our natural strengths – a high academic level, strong language skills, and good flexibility - we are convinced that Belgium will remain an attractive country for the pharmaceutical industry.”

*Note: Source for all the figures in this article is [www.pharma.be](http://www.pharma.be).*

Company	Number of employees in Belgium (2001)
Janssen Pharmaceutica	3,677
UCB Pharma	2,172
GSK Biologicals	1,617
Baxter	1,287
Pharmacia	1,231
GSK Bio Manufacturing	732
Alcon Belgium	644
AstraZeneca	540
Schering-Plough Laborat.	421
Innogenetics	406

Table G. Belgium's top 10 pharmaceutical companies by workforce. (Source: Trends Top 30.000, 2003)

Rank	Company	Turnover in 2001 in Euros / US\$
1	GSK Bio Manufacturing, GSK Biologicals and GSK Bio	1,689,469
2	Janssen Pharmaceutica	1,567,928
3	UCB and UCB Pharma	813,806
4	Baxter	747,326
5	AstraZeneca	412,829
6	Pharmacia	273,151
7	Alcon Belgium	169,610
8	Aventis Pharma	163,671
9	Bristol-Myers Squibb	134,269
10	Sanofi-Synthelabo	131,913
11	Schering-Plough Laborat. + Schering	122,843
12	AHP Pharma	109,471
13	Warner-Lambert Belgium	98,148
14	Pfizer AH	81,295
15	Beecham	48,796

Table F. Pharmaceutical companies in Belgium by turnover. (Source: Trends Top 30.000, 2003)





# GSK Biologicals: Vaccines for the World

## Strong Research, Responsible Marketing

The GlaxoSmithKline Biologicals Division is one of the world's largest and most important vaccine manufacturers. Headquartered in Belgium since the end of the 1960s, it has steadily grown to become one of GSK's most dynamic research centers and has been responsible for many decisive discoveries. The company's ambition is nothing less than to cover the vaccination needs of every man, woman, and child. This is particularly true for those living in the developing world, where GSK is taking part in numerous initiatives. GSK Biologicals boasts the sector's most extensive portfolio of vaccines currently in clinical testing.

*"GSK Biologicals introduced the world's first genetically engineered human vaccine."*

### Twenty-Five Vaccines per Second

The worldwide headquarters of GSK's Biologicals Division is at Rixensart, Belgium. It has specialized in the development of vaccines since it was first built in the 1950s. The site successfully produced the first anti-polio vaccine in 1957. That breakthrough and its many other subsequent development programs have contributed greatly to Belgium's worldwide reputation as a center of expertise in the areas of virology, bacteriology, and immunology.

Today, GSK Biologicals is the world's leading vaccine manufac-



Figure 1. Growing sales of hepatitis vaccines and pediatric vaccine combinations drove the increase in turnover at GSK Biologicals in 2002. (Source: 2002 GSK Annual Report)

turer with 25% of the global vaccine market. In 2002, GSK Biologicals distributed more than

800 million doses of vaccines to 156 countries. That represents a phenomenal average of 25 doses



Figure 2. The number of people employed by GSK Biologicals in Belgium has grown by more than 70% over the past decade. (Source: 2002 GSK Annual Report)

## GSK Biologicals: Vaccines for the World

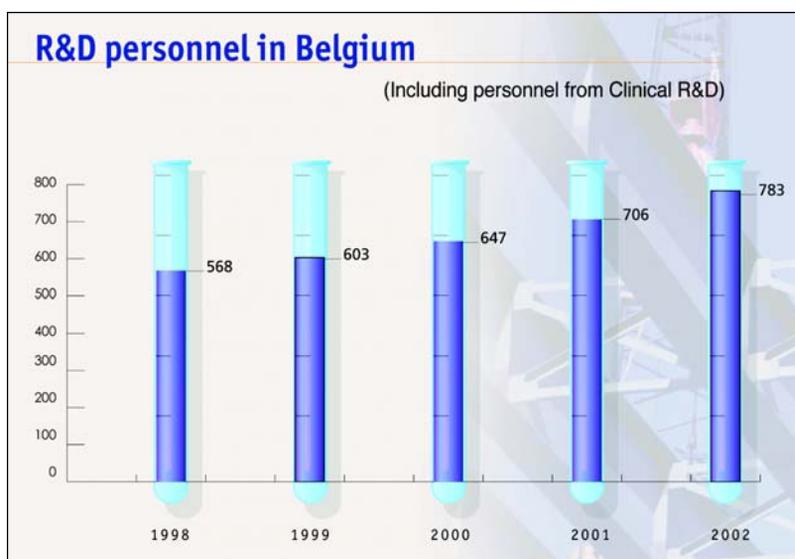


Figure 3. The number of researchers working on the development of new vaccines at GSK Biologicals in Belgium is steadily increasing. (Source: 2002 GSK Annual Report)

per second around the world. The company's best-selling products in 2002 were its *Infranix* pediatric vaccine combination and its *Havrix*, *Engerix-B*, and *Twinrix* hepatitis vaccines - *Figure 1*. GSK Biologicals also markets vaccines against numerous other diseases, including typhoid fever, meningitis, influenza, and salmonella.

### A Growing Team of Experts

The GSK Biologicals workforce has grown continuously over the past decade - *Figure 2*. The company's three Belgian sites are currently hiring one new person a day on average. Some 22% of the current 3,500 members of staff employed by GSK Biologicals in Belgium are dedicated to research and development. And, the number of researchers is increasing year by year - *Figure 3*. "Our R&D teams are involved in every step of the process, from molecular discoveries to the registration of new vaccines," says Jean Stéphenne, President and General Manager of GSK Biologicals. "If

we take into account our clinical tests, quality assurance, and regulatory affairs staff, the number of people employed in R&D exceeds 1,000. Approximately 20% of our turnover is invested in R&D every year. Without question, it is the beating heart of our business."

*"Interdisciplinary communication and exchange of ideas are fostered throughout the development cycle."*



Rixensart, near Brussels, Belgium, is the center of all GSK vaccine research, development, and production.

### Cross-Pollination

Research is organized into multidisciplinary project teams. Interdisciplinary communication and exchange of ideas are fostered all through the product development cycle. In the early stages, experts from various disciplines get together to stimulate cross-pollination. Specific techniques have been developed to improve brainstorming methods and knowledge management. In later stages, researchers frequently meet with business developers and staff from the clinical tests and registration departments. Together, they identify where the company stands in relation to the needs for new products and vaccines as well as what the competition is doing. Then they define priorities accordingly. This group also sees to it that the research portfolio remains well balanced. In other words, that there are always sufficient promising products at each stage in the development cycle.

## GSK Biologicals: Vaccines for the World



### Politics and Partnerships

"In recent years, the political and economic context in Belgium has been less favorable for research activities," states Jean Stéphenne, President and General Manager of GSK Biologicals. "Pharmaceutical research has not received sufficient support from the government. Likewise, universities have had to make do with restricted budgets. The result has been a notable brain drain. GSK Biologicals has therefore set up programs with the National Fund for Scientific Research to sponsor university doctorates in areas like immunology. The company also funds projects in a joint university research center which are in line with its research objectives and programs."

"Legal issues are another potential matter for concern," Stéphenne continues. "The pharmaceutical sector is closely following any new legislation by the Belgian government regarding the patenting of various aspects of the human genome or stem cells. Should the government decide on a legislation that is more restrictive than other countries, then large research projects in this promising area will almost surely move abroad."

The newly created European Agency for the Evaluation of Medicinal Products (EMA), on the other hand, has been warmly welcomed by the Belgian pharmaceutical sector. A single registration of a new vaccine authorizes it for all 15 European Union countries. This obviously saves a huge amount of time, administration, and cost of development. Because the evaluation procedures have been standardized, assessments are more consistent and of a higher quality. For the consumer, this also means a shorter time-to-market for much needed new vaccines.

### Research for the Real World

This carefully thought-out approach to R&D has produced numerous groundbreaking results. In 1986, GSK Biologicals developed and introduced Engerix-B. This was the world's first vaccine to use genetic engineering techniques against the human hepatitis-B virus. Genetic engineering methods have been a giant leap forward in the area of disease prevention. These recombinant vaccines can be produced much more quickly, on a larger scale, and in a more standardized way. This is of course critical in the event of a sudden outbreak in an area where vaccine stocks are low.

GSK Biologicals was also the first company to market combined vaccines against childhood diseases. Because they reduce the number of injections, these vaccines greatly

Product Development Pipeline December 2002

Therapeutic Area	Compound	Type	Indication	Phase	Estimated Filing Dates	
					MAA	NDA
Hepatitis Vaccines	Hepatitis E	recombinant	hepatitis E prophylaxis	II		
	Extra strength hepatitis B	recombinant	extra strength hepatitis B prophylaxis (poor/non-responders)	III	2003	TBD
	Twinrix 2 doses	recombinant	combined hepatitis A and B prophylaxis (child/adolescent)	Approved	A:Sep02	2003
Paediatric Vaccines	Rotarix	live attenuated - oral	rotavirus prophylaxis	II	2005	
	N. meningitidis	conjugated	meningitis prophylaxis	II	2004	
	Meningitis B (Cuba)	subunit	meningitis B prophylaxis	II		TBD
	S. pneumoniae paediatric	conjugated	S. pneumoniae disease prophylaxis for children	III	2005	
	MMR-varicella	live attenuated	measles, mumps, rubella and varicella prophylaxis	III	2005	
Other Vaccines	Infanrix/Pediarix PeNt-HepB-IPV	recombinant	diphtheria, tetanus, pertussis, hepatitis B and inactivated polio prophylaxis	Approved	A:Oct00	A:Dec02
	Infanrix HeXa-Hep B-IPV/Hib	conjugated/recombinant	diphtheria, tetanus, pertussis, hepatitis B and inactivated polio prophylaxis and Haemophilus influenzae type B prophylaxis	Approved	A:Oct00	TBD
	Dengue fever	attenuated tetravalent vaccine	prophylactic use	I		
Pharmaccines	HIV	recombinant	HIV prophylaxis	I		
	New Influenza	subunit	Influenza prophylaxis - new delivery	I		
	S. pneumoniae elderly	conjugated	S. pneumoniae disease prophylaxis	I		
	Staphylococcal antibodies**	monodonal antibody	prevention of staphylococcal infections	I		
	Epstein-Barr virus (EBV)	recombinant	EBV prophylaxis	II		
	Human papillomavirus (HPV)	recombinant	prophylaxis of HPV infections	II		
	Malaria	recombinant	malaria prophylaxis	II		
	Simplirix	subunit	genital herpes prophylaxis	III		
	Boostrix	subunit	adolescent/adult booster for diphtheria, tetanus and pertussis	Approved	A:Oct00	2004
	Boostrix IPV	subunit	adolescent/adult booster for diphtheria, tetanus, pertussis and inactivated polio	III	2003	
Pharmaccines	GSK/PowderJect**	recombinant	hepatitis B treatment	I		
	249553	recombinant	treatment of lung cancer/melanoma	II		

Figure 4. R&D teams at GSK Biologicals are making excellent progress in the advanced clinical tests of a number of new vaccines. (Source: GSK Biologicals Web site)

## GSK Biologicals: Vaccines for the World

*“One of our key strategic priorities is to simplify access to life-saving vaccines in developing countries.”*

Jean Stéphane

President and General Manager of GSK Biologicals

improve the comfort of newborn babies. They also reduce costs by freeing up medical equipment, personnel, and storage space. Combined vaccines are already greatly improving the efficiency of limited medical staff in both developing and developed countries.

### Promising Clinical Tests

Critical advances are being made in the clinical tests phase of vaccines under development. “Our product portfolio will certainly be greatly extended in coming years,” notes Stéphane. “New vaccines, in a wide variety of areas, have now entered the clinical tests phase. These include an HIV vaccine, a recombinant vaccine against chickenpox, a meningitis-B vaccine for teenagers, and a vaccine to fight malaria. It is a matter of public record that GSK Biologicals currently has the industry’s strongest product portfolio in clinical testing.”

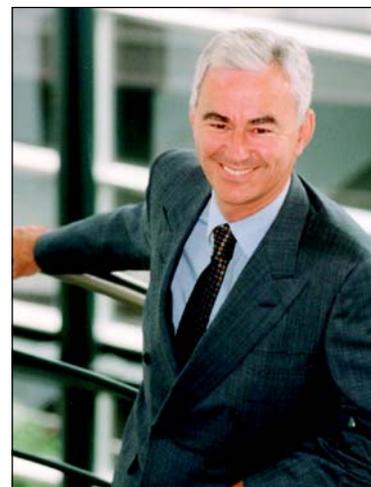
Encouraging results also have been obtained for products currently in Phase II and III clinical trials. These include a recombinant vaccine against cervical cancers due to HPV infections. Similarly, extremely positive results have been registered with a vaccine for rotavirus (infant diarrhea) that was tested in several Latin American countries. The Simplirix vaccine against genital herpes is also in its final testing stages. Diseases which affect mostly developing countries are one of GSK’s priority areas and the focus of

a great deal of research, especially resistant forms of tuberculosis and dengue fever and of course, HIV, and malaria - *Figure 4*. Much remains to be done however. Research continues unabated for a cure or prevention of Alzheimer disease, various types of cancer, and autoimmune affections such as allergies, asthma, and arthritis.

### Vaccines for Young and Old, Rich and Poor

No one questions the importance of a balanced research portfolio. But it is equally essential to cover all market needs. GSK Biologicals’ market strategy targets vaccines for the specific needs of various age groups; combined vaccines for infants, hepatitis or rubella vaccines for teenagers, hepatitis, salmonella or cholera vaccines for travelers, influenza vaccines for elderly people. This is a sound and efficient marketing strategy that aims to underline the company’s contribution to a better quality of life for every citizen of the world. It is an approach that is also fully in line with the GSK corporate motto to help everyone “Do more, feel better, and live longer.”

GSK Biologicals has made it a corporate strategy to provide countries in need with easier and cheaper access to essential vaccines. It has no intention of leaving the developing world to its own devices simply because they do not represent a profitable enough market. The whooping-cough component of some GSK combined infant vac-



cines, for instance, is produced at a lower manufacturing cost for developing countries. Community partnership projects also have been initiated whereby GSK Biologicals is distributing certain vaccines at no cost. The company’s active participation in UNICEF vaccination programs is well known and widely held up as a model for corporate responsibility. GSK Biologicals also has built a number of plants in Hungary, Russia, and China to be closer to developing countries. Additional plants in India and Latin America will follow soon. Since most vaccines require refrigeration, the shorter the transportation distance and time, the easier — and cheaper — it is to maintain and stock the necessary vaccines.

An important fact emerges upon a closer look at corporate income figures. North America and Europe currently account for two-thirds of GSK Biologicals’ revenue, but only one-third of their shipped volumes. Notes Stéphane, “The greater part of the vaccines we produce are going to developing countries. Our biggest challenge remains finding a cure to the three biggest health concerns facing the world today: AIDS, tuberculosis, and malaria.”



# Janssen Pharmaceutica: Built Around R&D

## 50 Years of Research, 75 Innovative Compounds



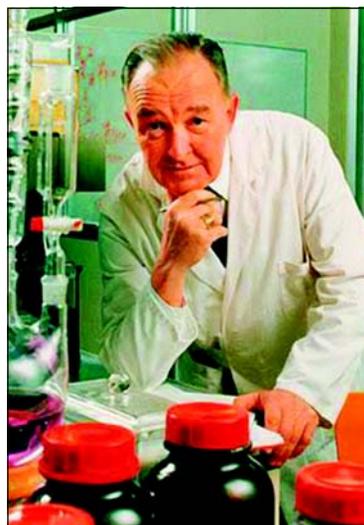
*“A good scientist is someone who succeeds in letting the different scientific disciplines work together harmoniously, just like the fingers of a hand can only function well if they cooperate fluently.”*

**Dr. Paul Janssen**  
Chemist, Pharmacologist, and Physician

The story of Janssen Pharmaceutica is extraordinary. Exactly 50 years ago, it all began in a small, simple laboratory in Turnhout, Belgium. Against all the odds and in spite of a skeptical world, Dr. Paul Janssen, M.D. began pursuing his ultimate dream: creating an independent and self-supporting research laboratory. Thanks to his incredible insight—you might even say genius – and his knack for spotting talented people, he

has achieved his dream. But, as it turned out, that proved to be only the beginning of the story.

Today, Janssen Pharmaceutica is part of the Johnson & Johnson Group, and one of the leading R&D sites worldwide. But it all began as a local initiative. Actually, Janssen got his inspiration from his general practitioner father, Dr. Constant Janssen. Back in the 1930s, disappointed that he could only help a fraction of his patients,



about one out of 200, the elder Dr. Janssen started looking for alternatives. He began importing Richter products from Hungary and sold them in his region, and later throughout Belgium, the Netherlands, and the Congo. It was mainly vitamin preparations, but it was a start.

### Pioneer in Linking Chemical Structure to Pharmaceutical Activity

In the 1950s, his son, Dr. Paul Janssen, took the idea a giant step further. He had studied both medicine and chemistry and was convinced that there must be a connection between the chemical structure of a compound and its pharmaceutical effects. He wanted to reconcile the two disciplines. It would be the fundamental concept of Janssen research: synthesizing molecules with the intent of detecting the relationship between the structure and their pharmaceutical activity. After only one year, the fifth molecule that he synthesized was a hit: R5 or ambucetamide. This antispasmodic proved to be

<b>Pain Management</b>	
Fentanyl®	Analgesic potency of several times that of morphine.
Sufenta®	An exceptionally potent analgesic (5 to 10 times more potent than Fentanyl) for use in heart surgery.
Rapifen®	Analgesic in general anesthesia for both short (bolus injections) and long (bolus, supplemented by increments or by infusion) surgical procedures.
Durogesic®	A Fentanyl transdermal patch used in chronic pain management
<b>Psychiatry</b>	
Risperdal®	Mental disorders
<b>Gastrointestinal Diseases</b>	
Imodium®	Antidiarrheal
Motilium®	Gastrointestinal regulator
<b>Mycology</b>	
Daktarin®	Antimycotic
Nizoral®	Antimycotic
Sporanox®	Oral antimycotic
Vermox®	Anthelmintic
<b>Neurology</b>	
Reminyl®	Alzheimer's Disease

Table A. Some of the main products developed by Janssen Pharmaceutica.

## Janssen Pharmaceutica: Built Around R&D

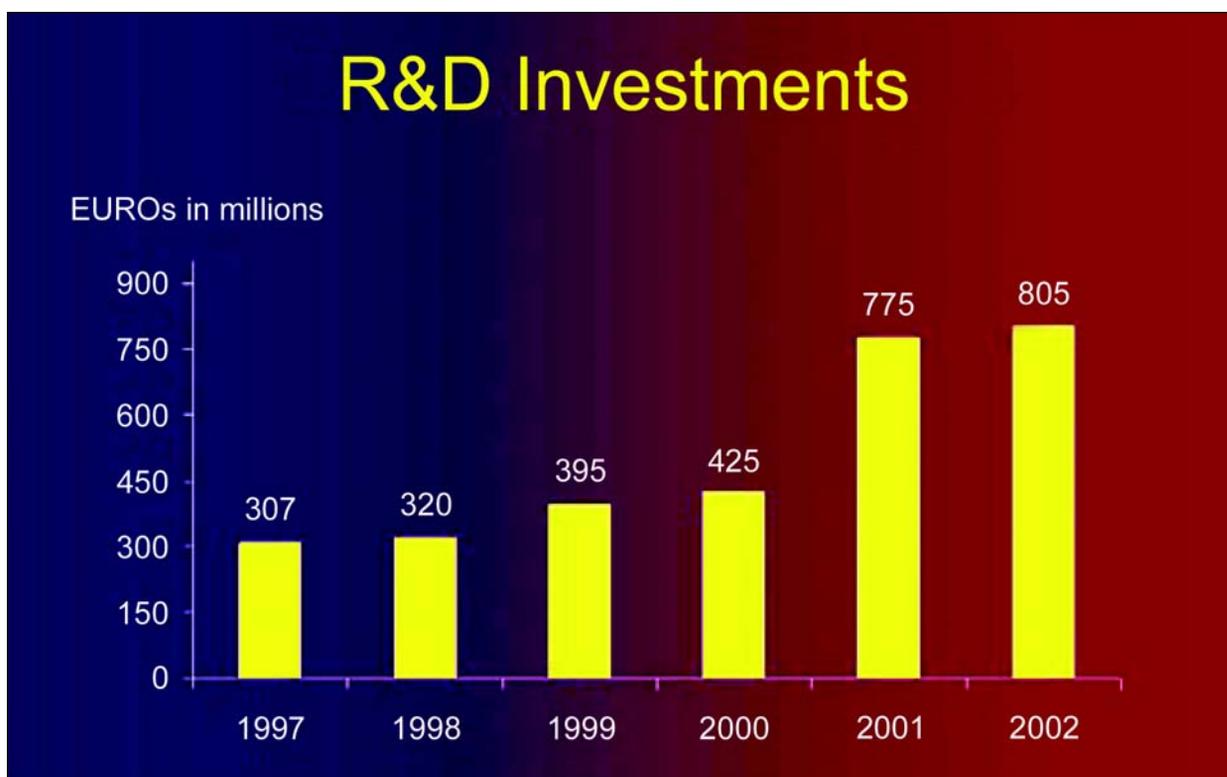


Figure 1. R&D investments at Janssen Pharmaceutica.

very effective against Premenstrual Syndrome (PMS). The product was launched in 1955 as Neomeritine® and is still available on the market today.

The second important molecule was R79, isopropamide iodide. Smith, Kline & French licensed it and then sold it as Combid and Darbid. A highly successful compound developed in the 1960s was R1132 (difenoxylyate). It was licensed by Searle and launched in the US as Lomotil. Interestingly, it even traveled to the moon with the Apollo astronauts in their medical kit.

### Evolutionary Products

Now, 50 years later, the record of achievements has grown to 75 synthesized compounds - *Table A*. Four Janssen medicines are cur-

rently listed among the 300 products in the WHO List of Essential Medicines. Stefan Gijssels, Vice President Public Affairs and External Communication notes that, "Annually more than 2 billion patient treatments with Janssen

products are being administered around the world. Our major areas of R&D focus are pain management and anesthesia, psychiatry, gastrointestinal diseases, mycology, oncology, gynecology, and neurology. We can honestly say that

### About Janssen Pharmaceutica

Janssen Pharmaceutica became part of the Johnson & Johnson Group in 1961. The company has expanded to an international organization with offices in 44 countries around the world, with a total workforce of 23,400. There are multiple sites in Belgium. These include Beerse, where the R&D department is seated together with pharmaceutical production and general services. In Geel, the chemical plant produces the active ingredients for more than 60% of the company's drugs. Together, they employ a staff of 4,200. This number has grown at an average of 100 employees a year over the past five years.

One of the main focuses of Janssen Pharmaceutica is quality. Dr. Ajit Shetty, CEO, states that, "We keep abreast of new regulations by maintaining a constant dialog with all of the appropriate regulatory agencies. All our sites are FDA and EMEA approved and our track record in this area is excellent."



## Janssen Pharmaceutica: Built Around R&D

*“During the last 10 years, we’ve seen a continuous increase in our production output, even against the economic tide. This is thanks to the quality and motivation of our employees.”*

**Dr. Ajit Shetty**  
CEO of Janssen Pharmaceutica

many of our products have affected a revolution in healthcare. Without Fentanyl® for example, which is up to 300 times stronger than morphine, the history of open-heart surgery would have been completely different. Fourteen million patients worldwide use Risperdal® (as the successor of Haldol®) to treat schizophrenia. It has changed the lives of countless psychiatric patients. One of our recent achievements is the production of the CYPHER™ Stent, the first coronary stent coated with antibiotics, a joint project with our sister company Cordis.”

### Successful Vision on R&D

The R&D staff of Janssen Pharmaceutica in Belgium has more than 30 different nationalities among its 1,300 researchers. This is one third of the entire worldwide pharmaceutical R&D staff, which now operates as a fully integrated entity with the name J&J BRD. In 2002, Janssen Phar-

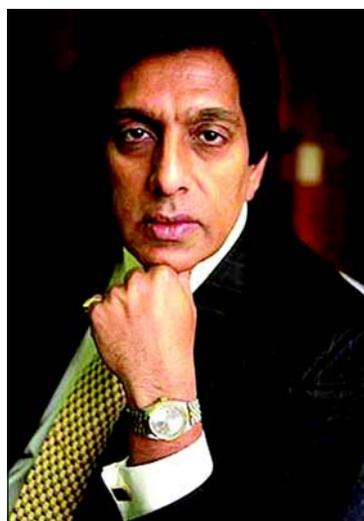
maceutica synthesized 9000 new compounds and screened 30,000 other compounds from external sources. Its record in bringing a new medicine onto the market, starting with the synthesis of new molecules, is one out of 5000, twice as high as the sector average. In 2003, Janssen had 38 new molecules in drug evaluation. It currently has four in late development, and has filed eight others for final approval.

Janssen Pharmaceutica has one big advantage. By integrating R&D and production sites, interesting exchanges between specialists take place. CEO, Dr. Ajit Shetty: “Janssen’s philosophy has always been to build research around people, rather than the other way around. We became a specialist in domains like parasitology and mycology after Paul Janssen began attracting people who had worked for many years in the former Belgian Congo. We also always see to it that there is a close interaction

between scientists and patients. When scientists are actually involved with the results of their work, they know that they are making a contribution. That is highly motivating.”



Figure 2. The R&D department of Janssen Pharmaceutica is situated in Beerse, together with the pharmaceutical production facilities and administration offices.



### With an Open Mind

This approach has resulted in an excellent track record, one that has been recognized by senior management of the Johnson & Johnson Group. R&D investments at Janssen Pharmaceutica have shown a steep increase in the past decade. In 2002, they reached a record level of 805 million Euro - *Figure 1*. Among those investments were a new Ultra High Throughput Screening and powerful computers for bioinformatics in order to gain new insights into diseases and to identify possible links with specific molecules. Dr. Shetty notes that “With our record of 50 years of continuous top-flight research, it’s not that difficult to convince J&J that their investments are in good hands. We can thank the productivity, quality, and drive of our employees for this.

“Our vision is to look beyond our own company and use - or add to - the expertise within the Group,” continues Shetty. “We study and learn from other industries, we keep an open mind as to how we can best capitalize on the exper-



## Janssen Pharmaceutica: Built Around R&D



Figure 3. One of the latest product innovations developed at Janssen is the Durogesic pain patch, combining the powerful analgesic Fentanyl® with the patch technology of Alza. This has been a breakthrough for the treatment of severe chronic pain.

tise of sister companies. We strive to create umbrella technology platforms. This has enabled us to get our products onto the market much quicker and to lower our costs.”

Shetty concludes with his thoughts on the future: “It is crucial that R&D and production continue to go hand in hand to safeguard the future health of people around the world as well as our company.”

Dr. Ajit Shetty, CEO of Janssen Pharmaceutica holds a PhD in Met-

allurgy from Trinity College, Cambridge University, a BA in Natural Sciences, and an MBA. He was born in India and has been living and working in Belgium for the past 20 years.

Dr. Paul Janssen, a leading Belgian researcher, pharmacologist, and general practitioner, is the founder of Janssen Pharmaceutica. Much of the growth of the company can be attributed to his passion for research and charismatic leadership. 

### Ajit Shetty's Thoughts on Belgium

“The business prospects for our Belgian company look good. Belgium has a central location which is especially attractive for other European researchers. The country's education level remains among the best in the world and is a good source for recruiting new researchers, engineers, and the other specialists and skills we need. Belgium has the largest per capita number of clinical trials in Europe, almost twice as many as number two on the list.

If you look at the combined levels of pharmaceutical industry capabilities, the quality of medical care, and academic and clinical research levels, then one can quite accurately state that Belgium is truly a world leader in pharmaceuticals and healthcare. The mutual reinforcement of all these factors creates a unique synergy and offers a very strong impetus for further investments and innovation.”

***“We believe our first responsibility is to the patients and the doctors, nurses, mothers and fathers, and others who use our products and services.”***

**Credo of  
Johnson & Johnson**



# Biotech Start-ups: Keepers of the Flame



**B**elgium has a long-standing tradition in the life sciences industry. The high standard of past achievements is being upheld and even expanded by the many start-up companies that have grown out of this research. Many of these companies are ready to follow in the footsteps of giants like GSK and Janssen. The combination of high quality academic research, industrial activity, entrepreneurship, and government financing makes Belgium exceptionally fertile ground.

Many of these new players are active in biotechnology which is playing an increasingly important role in developing, producing, and marketing new healthcare products and services. This focus is no coincidence. In the 1970s, Belgian researchers were the first to record the sequence of a gene and later a complete genome. They also were among the first to identify gene

defects and led the way in plant transformation. Belgian researchers such as Désiré Collen, Walter Fiers, Jeff Schell, and Marc Van Montagu are recognized as being among the best biotechnology scientists in the world.

These successes paved the way for start-up companies like Innogenetics, Tibotec, and Devgen. Today, Belgium has about 100 biotech companies. Half of them are active in the medico-pharmaceutical field. They are involved in a wide variety of activities, from the design and development of new applications and the testing and screening of new molecules and drugs to contract research.

### Specialized Newcomers

In recent years, successful cooperation between universities and the pharmaceutical industry has resulted in the success of several start-up firms, as well as the commercialization of academic re-

search. Pharmaceutical companies tend to focus on their core business of developing new therapeutic means and the marketing of registered products. "This paves the way for specialized newcomers who can carry out research assignments for or in collaboration with large pharmaceutical companies," says Jan Huybrighs of Innogenetics.

Since 1998, more than 25 new companies have been formed. Although many of them have not reached the stage where they are marketing products, there is every reason to believe that the number of biotech medicines marketed in the near future will increase rapidly.

### Belgian Entrepreneurship

Belgium certainly provides fertile ground for this type of spin-off. There are currently 16 universities and specialist research centers, along with several biotech parks in Belgium. The presence of adequate financing, one of the building blocks of biotechnology, also helps. Every stage – from academic research through product commercialization – can be addressed in Belgium. A wide array of financial sources are available, from private sector firms to government grant agencies. "These facts, combined with the Belgian entrepreneurial spirit, mean that innovators are not afraid of taking risks. This ensures the future of a thriving pharmaceutical industry in Belgium."

### Blazing the Trail

In Belgium, the early recognition of the importance of biotechnology has resulted in many of the start-ups establishing themselves in the pharmaceutical sector. A number of them are well beyond the pure research phase and have already commercialized their results. A few

	Number of Companies	Turnover (in Million Euros / US\$)	Turnover (% of total)	Number of Jobs	Jobs (% of total)
Large companies	17	1,368	84	5,732	79
SMEs*	80	230	16	1,428	21
Total	97	1,598	100	7,160	100
*Fewer than 200 employees					
Source: BIB 2000/BBA					

Table A. Biotechnology companies in Belgium (2000).

	Number of Companies	Turnover (in Million Euros / US\$)	Turnover (% of total)	Number of Jobs	Jobs (% of total)
Healthcare	48	1,250	78	5,589	78
Agriculture	17	284	18	1,026	14
Environment	9	9	1	132	2
Services	23	55	3	413	6
Total	97	1,598	100	7,160	100
Source: BIB 2000/BBA					

Table B. Breakdown by sector of Belgian biotechnology companies (2000).

## Biotech Start-ups: Keepers of the Flame

companies even have a long track record of successes to their credit.

### **Innogenetics**

Innogenetics provides high value-added diagnostics focusing on infectious diseases, neurodegeneration, and genetic testing. The therapeutics portfolio of the company is steadily expanding and consists of innovative candidates in the fields of hepatitis C, immune disorders, and wound care. Innogenetics was founded in 1985.

### **Tibotec**

Tibotec is a research and development company seeking the discovery of innovative HIV drugs and superior anti-infectives for diseases with high, but unmet medical need. The company is at the forefront of HIV research and has two anti-HIV compounds in early clinical development and several discovery programs for compounds highly active against resistant HIV strains. Tibotec was founded in 1994 and was acquired by Johnson & Johnson in 2002.

### **Virco**

Virco provides advanced diagnostic tools. These are based on pharmacogenomic principles for the clinical management of viral infections, HIV infection in particular. The company combines cutting edge technology in the fight against HIV with the active collaboration of doctors, patients, and researchers. Founded in 1995, Virco is a sister company of Tibotec.

### **Devgen**

Devgen focuses on the development and the industrial production of *Caenorhabditis elegans*. This is the model organism that has unique benefits over traditional animal

Creation	Company Name	Activities
2001	Ablynx	Therapeutics and diagnostics
1987	Analix	Electrophoresis kits, in vitro diagnostics
(*)	Baxter Healthcare	Vaccines, biosurgery therapies products, and services
1988	Beta-Cell	Cell therapy in diabetes
1996	Biosource Europe	Immunoassays, custom oligo synthesis, custom peptides and antibodies CDNA kits, Multiplex, Primers, and Tago immunologicals
1997	Biotech Tools	Vaccines correlated with allergies, gene therapy
2001	Brucells	Cell therapy, immunotherapy
1997	CAF-DCF	Human protein purification, plasma derivatives: factor VIII, Albumin, PPSB, immunoglobulins, and fibrinogens
1996	Coris-Bioconcept	Diagnostics
2001	Dyax	Development of monoclonal antibodies using phage display technology
1985	Eurogentec Bel	Customized production of oligonucleotides
1994	Euroscreen	Human receptors as drug targets
1983	Gamma	Diagnostics, monoclonal antibodies, home test, and blood bank
(*)	Genzyme Flanders	Therapeutics in Gaucher disease, serum phosphorus reduction, diagnostics for infectious diseases
(*)	GlaxoSmithKline Biologicals	Human vaccines
1985	INNOGENETICS	Diagnostics for infectious and autoimmune diseases, cardiovascular, neurological and genetic disorders, vaccine candidate for HCV (in phase II)
1999	MDS Nordion	Supplies products used in healthcare, diagnostics and therapeutics. Nuclear medicine
1950	Phibro	Veterinary vaccines and pharmaceuticals and temperature-sensitive vaccines
1998	R.E.D. Laboratories	Diagnostics tests and therapeutics for chronic fatigue syndrome, multiple sclerosis and other chronic immune diseases
2001	ReMYND	Drug testing for Alzheimer's disease and neurodegeneration
1994	Tibotec-Virco	Drug resistance testing (HIV, HCV, Tuberculosis) and two anti-HIV drug candidates (in phase II)
1999	Unibioscreen	In vitro cancer screening
1990	Zentech	RIA and EIA based diagnostics for human hormonology-thyroid and auto-immune diseases, genetically engineered proteins, prolactin, and CD4 panel
*Subsidiary in Belgium		
Source: BBA - Belgian BioIndustries Association		

Table C.

models or biochemical *in vitro* approaches for drug discovery. The company uses this model to rapidly analyze human disease states and identify and validate

high-quality screening targets for further drug development. Devgen was founded in December 1997 and employs more than 90 people. 

## Industry Associations and Related Bodies in Belgium

### AGIM-AVGI

**Belgian Pharmaceutical Industry Association**  
Square Marie-Louise 49  
1000 Brussels  
Tel: +32 2 238 99 76  
Fax: +32 2 231 11 64  
<http://www.agim-avgi.be/>  
E-mail: [info@agim-avgi.be](mailto:info@agim-avgi.be)

National trade association representing 146 pharmaceutical companies based in Belgium.

### DG Public Health Protection:

#### Medicinal Products

Bd Bischoffsheim 33  
1000 Brussels  
Tel: +32 2 227 55 00  
Fax: +32 2 227 55 55  
<http://www.afigp.fgov.be/>

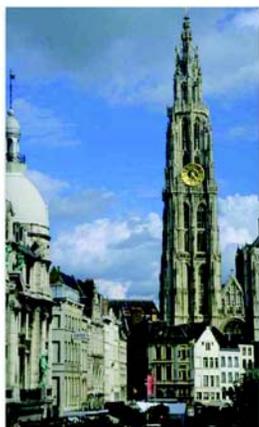
The DG Public Health Protection: Medicinal Products has as main duty to ensure that patients have high-quality, efficient and safe medicines and related products at their disposal and that they use them safely and effectively. This holds also true for veterinary medicines.

### Scientific Institute of Public Health (IPH)

Rue Juliette Wytsmans 14  
1050 Brussels  
Tel: +32 2 642 51 11  
Fax: +32 2 642 50 01  
<http://www.iph.fgov.be/>

The Institute tasks are: Reference activities; Monitoring; Epidemiological surveillance; Control of federal norms; Quality assessment; Risk evaluation; Evaluation of health data; National and international representation of the Belgian federal health authorities.

For information  
on the  
**ISPE Belgium  
Affiliate visit**  
[www.ispe.org/  
belgium](http://www.ispe.org/belgium)



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