Country Profile

A look at the Pharmaceutical Industry in

GERMANY AND SWITZERLAND

Produced in collaboration with ISPE Germany/Switzerland

ISPE

THE SOCIETY FOR LIFE SCIENCE PROFESSIONALS

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Dear ISPE Members,

On behalf of the ISPE Germany-Switzerland Affiliate, I am proud to present this overview of the pharmaceutical industry in our countries. You might ask why both countries are grouped in one profile, but this has something to do with the organization of our Affiliate. Within the global ISPE family, we offer essential benefits to industry professionals within the entire German-speaking region. Thus, the members of our Affiliate are located in the mother-countries of the pharmaceutical industry - mainly in Germany and Switzerland, but also in Austria. But when looking at the history and status of this pharmaceutical industry, we see two distinct stories, each with its own highlights. Hence, this profile is presented in two sections.

Our Affiliate is representing a region with the largest population in Europe and globally the third largest economy, giving immediate access to a vast domestic market for manufacturers as well as vendors and suppliers. The availability of this market also has lead companies to grow and thrive, promoting a stage for excellent R&D and export.

Both Switzerland and Germany are renowned for their thoroughness in design and manufacturing in all industries. This is also the reason why many of the world's most famous equipment suppliers for the pharmaceutical industry are located in this area. The excellent education systems deliver well-trained professionals guaranteeing a stable and highly qualified workforce. A close collaboration between private and academic research institutions provides an innovative climate, attracting new investments in an ever-growing pharmaceutical industry.

ISPE Germany-Switzerland started activities in 1992 and is today – with more than 800 members - an active contributor to the ongoing education of life science professionals, through the organization of seminars, training courses, site visits, and active cooperation with ISPE in the publication of German-language versions of technical documents. More information about ISPE D/CH can be found on http://www.ispe.org/germany-switzerland/.

I hope you will enjoy reading these pages and that they will contribute to completing your knowledge about the pharmaceutical industry in this part of the world. Welcome into our region in the heart of Europe.

Mit besten Grüssen,

Werner H. Oesterle
Chairman, ISPE D/CH

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 Brazil in the March/ April issue of *Pharmaceutical Engineering*.

A Look at the Pharmaceutical Industry in Germany

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Despite strong regulation and federal budgets, the German pharmaceutical market is still one of the strongest with nearly 8% of global sales, considering it only comprises 1.3% of the world population. In the EU, the German market leads in sales as well as in the production of medicines. Sales increased 7.8% in 2002 due to an intensified prescription of innovative drugs after a period of strong budgeting.

With a market participation of 27%, generic drugs are pressuring prices of innovative products after the end of patent protection. Continuously increasing re-imports have caused a significant sales loss for the national pharmaceutical industry.

The market covers "public" and hospital pharmacies. In 2002, public pharmacies, (nearly 50,000 which are actually all privately-owned and which have a monopoly over drug dispensing except to hospitals), sold drugs for €18.7 billion while hospitals purchased drugs with an ex-factory volume worth €2.5 billion. Distribution by drugstores is 7%, and does not play an import role in the market of OTC products.

Pharmacy surcharges and the taxes are among the highest in west European countries. In Germany, full VAT is applied for drugs, but several consumer goods like food, books, etc., have a reduced VAT rate. For the market, 9,500 drugs are registered, but only 2,300 generate 90% of total sales.

With 79% and €18 billion, prescription drugs comprise the most important part of the market. In 1997, the average number of prescriptions per patient was 12.1, with an average of 18.6 prescribed packs. General practitioners, 18% by internists and 7% by pediatricians, prescribed more than 55% of all prescriptions.

As a result of continually rising economic barriers in the national health system, many substances are no longer reimbursable and self-medication has become more important to the population. In the future, patients will try to treat less severe diseases with OTC products first, before consulting a physician, due to a relevant change in the health system where patients are obligated to pay up front.

In the area of self-medication, patients are favoring brand name OTC products even though physicians have a broad portfolio of drugs they can prescribe.

The increase of 66% in the prescription drug market is based on the introduction of new innovative substances for severe and life threatening diseases. Approximately 30 drugs per year get approval.

For the purposes of international comparison, the health status of the German population can be illustrated using certain health indicators. Cardiovascular and non-malignant lung disease mortality rates in Germany are well above the European average. In 1991, unified Germany had a life expectancy that was slightly below the EU average. Current health concerns are mainly related to diseases associated with the age structure and demographic trends of the German population. Important demographic and health-related trends that are currently observed include an increase in the number of one-person households, and an increase in long-term chronic-degenerative diseases.

Future changes in the structure of the population will lead to a moderate increase in the elderly population's need for therapy, rehabilitative care, and nursing care whereas the morbidity transition will result in less need for curative medical intervention. It is also expected that there will be an additional need for health services responding to obstructive lung dis-

Figure 1. Global versus German pharmaceutical market.

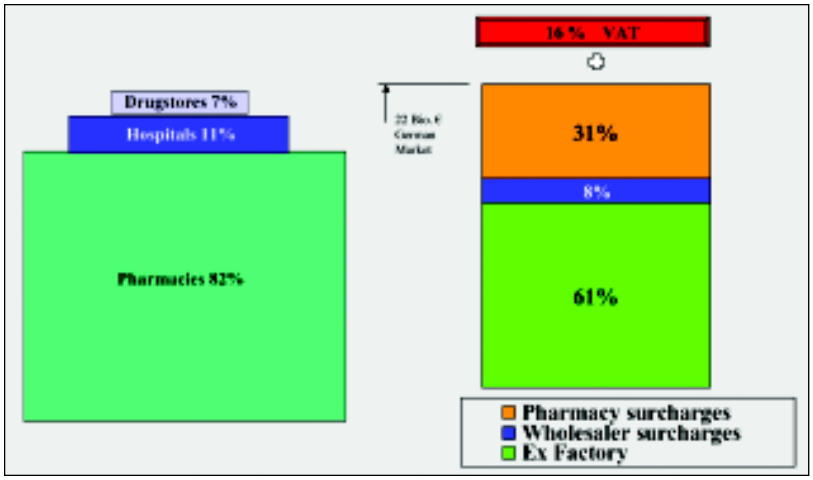


Figure 2. Distribution channel and price structure.

eases, diseases of the cardiovascular system, urogenital diseases, and cancer diagnosis and therapy. A large preventive potential for coronary and circulatory diseases, respiratory diseases, and accidents is also foreseen.

National Health Care System

The modern German health care system started with the introduction of mandatory health insurance on a national level in 1883. Germany is recognized as the first country to have introduced a national social security system. The prominence and structural continuity of social insurance is one of the key features of the historical development of Germany's health care system to the present day. Contributions and expenditure increased substantially during the 119 years of statutory health insurance. This was the result of the extension of benefits – often following decisions by the civil courts – through state intervention, but mainly by the self-administered funds themselves or by joint committees between funds and physicians. While initially the statutory health insurance scheme aimed primarily at preventing impoverishment by compensating income in cases of illness, sickness funds increasingly funded services and the prescriptions of specialized professionals.

Health insurance is provided by autonomous sickness funds, which are organized on a regional and/or federal basis. In mid-1999, there were 453 statutory sickness funds with about 72 million insured persons (50.7 million members plus their dependants) which represent 88% of the population. Fifty-two private health insurance companies covering around 7.1 million private health insured people.

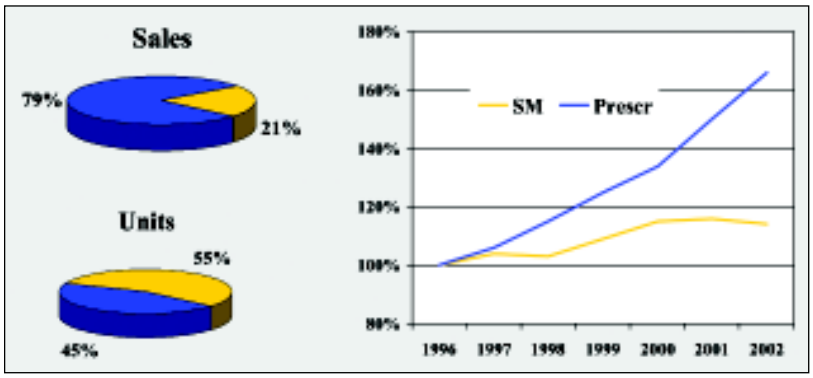


Figure 3. Self medication versus prescription.

Contributions are dependent on income and not risk, and include non-earning spouses and children without any surcharges. By law, sickness funds have the right and the obligation to raise contributions from their members which includes the right to determine what contribution rate is necessary to cover expenditure. Currently, they cover between 12% to 15% of gross salary of the insured persons. Contributions are shared equally between the insured and their employers.

Germany's health care system is expensive by international comparison, both in absolute figures and, even more visibly, as a percentage of GDP.

The basic principle behind "German-style" cost-containment was an income-oriented expenditure policy to guarantee stable contribution rates. This was an important objective in a time of economic restructuring and growing international competition since employers and employees jointly pay the contributions. Therefore, increases in contribution rates were (and still are) perceived to be a question of international competitiveness.

The drive for cost-containment was realized through a long series that employed various measures including:

- the introduction of legally fixed budgets or spending caps for the major sectors of health care
- reference-price setting for pharmaceuticals
- restrictions on high cost technology equipment
- increased co-payments on prescribed drugs
  - small packs N1 €3
  - medium packs N2 €4
  - large packs N €5

- the exclusion of young people from certain dental benefits

The idea behind reference prices was to establish an upper limit for the costs reimbursable through the sickness funds. Due to lowered prices for drugs formerly above the reference price, these regulations led to decreasing prices for reference priced drugs.

Health care service is provided by approximately 30,000 physicians, 45% office-based, 41% hospital, 11% care services and rehabilitation, and 3% state prevention services.

There are around 3,600 hospitals with approximately 750,000 beds (6.2 beds per 1000 inhabitant) and an average occupancy rate of a little more than 80%. All ambulatory care, including both primary care and outpatient secondary care, has been organized almost exclusively on the basis of office-based physicians. The majority of physicians have a solo practice; only around 25% share a practice. Germany has no gate keeping system, instead patients are free to select a sickness-fund-affiliated doctor of their choice, but this will probably change in the future.

Pharmaceutical Industry

The profession of the pharmacist was established in Germany about 800 years ago by a written regulation of the German emperor Friderich II. It was the first time the profession of physician and pharmacist were divided. These laws influenced the development of pharmaceutical manufacturing that pharmacists dedicated purely to the manufacturing and distribution of drugs. Pharmacists could increase their manufacturing scale from simple pharmacy labs (Uffizin) to industrial production by discovering the scientific based

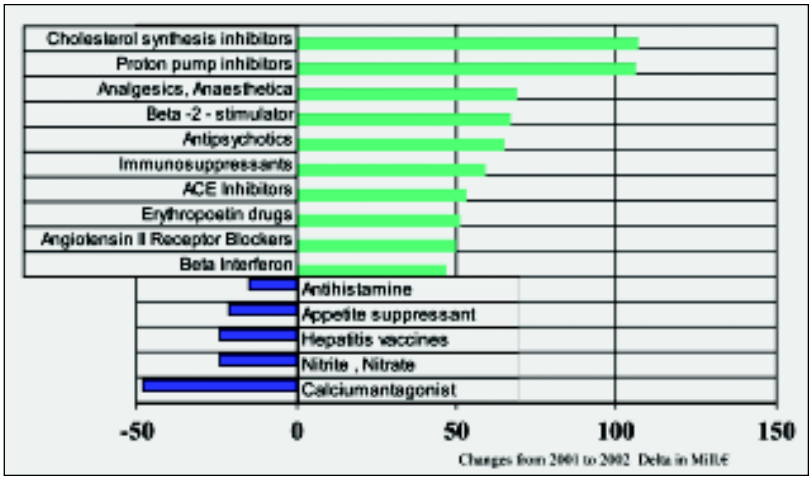


Figure 4. Drugs with major change in sales.

synthesis in the 19th century. Organic chemicals were being more widely used for pharmaceuticals. New formulations like tablets, capsules, and ampoules were developed. Now drugs were reachable in terms of finance for the majority of the population. The majority of the pharmaceutical companies started with fine chemical activities. Only a few were dedicated merely to pharmaceutical production.

Germany was the spearhead of this evolution. From that time it had its name "Apotheke der Welt" (Pharmacy of the World), because with the increase in pharmaceutical production, exportation started shortly thereafter. At end of the 19th century, the first German sales representatives were selling drugs even in Chinese deserts. After World War I, most German companies lost their foreign subsidiaries and, even more painful, their trademarks. The pharmaceutical industry could not advance

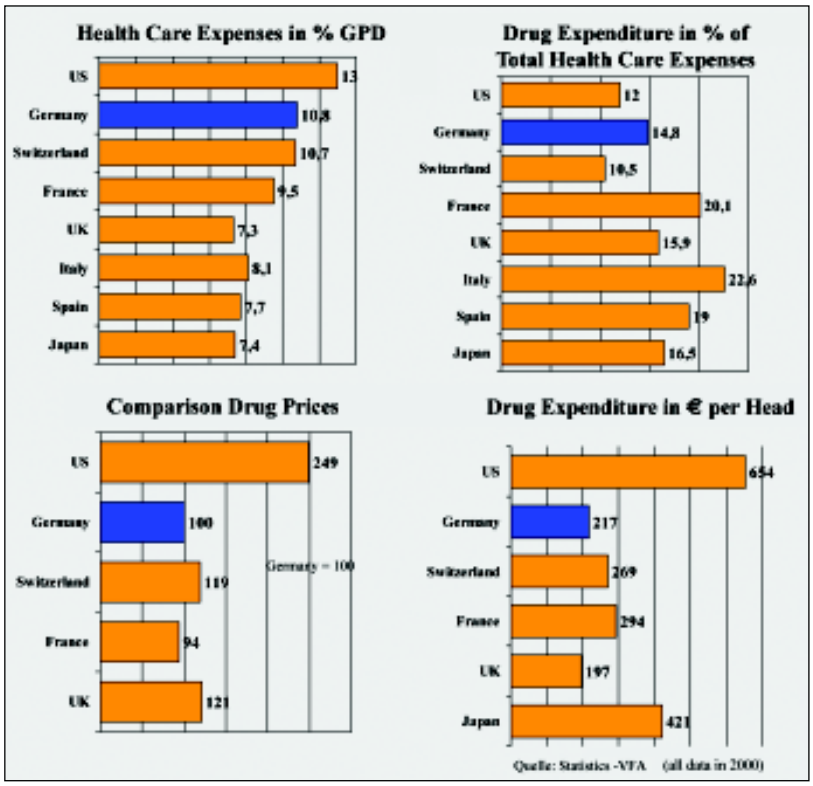


Figure 5. German healthcare expense statistics.

	Sales/Mill.€	Marketshare/%	Development	Units/Mill.
PFIZER	1,510	6.8	7.3	3,810
AVENTIS	1,190	5.4	4.4	2,310
NOVARTIS	1,090	4.9	2.2	6,710
MERCKLE	1,060	4.8	13.5	10,710
ROCHE	900	4.1	12.2	2,960
KOHL MEDICAL AG	810	3.7	17.1	1,220
ASTRAZENECA	790	3.6	4.0	1,510
MERCK & CO	750	3.4	8.2	1,060
HEXAL GROUP	750	3.4	20.5	4,710
GLAXOSMITHKLINE	720	3.3	-1.0	1,330
SANOFI-SYNTHELABO	560	2.5	2.6	2,650
BOEHRINGER INGELHEIM	520	2.4	8.3	3,210
JOHNSON & JOHNSON	510	2.3	5.8	760
BAYER	450	2.0	-8.1	1,900
SCHERING AG	420	1.9	5.5	660
STADA	420	1.9	20.4	3,080
BRISTOL-MYERS SQB.	390	1.8	0.3	420
LILLY	380	1.7	13.7	310
ALTANA	370	1.7	8.5	670
NOVO NORDISK	320	1.5	2.7	300
Subtotal	*13,910*	*63.1*	*7.2*	*50,290*
Rest of market	8,123	36.9		54,030
Germany incl. Hosp.	**22,033**		**6.9**	**104,320**

Figure 6. Leading pharmaceutical companies in Germany - MAT/2Q.2003.

during the turbulent years of economical crisis. And leaving this crisis, the pharmaceutical industry was integrated in the preparation for World War II.

After the war, the Allied Forces placed most companies under the control of the allied officers. Some of the companies were to be dissolved and the assets made available for war reparations, but soon they allowed production to resume as well, as the chemical industry's products were essential to supply the population.

The reconstruction of the pharmaceutical industry was closely linked with the Wirtschaftswunder, or "economic miracle" in the Federal Republic

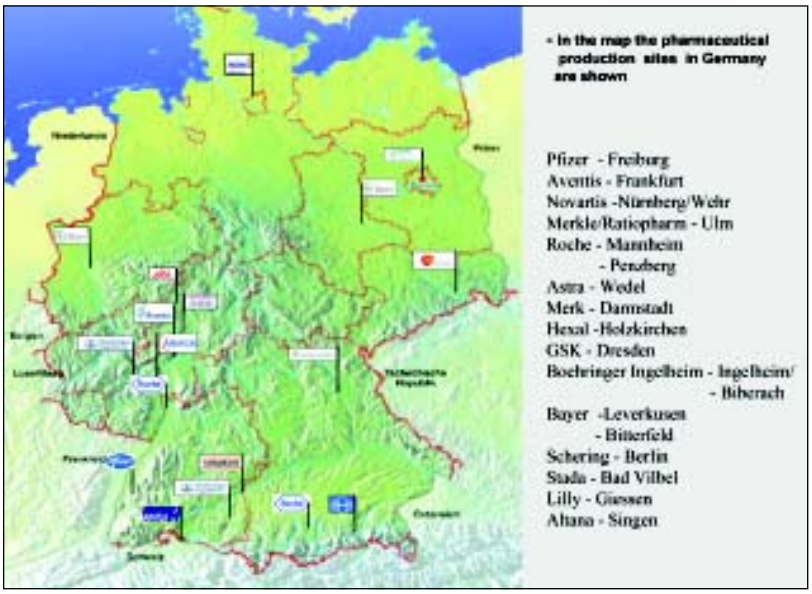
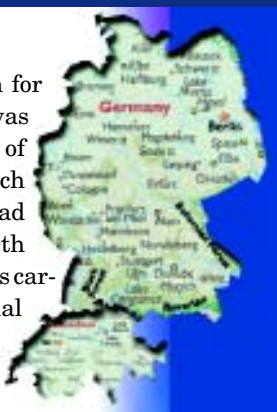


Figure 7. Regional distribution of 20 leading pharmaceutical companies.



of Germany. The foundation for this positive business trend was not only the reestablishment of operations, but also research and development - as it had been at the end of the the 19th century. New products such as cardiovascular medicines, dermal antifungals, and broad-spectrum antibiotics emerged from the pharmaceutical laboratories. During that period, new pharmaceutical companies were founded by strong entrepreneur characters. Although the expansion across the frontiers of Europe was done originally by representations, the companies emerged in the fifties by developing foreign production sites or acquisitions.

At the end of 1980s, the continuously increasing cost and the limitation of the budget in the health care system resulted in the first cost cutting measures temporarily slowing down the growth of the pharmaceutical industry. But in the wake of the radical political changes that took place in Germany and Eastern Europe after 1989, the companies could increase their focus on these promising markets.

A crucial change has taken place during the 1990s in orientation of the major players in the German pharmaceutical industry, including:

- some companies focused all their activities on pharmaceuticals and separated their chemicals, while others sold their pharmaceutical branch

- new generic companies entered the market due to changes in legislation supporting generics and re-imports

In Germany, the same big players, as in most OECD countries, are leading the industry. The leading pharmaceutical company of national origin is Boehringer Ingelheim. Generic manufactur-

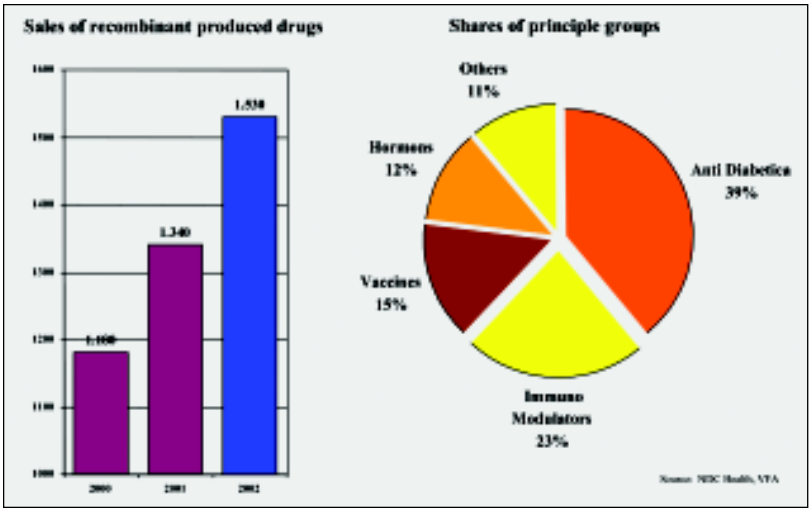


Figure 8. Market of recombinant produced drugs.

ers or re-importers are gaining market share due to German legislation. In total, there are 600 pharmaceutical manufacturers present on the national market. The pharmaceutical industry is employing about 115,000 workers, where more than 83,000 are with R&D based companies. But only 3.7% of all expenses of the national health security system are related to innovative drugs.

Another reason for recession in international competitiveness is the political initiated promotion of re-imports with a fixed sales quota of 5.5% in 2002 and up to 7% in 2003 for reimbursed drugs by GVK. Due to the political instruction, the prices of re-imported drugs had the chance to approach the prices of original products. This created financial gains for the distributor only but not for compulsory health insurance, the pharmaceutical manufacturer, or the patient.

Another problem on the horizon is that for the first time ever the importation of drugs has surpassed exportation. Exportation decreased in 2002 by 15.5% due to the negative general pharma-economical conditions in a high cost labor country.

The pharmaceutical industry is mainly concentrated in the southwest of Germany. Along the river Rhine, the traditional chemical – pharmaceutical industry has its origin. Also there is strong contact with the Swiss pharmaceutical industry situated in Basel, as well as the Rhine river valley. Pharmatechnology suppliers are concentrated in this area, especially engineering firms. After reunification of Eastern Germany some state owned facilities were sold by the government to West German or international companies. After renovation of obsolete equipment and buildings, they have reached high competitive level in GMP and efficiency. Most known is the large scale Aspirin factory of Bayer in Bitterfeld.

Research and Development

About 14,500 professionals are engaged directly in research and development in Germany. The involved pharmaceutical companies are investing €3.6 billion in R&D annually, that means more than €10 million per day. They spend in average of about 16% of sales for R&D activities.

Companies with R&D activities have invested during the last few years an average of more than €1.3 billion annually, which means their investments increased faster than sales.

In the year 2000, the Federal Institute for Drugs and Medicinal Product (BFArM) received 431 Phase I, 292 Phase II, and 492 Phase III study applications. With improved political-economical conditions, it would be possible to conduct much more studies than now. A change could result with the upcoming amendment of the German drug law, by which the EC regulation regarding the harmonization of clinical trials in Europe has to be adapted to German law.

Biopharmaceuticals

In Germany, biotech has two aspects: the research and development and production with export. In the German market, there are 102 genentechnical-produced drugs based on 74 molecules registered. The share of genetic produced drugs is increasing continuously with sales of €1.53 million and participation of total market (pharmacies) of 8.3% in 2002. Ad-

Drug	Main Indication	Company	Trade Name
Insulin, human	diabetes mellitus type 1	**Aventis**	Insulin Aventis Insuman; Lantus
Erythropoietin beta	renal anemia	**Roche**	Recormon
Interferon gamma 1b	chronic granulomatosis	**Boehringer Ingelheim**	Imukin
Interferon gamma 1b	chronic granulomatosis	**Schering**	Betaferon
tissue plasminogen activator, t-PA	coronary thrombosis, thrombosis	**Boehringer Ingelheim**	Actilyse
Tenecteplase	coronary thrombosis, thrombosis	**Boehringer Ingelheim**	Metalyse
Gewebe-Plasminogen-Activator, r-PA	coronary thrombosis, thrombosis	**Roche**	Reteplase

Figure 8. Recombinant drugs produced in Germany.

ditionally, there are sales in the hospital segment, but currently there is no data available.

Today, Germany is the most important location for production of geneticly modified drugs in Europe. With fermentation production capacity of more than 470,000 liters, mainly in the most modern facilities in the world, Germany passes its European concurrent and reaches the second position after the US.

Currently, 15 genetic modified drugs are produced and exported worldwide. Those are medications for the treatment of diabetes, anaemia, hepatitis C, cancer, rheumatic arthritis, and myocardial infarction.

Last year Germany conducted for the first time a statistical survey for biotechnical activities by the German federal statistical secretary. The data available are for the year 2000. The survey identified five categories:

- Category I - biotech core companies with modern biotechnical processes according to OECD definition
- Category II - suppliers of technical products and services for biotech companies
- Category III - combination of Category I and II
- Category IV - major companies from the Life Science Industry with significant biotechnical activities
- Category V - consultants and financial services of the Biotech branch

OECD definition: the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.

The survey includes all types of Biotech activities, but the "red" Biotech, with human, veterinary medical, or pharmaceutical activities is dominating, reaching 70% in the number of Category I companies in the Biotech area. The focus of this article are the companies of Category I and IV, but in the table "general numbers" are also listed for the other categories.

	Companies				
Attributes	I	II	III	IV	V
Number of companies	**313**	209	24	**24**	96
Employees	**9,906**	17,786	1,332	**8,933**	327
Employees in R&D	**3,337**	-	247	**2,401**	-
Sales in € million	**594**	1,200	136	**3,500**	37
R&D expenses in € million	**399**	-	19	**368**	-

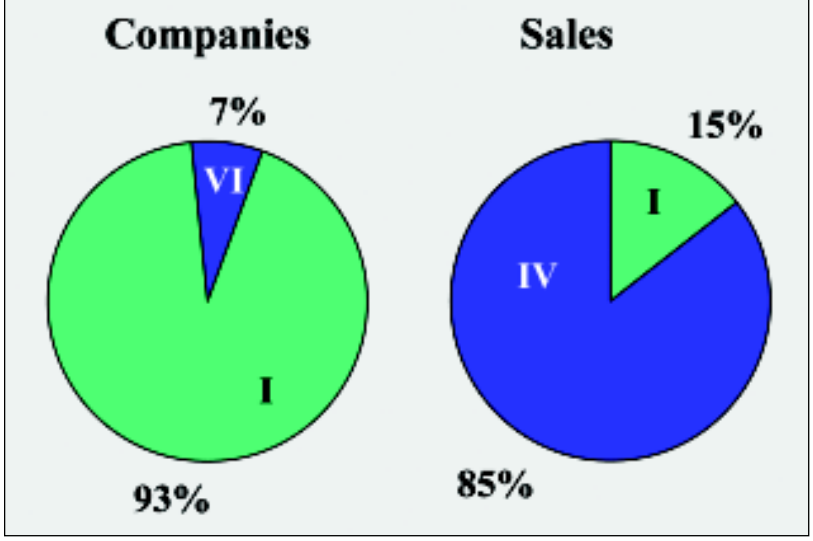


Figure 10. General numbers Biotech Germany.

From the 313 companies in which Biotech is the core business (Category I), about 50% of the 9,906 employees are working in 21 companies with more than 100 employees. That means the rest of the 290 companies are medium size with about 20 employees. In these smaller companies, the participation of employees in R&D reaches nearly 66%, whereas the average in Category I is 34%.

Analyzing the ratio of sales (€594 million) to the expenses for R&D (€368 million) in this category, it can be assumed that most of the companies in 2000 were still start-up companies, far away from gaining profits.

The major companies from the Life Science Industry are contributing mainly to economic power of the biotech branch in Germany. The six leading companies are responsible for €3.150 million, in other terms 90% of all sales in the Biotech Life Science Industry. Each of them reach sales above €100 million annually. The Biotech activities in Germany are concentrated in the states of:

- Baden-Wuerttemberg - with local spots of BioValley in the trinational region (Germany/France/Switzerland), BioRegion Ulm and the surrounding of the university place Heidelberg
- Bavaria - with the local spot of Martinsried near Munich
- Hessen - concentrated around the city of Frankfurt
- Nordrhein-Westfalen

Biotech is made up of about 60% of the investments of venture capital and private equity related to health orientated industry (Biotech, small molecules pharmaceuticals, medicinal technique, consumer the health care). Although the investments decreased with the stock crisis in 2001/2002, biotech achieved €8,500 million in 2002.

In the future, the next solid basis for venture capital in biopharmaceuticals is given by the solid pipeline of new drugs. Venture capital is not only relaying anymore to brilliant ideas and business models of pioneers, but more and more to developed molecules passing through the phases of clinical studies to the market.

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Pharmaceutical Engineering Know-How in Germany and Switzerland
Interview of Klaus Köhler, Pharma Industry Manager, Endress + Hauser Germany

An Overview of German/Swiss Equipment Suppliers
A general overview of pharmaceutical industry machinery suppliers in the German-Swiss region.

A Country Profile of Switzerland

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The Swiss Paradox

Switzerland could be considered as a country of paradox, as a small country with an insignificant domestic market for pharmaceuticals, though, it is one of the major drug manufacturers of the world. Scientists in Switzerland have contributed substantially to expand the frontiers of biomedical research for the benefit of mankind.

In comparison with similar developed countries, the Swiss inhabitant devotes less money for drugs. For example, in the USA, France, Italy or Germany, the expenses for drugs per inhabitant are 1.5 times higher than in Switzerland. However the major[1] Swiss pharmaceutical companies represent 7.5% of the world wide pharmaceutical market with a turnover of $30 billion.

Public Health Care

There are a large number of providers of health care products and services in Switzerland. The quality of the health care system is acknowledged to be excellent, but costs are correspondingly high. Between 1970 and 2001, the number of practicing physicians more than doubled, from 5,500 to 14, 178. While the number of pharmacies was still rising up to 2000, more than 300 drugstores closed down between 1970 and 2001.

Table A shows the evolution of resources in public health care between 1990 and 2001.

	1990	1995	1999	2000	2001
Practicing Physicians	**10,398**	**12,327**	**13,622**	**13,935**	**14,178**
– per 10000 inhabitants	15.3	17.5	19.0	19.3	19.5
General Practitioners	**3,858**	**4,364**	**4,604**	**4,849**	**4,877**
– per 10000 inhabitants	5.7	6.2	6.4	6.7	6.7
Specialists	**6,540**	**7,963**	**9,018**	**9,086**	**9,301**
– per 10000 inhabitants	9.6	11.3	12.6	12.6	12.8
Dentists working in their own practice	**3,788**	**3,790**	**3,933**	**3,941**	**3,929**
– per 10000 inhabitants	5.6	5.4	5.5	5.5	5.4
Physiotherapists	**2,016**	**2,801**	**3,400**	**3,400**	**3,670**
– per 10000 inhabitants	3.0	4.0	4.7	4.7	5.1
Chiropractors	**153**	**188**	**205**	**213**	**215**
– per 10000 inhabitants	0.2	0.3	0.3	0.3	0.3
Pharmacies	**1,536**	**1,641**	**1,654**	**1,677**	**1,669**
– per 10000 inhabitants	2.3	2.3	2.3	2.3	2.3
Drugstores	**978**	**883**	**839**	**829**	**796**
– per 10000 inhabitants	1.5	1.2	1.2	1.2	1.1
Hospitals[1]	**530**	**555**	**585**	**565**	**592**
– per 10000 inhabitants	0.8	0.8	0.8	0.8	0.8
No. of people employed in public health care, approx.[2]	**317,000[3]**	**358,000**	**395,000**	**399,000**	**408,000**
– per 10000 inhabitants	466	506	551	554	562

[1] Hospitals with in-house pharmacy only [2] Incl. social care [3] Figure for 1991

Table A. The evolution of resources in public health care between 1990 and 2001 (Source: Pharma Information, Basel; Swiss Medical Association (FMH), Berne; IHA-IMS Health, Hergiswil; Swiss Physiotherapists Association (SPV), Zurich; Swiss Chiropractors Society (SCG), Berne; "Statistisches Jahrbuch der Schweiz", various years; and Federal Statistical Office, Neuchâtel).

At the same time, this increasing of health care resources is associated with a significant increasing of the health care costs, as shown in Figure 1.

Since 1995, total health care costs rose from CHF 36.2 billion to CHF 43.3 billion between 1995 and 2000, an increase of 20%. In 2001 there was no increase in the price index for medical treatment. The price index for drugs was the lowest at 99.8, below the 100 mark set in 1993. Despite only a slight increase of 0.8 percentage points, the price index for hospitals was still the highest (115.6).

As in previous years, outpatient treatment by physicians, hospitals, physiotherapists, home care (Spitex) and chiropractors accounted for the highest gross costs within compulsory health care insurance in 2000: 47%. This was followed by inpatient treatment in hospitals and nursing homes, accounting for 32% of costs, and by drugs, accounting for just under 21%. Outpatient treatment in hospitals posted the greatest growth in 2000 (12%), followed by drugs (11.6%). The total cost of compulsory health care insurance rose by 5.9% in 2000, 1.6 percentage

points more than in 1999.

One third of the costs of health care were paid directly by private households, its actual burden however, was twice as high, 66.9%. The health insurance costs represent 5.8% of the expense for each Swiss private household.

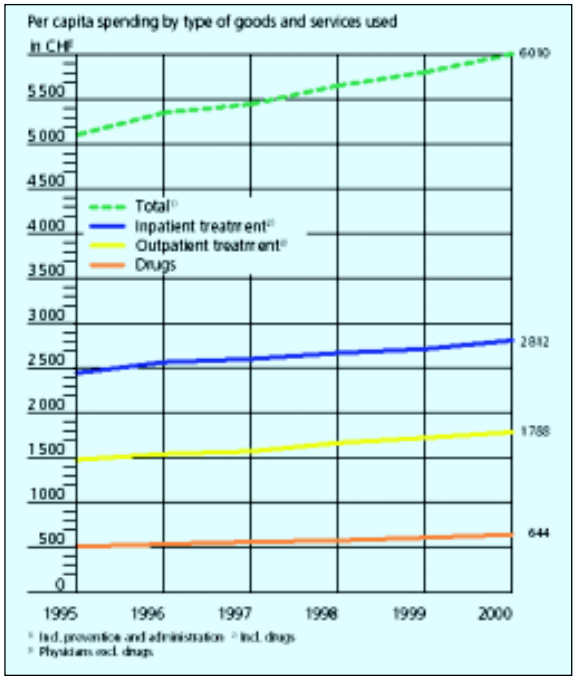

Figure 1. The increasing of health care resources is associated with a significant increasing of the health care costs (Source: Pharma Information, Basel).

The Pharmaceutical Market

Currently in most OECD countries, more than 10% of the health care expenses are devoted to drugs. In France and Italy, this ratio is greather than 20%. In Switzerland, this ratio is around 11%. Indeed each Swiss inhabitant spends 1.5% of his income for drugs. This should be considered in comparison with other expenses like housing rent (14.5%), income taxes (11.9%), car (5.4%), restaurant (5.0%) or phone (1.5%).

Registered Drugs

All drugs available in Switzerland from Switzerland are registered by a federal public agency for therapeutic products: Swissmedic, in Berne. In 2001, the Swissmedic list contained a total of 7,890 drugs for human and veterinary use. In 1985, the number of registered items was 3,137 higher (11,027 drugs and medical devices).

Since 1998, medical devices have ceased to figure on the Swissmedic registration list. On the basis of the relevant risk/benefit ratio, Swissmedic divides human drugs into various lists, which also provide information on who is authorized to dispense them. In 2001, the drugs on lists A and B (prescription drugs) accounted for approx. 53% of all registered drugs.

Drugs Covered by Health Insurance

Not all drugs are covered by compulsory health insurance. The drugs subject to cover are contained in the "List of Proprietary Medicines" ("Spezialitätenliste", SL) published by the Federal Social Insurance Office ("Bundesamt für Sozialversicherung", BSV). The criteria for inclusion in this list relate not only to the efficacy and suitability of a drug but also to its cost-effectiveness. This decision is made by the BSV, normally at the request of the Federal Drug Commission ("Eidgenössische Arzneimittelkommission", EAK).

In 2001, the list contained approximately 2,499 drugs in 6,502 different packaging units. 79.9% of the items were prescription drugs (sales categories A and B) and 20.1% were non-prescription drugs (sales categories C and D). In contrast, there were 4,547 drugs (64.5%) which were not covered by the health insurance organization (obligatory sick funds or private insurance companies).

Distribution Channel

Owing to the liberalization of the pharmaceuticals market and the introduction of the new service-based compensation model ("LOA") for pharmacies, an accurate survey of sales in the different distribution channels is difficult. The most adequate way for comparison is therefore at the level manufacturers' prices.

In 2002, CHF 3,644 million was spent on pharmaceutical products, 6.6% more than in the previous year. The average annual growth during the last three years comes to 7%.

Prescription Drugs

In 2002, prescription drugs, at manufacturers' prices, accounted for 78.8% of total drug sales (CHF 2,870 million). Prescription drugs are classified as types A and B on the sales lists of Swissmedic, and are distributed by pharmacies, hospitals, and SD physicians.[2]

Non Prescription Drugs

Non-prescription drugs can be purchased over the counter (OTC) at pharmacies and drugstores, or can be prescribed by SD physicians or in hospitals. Non-prescription drugs include medicines bought in pharmacies and drugstores without a prescription and medicines prescribed in medical practices and hospitals. In 2002, non-prescription drugs accounted for 21.2% of the total drug market in Switzerland.

Generics Market

Between 1990 and 2002, the volume of the generics market grew from CHF 27.2 million to CHF 102.7 million at manufacturers' prices. In 2002, they accounted for 3% of the market, which corresponds to sales of CHF 102.7 mil-

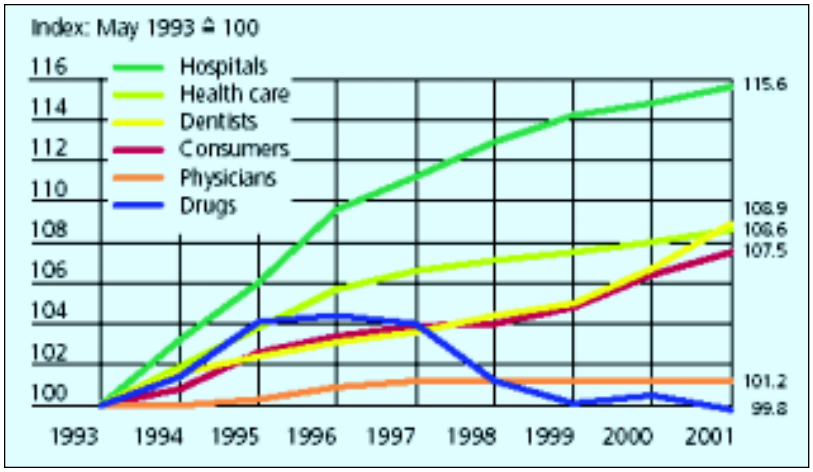

Figure 2. (Source: Pharma Information, Basel).

lion at manufacturers' prices. Patent-protected original brands accounted for 60.4% of the market. Thus the sector offering potential for generics amounted to 37.2% of the market. This sector consisted of off-patent original brands (27.5%) for which no generics existed, and of off-patent original brands (9.7%) for which generics existed.

Distribution Channel	At Manufacturers' Packs Prices	Packs
Pharmacies	CHF 2,024 m	110.5 m
SD Physicians	CHF 807 m	29.7 m
Hospitals	CHF 671 m	23.5 m
Drugstores	CHF 142 m	20.6 m
Total Sales	**CHF 3,644 m**	**184.3 m**

Table B. (Source: IHA-IMS Health, Hergiswil/ Pharma Information, Basel).

Distribution Channel	At Manufacturers' Packs Prices	Packs
Pharmacies	CHF 1,501 m	40.7 m
SD Physicians	CHF 733 m	20.8 m
Hospitals	CHF 636 m	18.6 m
Total Sales	**CHF 2,870 m**	**80.1 m**

Table C. (Source: IHA-IMS Health, Hergiswil/ Pharma Information, Basel).

Distribution Channel	At Manufacturers' Packs Prices	Packs
Pharmacies	CHF 522 m	CHF 69.8 m
Drugstores	CHF 142 m	CHF 20.6 m
SD Physicians	CHF 74 m	CHF 8.9 m
Hospitals	CHF 35 m	CHF 4.9 m
Total Sales	**CHF 773 m**	**104.2 m**

Table D. (Source: IHA-IMS Health, Hergiswil/ Pharma Information, Basel).

Rise in Imports

About 28% of drugs sold in Switzerland in 2001, representing sales of CHF 962 million (at manufacturers' prices), are manufactured in Switzerland itself. Of these, the Interpharma companies Novartis, Roche and Serono (and their subsidiaries) account for 60%, or 16.9% of the total Swiss pharmaceutical market. About 72% of the drugs sold in Switzerland are imported.

The Swiss Association of Importers of Proprietary Medicines ("Vereinigung der Importeure Pharmazeutischer Spezialitäten", VIPS) comprises 70 companies active in Switzerland. They are subsidiaries of foreign pharmaceutical companies or Swiss pharmaceutical importers.

VIPS members and other importers account for about 72% of the Swiss pharmaceutical market. In 2001, their retail sales came to CHF 2,423 million (at manufacturers' prices).

The Swiss Pharmaceutical Industry

The pharmaceutical industry and its employees represent an important factor in the economic life of Switzerland, as well as of Basel and its neighboring areas. In the canton of Basel City alone, Novartis and Roche account for one third of total revenue from taxation, and it is the source of one fifth of income in the Basel region. This industry is also responsible for 52% of regional net product.

Switzerland numbers about 420 companies whose chief business is the manufacture and trade of pharmaceutical products. Of these 420 companies, only 130 have manufacturing facilities and only ten employ more than 500 people. However, the structure of the pharmaceutical industry in the country is dominated by the two major enterprises Novartis and Roche, both located in Basel (see map below).

Why Basel? A number of factors coincided towards the close of the 19th century to make Basel a favorable site for the establishment of the chemical industry, which is the base of the pharmaceutical industry. The prominence of Basel as an economic and cultural center can be traced back to the Middle Ages. At that time, the Rhine Bridge in Basel (built 1226) was the only one, looking downstream, until well into the lower reaches of the river at Cologne. As a result, the city became a major commercial and trading center, as well as a station on the important north south transalpine route. The foundation of the university in 1460 brought a new dimension to the city: it became an influential center of learning and culture. Apart from the city's trade links, good communications and its role as a university town, there was a further factor favoring the growth of the chemical industry in the region; namely the local silk-ribbon and cotton industry, which had developed in neighboring parts of Switzerland, the French Alsace and German Baden in the 18th century.

The oldest firm within the

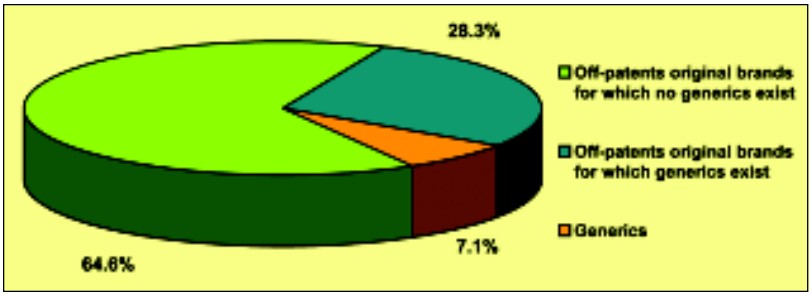

Figure 3. (Source: IHA-IMS Health, Hergiswil/Pharma Information, Basel).

chemical industry at that time - J.R.Geigy Ltd. - began in 1758 as a dealer in chemicals, dyestuffs and drugs of all kinds. Shortly before the start of the Second World War, Geigy achieved a breakthrough with the discovery of DDT. Its discoverer, Paul Mueller, was awarded the Nobel Prize. Geigy marketed its first drug in 1938, but its first real breakthrough in pharmaceutical research came with the development of Butazolidin, an anti-rheumatic agent. In 1859 Alexander Clavel's factory and in 1886 Kern & Sandoz, also began producing new dyestuffs in Basel. Clavel turned its name into Ciba in 1884. As early as 1889, Ciba showed its first pharmaceutical products at the International Exhibition in Paris. Antipyrine, an agent to reduce febrile temperatures, was particularly successful. After two years as a pharmacy, Hoffmann-La Roche began to develop and manufacture pharmaceutical specialties in 1896. Roche made use of the innovation to publicize one of its first products, Siroline, a cough syrup that remained on the market until 1964. Roche was also the first European company to publish its own scientific journal. In 1917, Sandoz established a pharmaceutical division. In 1921, Gynergen, an important preparation in the field of obstetrics, appeared on the market. The period before the Second World War also saw the formation of the first subsidiary companies and branches abroad (England, France, USA) of these important enterprises. The development of the pharmaceutical industry in the post war years might almost be described as explosive. In 1971, Ciba and J.R. Geigy initiated the first Basel fusion within the chemical/pharmaceutical industry. 25 years later, in 1996, Ciba-Geigy and Sandoz merged and founded Novartis.

To complete the chemical and life sciences position of Basel, the foundation of Syngenta in November 2000 should be mentioned. Syngenta was founded by the merger of Novartis Agribusiness and Zeneca Agrochemicals. It is the world's largest dedicated agribusiness, employing more than 20,000 people and operating across all important areas of crop protection and seeds.

From the outset the fact that the chemical-pharmaceutical industry was located in a country with few raw materials meant that the companies had to produce highly processed, high quality goods. The main fields of research and development of the major companies are, cancer, cardiovascular and geriatric diseases, immunology, rheumatism, central nervous system, infections, and dermatology. Today, biotechnology and genetic engineering are the most important tools in R&D. About 26,000 people work in this industry, worldwide the Swiss pharmaceutical companies employ 82,000 persons approximately.

Strong Export Position

In 2002, according to the international drug market statistics compiled by Information Medical Statistics[3] (IMS), the three biggest Swiss pharmaceutical companies - Novartis, Roche and Serono - represent 7.5% of the global pharmaceutical market and contribute significantly to the very positive pharmaceutical balance of trade.

Drugs are high-tech quality products and, in 2001, once again produced excellent trade results. Pharmaceutical exports were valued at approximately CHF 27.7 billion. This corresponds to 66% of Switzerland's total chemical exports or 20% of the country's total export volume. Switzerland earned an export surplus of CHF 14 billion on pharmaceutical products in 2001. More than 90% of the drugs manufactured in Switzerland are destined for export. Europe is the largest buyer (CHF 18.1 billion), followed by America and Asia. 82% of imported pharmaceutical products are manufactured in Europe. In terms of value, this is equivalent to CHF 11.3 billion.

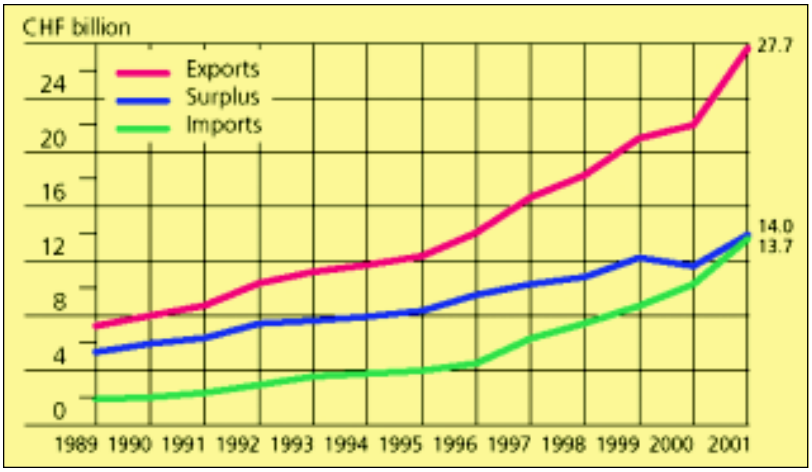

Figure 4. (Source: Federal Customs Administration Statistics, 2001, Berne/ Pharma Information, Basel).

Research and Development

This strong position of the Swiss pharmaceutical industry on the global market is the result of an active research strategy. The three Interpharma companies – Novartis, Roche and Serono – spent around CHF 7.0 billion on researching and developing new drugs worldwide in 2002. This figure is equivalent to 17.3% of their total pharmaceutical sales.

In 2002 the three companies sold drugs worth CHF 507 million in Switzerland, just 1.2% of their global sales. Nonetheless, Novartis, Roche and Serono spent some CHF 3.0 billion on pharmaceutical research and development in Switzerland in the same year. This represents 44% of their global outlay on pharmaceutical research and development.

In 2002, the total expenses for research and development in Switzerland were CHF 10 billion. Around 69% of these are supported by private companies, 23% by the Confederation and the Cantons, non-profit organizations and engineering institutes brought 3.4%.

Year	Product	Company	Indication
1992	Hivid	Roche	AIDS
	Lentaron	Novartis	Breast cancer
	Leucomax	Novartis	Neutropenia during cancer chemotherapy
	Navoban	Novartis	Emesis during cancer chemotherapy
1993	Lescol	Novartis	Cholesterol lowering
1994	Vesanoid	Roche	Acute promyelocytic leukemia
1995	CellCept	Roche	Kidney transplants
	Cymevene	Roche	Viral infections (CMV)
	Gonal-F	Serono	Follicle-growth disorders
1996	Diovan	Novartis	Hypertension
	Femara	Novartis	Breast cancer
	Invirase	Roche	AIDS
	Serostim	Serono	AIDS cachexia
1997	Exelon	Novartis	Alzheimer-type dementia
	Mabthera	Roche	Non-Hodgkin's lymphoma
1998	Rebif	Serono	Multiple sclerosis
	Simulect	Novartis	Organ transplants
	Xeloda	Roche	Breast cancer
	Xenical	Roche	Obesity
	Zenapax	Roche	Organ transplants
1999	Comtan	Novartis	Parkinson's disease
	Herceptin	Roche	Breast cancer
	Tamiflu	Roche	Influenza
2000	Luveris	Serono	Infertility
	Ovitrelle	Serono	Infertility
	Starlix	Novartis	Diabetes
	Zometa	Novartis	Malignant hypercalcemia
2001	Zelmac	Novartis	Irritable colon
	Pegasys	Roche	Hepatitis C
	Glivec	Novartis	Leukemia (CML)

Table E. Major achievements in pharmaceutical research between 1992 and 2001 (Source: Pharma Information, Basel).

Innovation at Interpharma Companies

Table E lists some important drug products developed in the research laboratories of the Interpharma companies worldwide in the last 10 years. All these products are new chemical entities (NCEs) and are therefore classified as "innovative drugs". The Interpharma companies' research laboratories develop an average of three new active substances each year which are submitted for registration.

Biotechnology

There is a long history of Swiss contributions to the evolution of modern biotechnology which started with Friedrich Miescher's discovery of DNA in the late nineteenth century, continued with Werner Arber's Noble Prize winning discovery of the restriction enzymes (the so-called gene scissors), Noble laureates Jerne, Tonegawa and Köhler from the Basel Institute for Immunology, and the Nobel laureate in medicine, Rolf Zinkernagel and Kurt Wüthrich. Swiss scientists have been in the forefront of expanding scientific knowledge for the benefit of mankind. Whether it is in the search for the causes of "mad cow disease" (BSE), where the European Community turned for advice to Charles Weissmann in Zurich and highly innovative research groups working in Zurich and Geneva, or the quest for an understanding of Alzheimer's where scientists from Novartis in Basel were able to develop an animal model for the study of the disease. Research in Switzerland can compete with the world's leading science laboratories.

The Swiss role in modern biotechnological research is sometimes undervalued. Even usually

well-informed observers of the Swiss economy often erroneously believe that most of Swissfunded research is carried out in the United States where most of modern biotech companies reside. However, whereas it is true that the thriving US biotech industry with its more than 1,000 start-up companies is unmatched in Europe, the existing strength and potential of biotechnology in Europe and, in particular, in Switzerland should not be misjudged. Almost half of the research jobs of Swiss pharmaceutical research companies Novartis and Roche are based in Switzerland, 2,200 out of 4,600. A study done by the Zurich Polytechnic (ETH), based on 1994 figures, showed that Swiss companies spent 17% of their CHF 4 billion research budget on genetic research, with an above average amount spent in Switzerland. But modern biomedical research is not a reserve of industry. Noteworthy that some 70 percent of research projects applying gene technology in Switzerland were done within university and hospital laboratories.

Sales of the 63 genetically manufactured products (55 drugs and 8 vaccines) which had been approved in Switzerland up to February 2002 accounted for CHF 159 million in 2001 (at manufacturers' prices). The highest sales figures were for medicines for the treatment of disorders of blood formation (e.g. for treating myocardial infarction), with 25% of the market in terms of value, followed by anticancer drugs (19%). Vaccines accounted for 8% of total sales in this area.

References

1. Members of Interpharma: Novartis, Roche, Serono.

2. Doctors with their own dispensary.

3. In 2002, the consolidated IMS figures covered about 70% of the total market in prescription drugs (excluding hospitals) at manufacturers' prices and may therefore diverge from the figures published by the companies. The global market is estimated at about $400 billion.

Additional Source

InterPharma, Basel, OECD Health Data, 2002.

Approval of Drugs Subject to Coverage by Health Insurance Companies

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