Chapter 1
The Process Industry

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1.1 Segments of the Process Industries

Process industries cover a wide range of businesses, typically from the chemical, pharmaceutical or life science, oil, gas, steel, paper, and glass industries, but also from the consumer goods sectors like cosmetics and food. However, the literature on the subject does not provide a single common definition of the process industry.

The production processes used in process industries differ significantly from those used in discrete manufacturing. While discrete manufacturing is based on discrete unit production, that is, component-based production and assembly processes, process manufacturing is characterized by continuous or discontinuous (batch) production processes. This results in the production of quantities or volumes rather than units. In process manufacturing, products are manufactured in production networks linked to each other via a distribution network. Typical for the industry are also regulatory standards and quality management requirements, which present their own particular challenges for production and logistics.

This book does have a focus on the chemical and pharmaceutical industries. Other segments are not considered. There are significant differences between pharmaceutical and chemical industries: the introduction of different technologies, changes in downstream markets, growth perspectives, drivers of success, approaches to innovation and changing shareholder expectations (CEFIC 2004). Since these are the crucial factors for economic success, the chemical and pharmaceutical industries are examined separately in this book.

1.1.1 The Chemical Industry and its Share in the Economy

The chemical industry refers to companies that, in the widest possible sense, are dealing with the processes of transforming natural and manufacturing synthetic raw materials. These materials are typically used by other industries to create products mainly for the industrial and less for consumer products markets.

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Similar to process industries as a whole, there does not exist a common agreement which industry fields belong to the chemical industry. Therefore, a precise definition is not possible. Considering the official classifications throughout the world, there is also less convergence. Historically, the chemical producers have seen themselves belonging into one of the five main segments: basic chemicals, specialty chemicals, agricultural chemicals, pharmaceuticals, and consumer products. The differences apply to the structure, growth dynamics, markets, and other special issues, but in many cases a clear distinction is not possible (ACC 2011).

Generally, the chemical industry can be divided into two sectors:

Basic (*or commodity*) *chemicals* are produced in large volumes with no product differentiation. They are primary products for further processing. These include inorganic chemicals, bulk petrochemicals and organic chemical intermediates, petrochemical derivatives and other industrial chemicals, plastic resins, synthetic rubber, and synthetic fibers.

Basic chemicals are a mature business. Prices are highly correlated with capacity utilization and feedstock costs. Companies generally employ low-cost leadership strategies. The low profit margins and a strong sensitivity toward economic cycles are typical features. Availability of feedstock and large capital (plant size, technology) and energy requirements are strong barriers to entry (ACC 2011).

Specialty chemicals (*or specialties*) are differentiated and often technologically advanced products. They are manufactured in lower volumes than basic chemicals and are used for a specific purpose—basically as solutions to problems. A feature distinguishing specialties from basic chemicals is their large customer servicing or technical servicing component. That is, they are sold for what they do, rather than for what they contain. Included are for example coatings, adhesives, and sealants.

Specialty chemicals companies are generally niche players and fragmented along specialty market lines. Nevertheless the long-term growth prospects for specialties are mostly more dynamic than for basic chemicals. The customer industries needs are rising and the lower volumes allow easier transportation. Specialty chemicals prices tend to be set by "value-in-use", not by cost and historically their earnings have not been impacted as much by demand pressures. In general, specialty chemicals represent a small portion of customers total cost, but they are essential to enhancing productivity and performance. Innovation is critical there and producers of specialties typically spend 4–8 % of their revenues on research and development. Strong technical servicing, marketing and distribution competencies are a must. Patents and technology requirements are high barriers to entry (ACC 2011).

Agricultural chemicals can be seen as a part of specialty business. A distinguishing feature is that only one end-use customer industry—farming—clearly dominates. This sector produces primary fertilizers and crop protection.

Segments like food, cosmetics or detergents are often labeled as *consumer products* within the process industries, because they are manufactured in batch-type operations. Consumer products feature a high degree of differentiation along branding lines. Markets are segmented along distribution channels, price points, and customer demographic lines. Brand advantages and product development are

extremely important, as is the management of distribution channels. The profit margins are higher than for basic chemicals although long-term prices are falling fast. This context makes the analogy to consumer products in other industrial segments clear. Since consumer products are subject to the book "Innovative Design of Business Processes in the Consumer Goods Industry", they will not be further discussed.

The world chemical turnover share by segments shows, that basic chemicals are predominant in the global business of chemistry (Fig. 1.1).

The chemical industry produces a high number of different products for all manner of applications. The products can be found in almost all manufactured goods. According to the American Chemistry Council, over 96 % of all manufactured goods in the US are directly touched by chemistry. Including indirect support, chemistry touches 100 % of manufactured goods (ACC 2011). This implies that the chemical industry has a great impact on the economy. The pricing and quality directly influence the downstream production. The scientific improvements enable better productivity, health, and safety. Longer lasting paints, stronger adhesives, better packaging materials, faster microprocessors, lightweight automobile parts, synthetic fibers and permanent-press clothing, health-improvement products are only a few examples. The commitment of the chemical industry to the goal of the sustainable world economy is essential for the success of the topic.

Vice versa, as chemicals are being a part of nearly any manufactured good the economic climate itself has a bearing on the sales and profits made by chemical companies. As a result, compared with the pharmaceutical industry, for example, the chemical industry is strongly influenced by economic cycles.

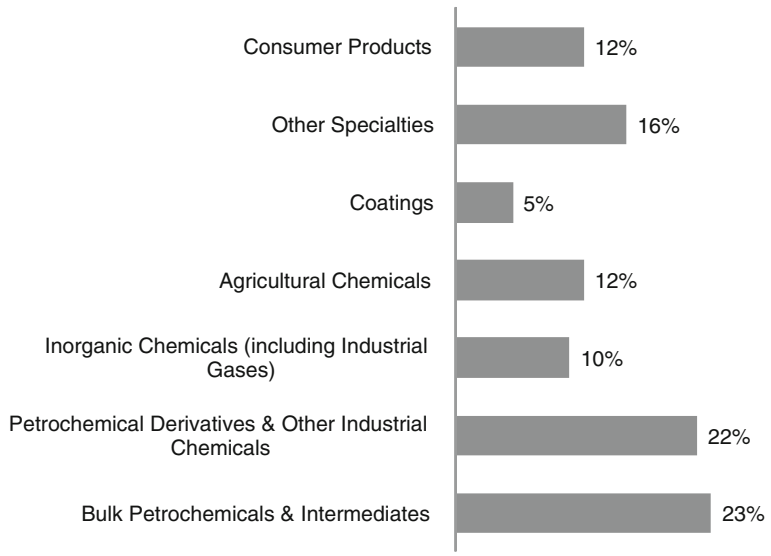


Fig. 1.1 Global chemical shipments by segment (2010, percentage) (ACC 2011)

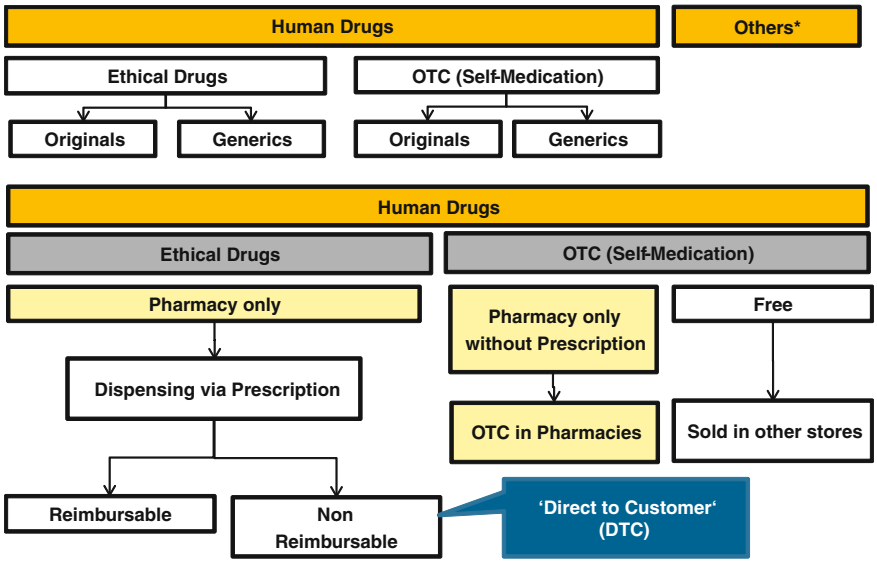
1.1.2 The Pharmaceutical Industry and its Share in the Economy

The pharmaceutical industry refers to companies that produce and/or sell drugs. It is the main group in the life sciences industry next to the manufacturers of veterinary medical products, the diagnostics industry and the producers of medical equipment and dressing materials.

The products from the pharmaceutical industry fall into two categories: products available only on prescription (also known as ethical drugs) and products available over the counter (Fig. 1.2). While ethical drugs are sold on medical prescription, the OTC-products are available to purchase directly without prescription.

The manufacturers of pharmaceutical products can generally be divided into pharmaceutical research manufacturers (originators) and producers of generic drugs.

Research companies are pharmaceutical companies that develop drugs and apply to have them licensed. These companies then possess the patents for these drugs for a fixed period of 20 years. When the patent protection for a drug expires, the originator no longer has exclusive manufacturing rights and the product is opened up to the general manufacturing market. It is at this point that generic drug manufacturers come into play. Generic drugs are a copy whose active ingredients match those of the original product but whose galenics may vary and for which the manufacturing technology may differ. The therapeutic effects of the generic drug must match those of the original product.



* Others: animal health, diagnostic, surgical and hygienic products

Fig. 1.2 Product differentiation in the pharmaceutical industry (in Germany)

Generic drugs are usually far less expensive than the original product because the level of spending required for research and development as well as for registration is either much lower or non-existent, which means this outlay does not have to be recouped through the sales price. A prominent example of a generic drug is the active ingredient acetylsalicylic acid. Developed and established under the name "Aspirin" by Bayer, this active ingredient is also available as a product from a wide range of other manufacturers besides Bayer under various different names.

Industry practice shows that there are often mixed forms, for example, originators with their own generic drug line or generic drug manufacturers who focus strongly on research.

1.2 The Global Chemical Market

1.2.1 Key Figures

Global Chemical Sales

Chemical products play a fundamental role in most of the countries in the world. However, more than 90 % of the world chemical output is provided only by 3 regions: Asia (48 %), Europe (25 %), NAFTA (19 %) (Fig. 1.3). It is also remarkable that the Asian (48 %) chemical production is higher that the European (25 %) and American (19 %) together. In 2008 the ratio was yet 38 % (Asia) to 51 % (EU-27+NAFTA). The world chemical sales amounted to 1,950 billion euro in 2008, two years later it was 2,353 billion euro. It is obvious, that the emerging countries essentially contributed to the recovery of the sector after the world financial crisis in 2009 (CEFIC 2011).

Considering the countries, the differences are even more apparent. Only four countries: USA, China, Japan, and Germany account for more than 50 % of the world chemical output (Fig. 1.4). In 2008 the US was the world leader with 374 billion euro chemical sales, in 2010 the US achieved a rise to 395 billion euro. However, China gained the first position in 2010 with 575 billion euro, which is more than a 70 % growth to 337 billion euro in 2008 (CEFIC 2011).

Global Chemical Growth

The long-term figures of the growth show a non-surprising lead of the Asian region (Fig. 1.5). In the five-year-period from 1999 to 2004, the European and North American chemistry achieved only moderate growth. In the next five-year-period until 2009 there were even negative growth rates. In contrast, the Asian-Pacific Region[1] was booming with average growth rates of about 5 % in both periods.

[1] Asian–Pacific Region includes Australia, Bangladesh, China, India, Japan, Korea, Malaysia, Pakistan, Philippines, Singapore, Taiwan and Thailand.

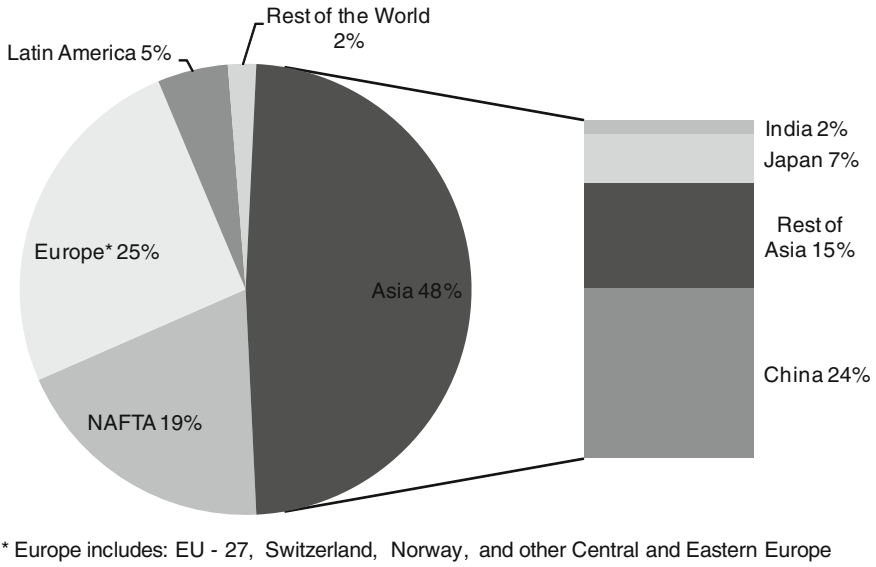


Fig. 1.3 Regional breakdown of world chemical sales (2010, percentage) (CEFIC 2011)

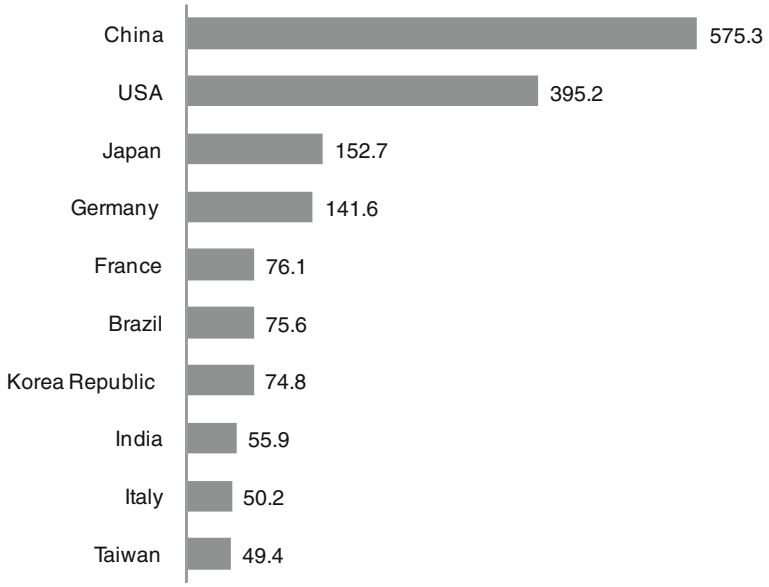


Fig. 1.4 World chemical sales by country (2010, billion euro) (CEFIC 2011)

Throughout the whole ten-year-period (1999–2009) the EU grew only by 0.1 % and the average growth rates of the NAFTA-region counterbalanced themselves to 0 %. Despite of the strong reduction in the second period, Latin America still

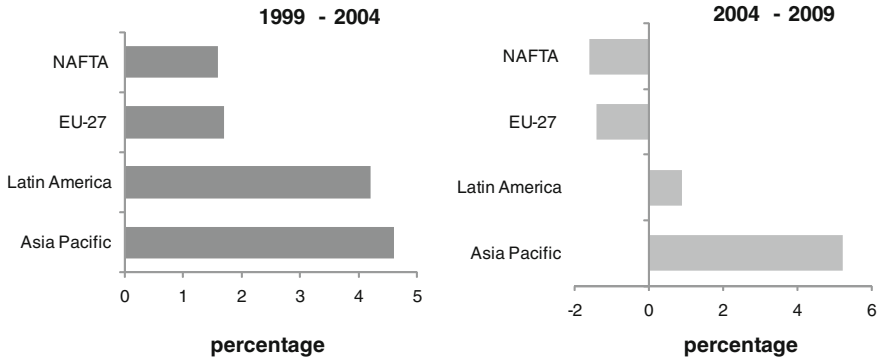


Fig. 1.5 International growth rate by region in two five-year-periods (1999–2004, 2004–2009, percentage) (CEFIC 2010)

achieved growth rates of 2.5 %. Asia–Pacific kept the growth rates at an average level of 4.9 %. Since Japanese growth rates are at a similar level as those of EU and NAFTA, it is primary the Chinese chemical market causing the rise (CEFIC 2010).

Already in the ten-year-period previous to the crisis (1997–2007) the average growth rate in China was 16.5 % (Fig. 1.6). The world average growth rate was 4.8 % in this period and the industrialized countries (Japan, USA, Canada, EU-27 and Switzerland) remained below that threshold (CEFIC 2009a).

In 2010—the year of the economic recovery—chemical sales (incl. pharmaceuticals) increased in all regions. The worldwide growth rate reached 21 % with the highest rate of 30 % in the Asia–Pacific region. Figure 1.7 shows the cumulated growth rates in the three regions with the largest production over the last ten years (ACC 2011).

Global Chemical Market Share

Following the trends in the growth, the chemical world market share has changed rapidly already in the years previous to the crisis. The United States, the European Union, and Japan have lost their market shares and China was the winner with 8 % within the five-year-period (2003–2008) (Fig. 1.8).

There is also one another factor fostering the change in the global market share. The world market as a whole was growing much faster in the last years. World chemical sales increased by almost 64 % in 2010 compared to 2000 (Fig. 1.9).

Global Chemical Trade

The chemical trading statistics[2] give a slightly different view as those of sales. In 2010 the European Union remains the largest trading block[3] (Fig. 1.10). It is losing

[2] Pharmaceuticals included.

[3] The intra-European trade is included, mainly for reasons of comparison with other regions. The European Union remains the largest exporter for chemicals even after eliminating the intra-European trade.

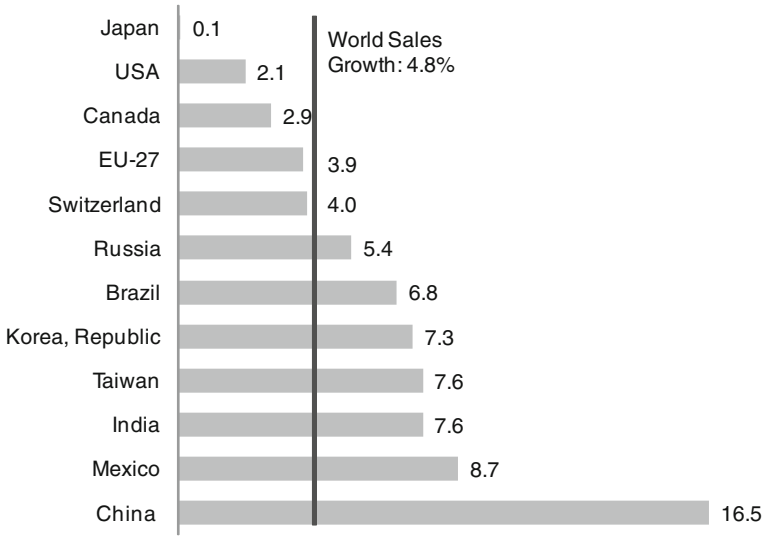


Fig. 1.6 Chemical sales growth rates of selected countries and regions (1997–2007, percentage) (CEFIC 2009a)

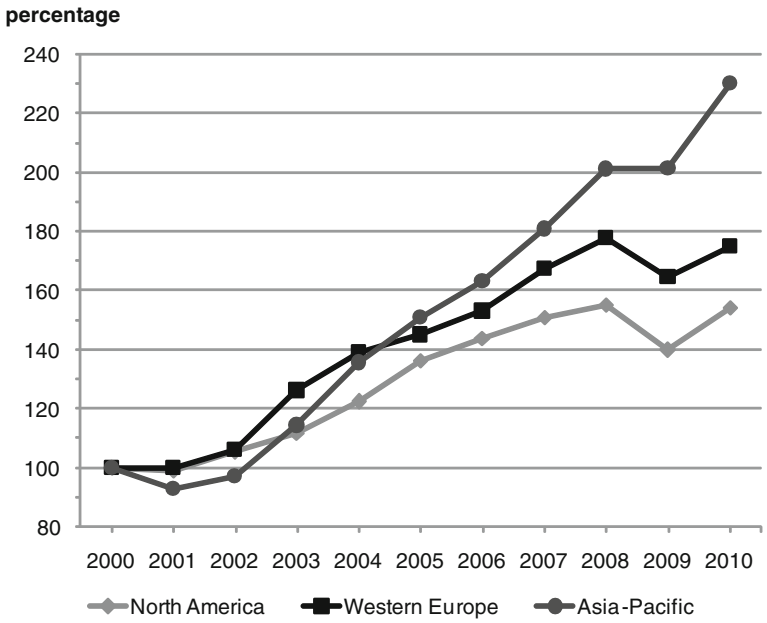


Fig. 1.7 International comparison of the sales growth (cumulated) (2000–2010, percentage) (ACC 2011)

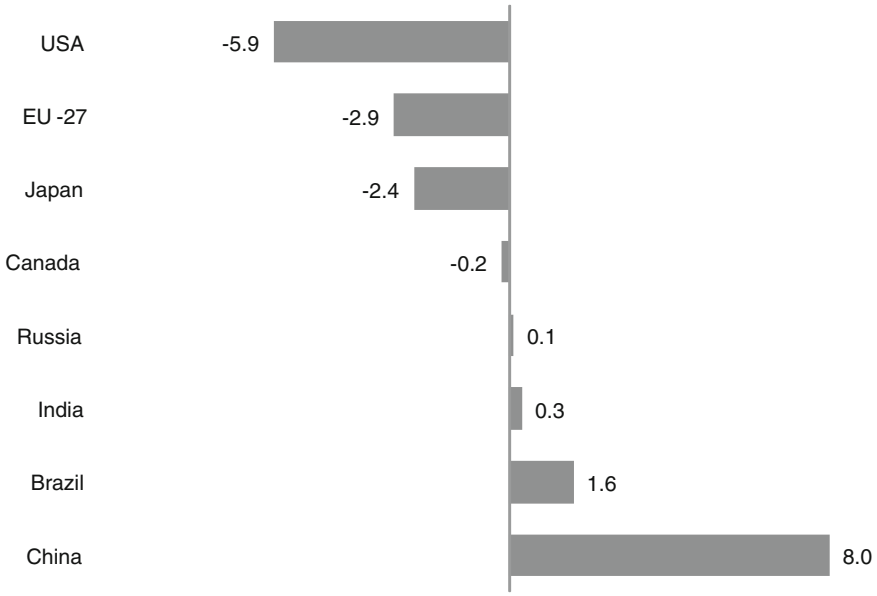


Fig. 1.8 Shift in the world market share in major countries (2003–2008, percentage) (VCI 2010)

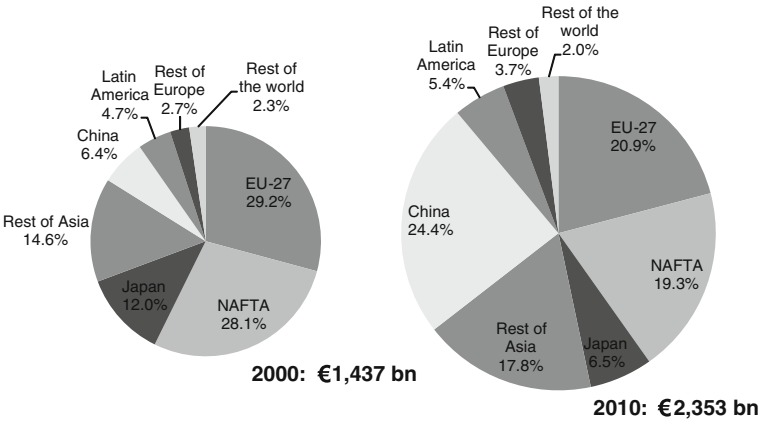


Fig. 1.9 World chemical sales by region (2000 vs. 2010, billion euro) (CEFIC 2011)

the trade share to Asia, but slowly. In 2000, Asia shared only about 22 % of the world exports, ten years later about 26 %. The EU-27 accounted for 54 % of the world chemical exports in 2000, in 2010 the export-share dropped to 50 %. Imports also only decreased from 45 to 44 %. In contrast, NAFTA reduced the exports and imports share by about 4 % each in 2010 comparing to 2000 (ACC 2011).

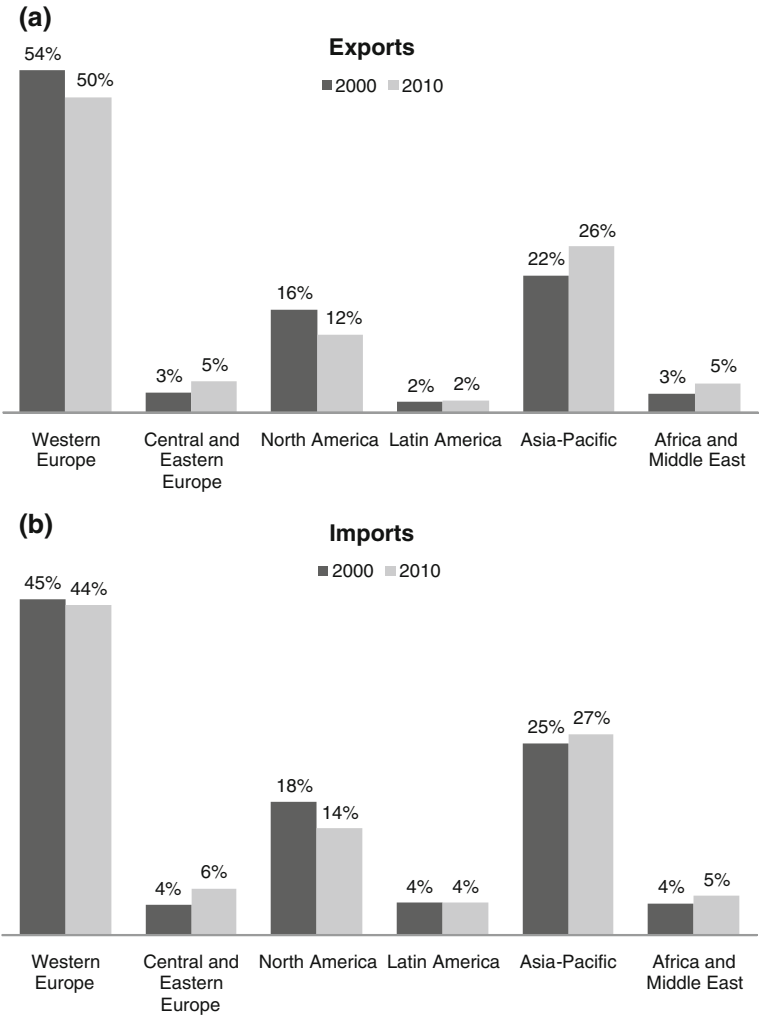


Fig. 1.10 Regional shares in world exports and imports of chemicals (2000 and 2010, percentage) (ACC 2011)

The main competitive disadvantage for the EU-countries was the USD/EUR exchange rate, which picked up rapidly. The exports became expensive and the threat from new imports on the own market higher. The European manufacturers could counterbalance this only by exports to booming parts of Asia (DBR 2008).

Demand for chemical products in China is strong. Both the demand from the major customer industries (construction sector, automobiles, electrical engineering, and textile industry) and the private consumption are growing rapidly. In the basic chemicals segment, the high speed of building new capacities does not suffice the even higher speed of increasing demand and also meets the shortage of

raw materials (DBR 2008). In the special chemicals segment, China had a positive trade balance in the first half of 2009 (CPCIF 2009). There was a strong dependence on imports of high-tech specialty chemicals in the first booming years. Though China started own sufficiency plans in the recent years, thus we may expect a lower export opportunities for western companies in some sub-segments in the future (DBR 2008).

According to the statistics of American Chemistry Council the US had a trade deficit in chemicals in 2002 for the first time. Reaching the peaks in 2003 (9.5 billion US dollar) and 2005 (8.8 billion US dollar). Since 2010 the US has a positive trade balance again. China had an increasing trade deficit in chemicals in the past. In 1998 this was only 12.5 billion, in 2000 17.4 billion but in 2010 already 35.6 billion US dollar. In Western Europe and Japan, the chemical trade surplus has been steadily growing since 2001 up until the crisis in 2009 (Fig. 1.11) (ACC 2011).

Considering the trade balances in chemicals in 2008 between the four main regions: Japan had a trade surplus only with China. China had trade surplus with the US and the EU-27. The US had a trade surplus only with Japan. The EU-27 had a trade surplus with USA and Japan.

Global Chemical Companies

In 1960s chemical companies began to enhance their activities in foreign countries. In the following years the conditions for international trade were improving rapidly: reduction of tariffs and other barriers advances in telecommunications and

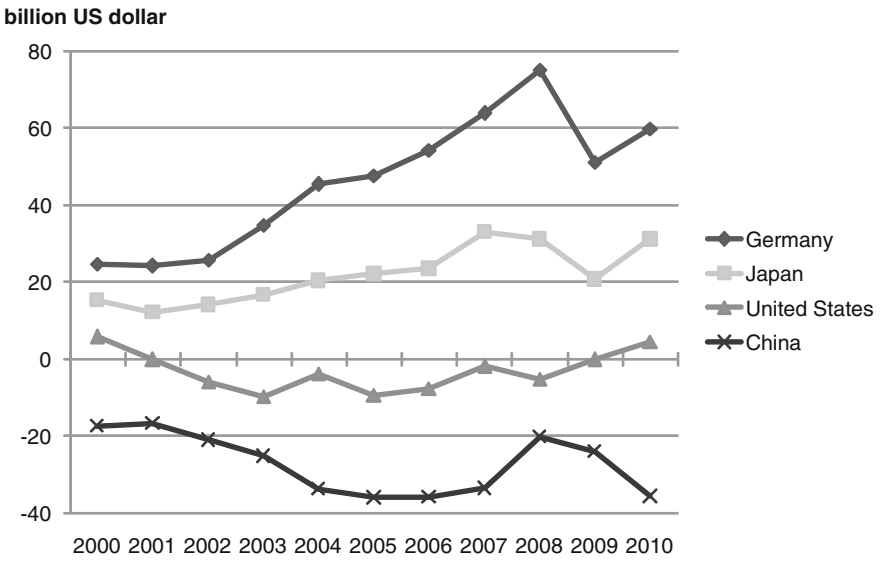


Fig. 1.11 Global chemical trade balances in Germany, Japan, United States and China (2000–2010, in billion US dollar) (ACC 2011)

transportation and increasing world economic growth. These movements established the world market with prices set by global supply and demand.

During the 1980s and 1990s the international investments of western companies grew even faster than in the years before. In 1990s companies originating in emerging countries also started to expand by abroad investments. Thus apart from the world market and worldwide spread of industry resources, also the emergence of multinational companies was enabled in the course of globalization (ACC 2009) (Fig. 1.12).

The Global Financial Crisis

During the years 2008 and 2009, the world economy was suffering one of the biggest crises in the history. In all world regions in parallel, the financial system broke down, all important industrial segments were struggling, the raw material prices became highly volatile and the deflationary pressures increased (CEFIC 2009b).

The chemical industry was hit hard by the global financial and economical crisis. The demand for chemical products dropped in all chemical end markets, especially in construction and automotive. The chemical companies had to face both falling the sales and the prices with the unelectable consequence of financial stress. Moreover, in the 4th quarter of 2008 and 1st quarter of 2009 all industries began destocking, because of a lack of capital, waiting for prices to drop down and to reduce stocks in general. The nonfunctioning banking system in all regions of the world made it impossible to obtain a credit to finance the depths or missing working capital. Many companies did not last the pressure (Dvorocsik 2010).

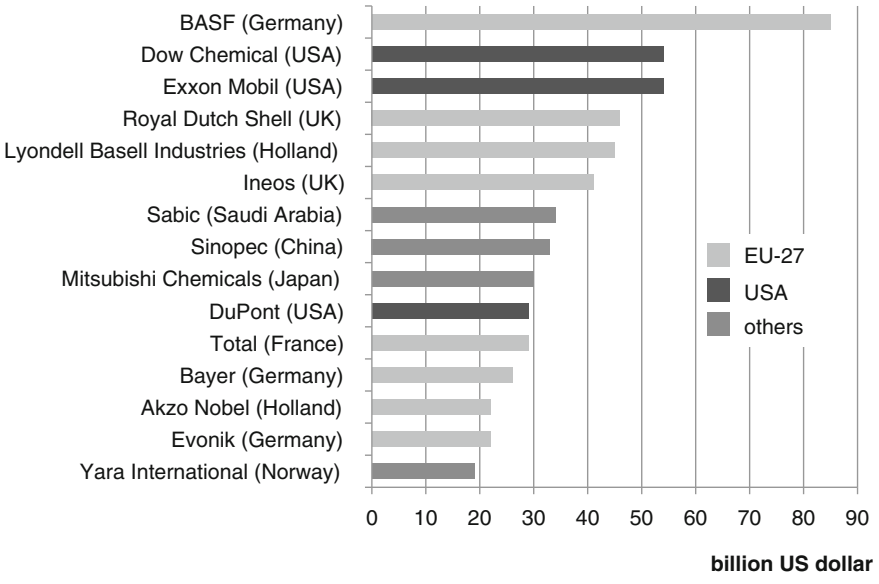


Fig. 1.12 Top 15 chemical companies in the world (2007, according to sales in billion US dollar, including pharmaceuticals) (CEFIC 2009a)

In 2009, governmental intervention helped the credit market to start working again. Since most of the chemical industry products are used for further processing, the demand is strongly linked to the changes in economic output. Statistics show that the gross domestic product (GDP) has been improving again passing the bottom in 2009 (Table 1.1). There are still two major concerns about the future progress: whether there is a serious risk of next crisis and how nations will cope with the financial burden of governmental support programs. However, among the experts prevails the positive attitude (Chang 2010).

1.2.2 The Market Environment of the Chemical Industry

The market environment of the chemical industry is shaped by three main issues: globalization, regulations and sustainability. There are manifold effects hidden behind each of these issues. Globalization is facilitating the rise of emerging markets, thus opportunities like new markets, investments or M&A-deals are opening up. On the other hand margin pressure, volatility of global prices, commoditization rate and market dynamics are increasing. Considering these changes as opportunities or threats is a matter of individual capability of each chemical company. The same is true for the impact of regulations protecting health, environment and intellectual-property-rights. The goal of sustainability also cannot be seen only as a restrain, it implies opportunities in form of demand on renewable energy sources and environmental friendly products. Other global mega topics like health and mobility have similar effects.

The following chapter gives an overview on the central trends in the world of chemistry. The topics have been divided into four groups: economical, technological, political and legal, and demographic market environment. A differentiation like this is only possible on the analytical level. The strong interdependencies between the issues and in some cases various implications make the situation much more complex.

The complexity is, indeed, the main issue chemical companies have to face. In the globalized environment each strategic or operational decision has to consider the world market. For instance in the supplier selection items like price, legal compliance, reliability get a whole new dimension. The globalized market also brings up issues of its own, such as new possibilities for investments, business-location, partnership, customer needs or innovation and also new restrains through new competitors and

Table 1.1 World economic activity: GDP growth in selected regions (outlook 2008–2010, percentage) (CEFIC 2009c)

	EU-27 (%)	North America (%)	South America (%)	Emerging Asia (%)	Japan (%)	Eastern Europe (%)
2008	0.8	1.0	5.4	6.1	−0.7	4.5
2009	−3.9	−3.2	−0.7	2.4	−5.5	−2.4
2010	0.0	1.4	2.9	5.6	0.5	1.8

regulations. The pressure for change in an increasingly dynamic environment makes it even more difficult. The obvious consequence of the globalized world is that the risk is rising. Controlling the complexity is the key to the success.

According to the recent Gartner study[4] 58 % respondents chose 'managing risk resulting from complex demand and supply chains' as one of the critical business drivers. It keeps the issue of complexity on the first place outplaying the innovation (56 %), regulatory pressures and costs (54 %) and operations (54 %). The results are even more evident considering the question about the most critical driver to overall success. Managing complexity scores 35 %. The second place took innovation with only 18 % (Lord et al. 2010).

This result is a clear implication of the economic downturn in 2009. Following the wake-up call chemical companies were forced to review their portfolios of customers, channels, products and suppliers in search for optimizing potential. Managing the complexity is seen as the key. A. T. Kerney Consulting states increasing margins by 2–5 % as a release of hidden earnings potentials due to controlling complexity. The executives of the industry believe, that the companies, which are able to manage complexity better than others are able to grow twice as fast with a 70 % higher profitability (Kerney 2010). Thus managing complexity enables both protecting margins and keeping resources focused on growth.

1.2.2.1 Economic Market Environment

Globalization is the superior factor for most aspects of the market environment, providing various opportunities and threats. Making no claim to be exhaustive, this chapter covers following main issues and their implications: rise of emerging countries and a changing competitive landscape.

The rise of emerging countries

In the 1980s many developing nations started to run programs to establish globally competitive chemical industries. The newly industrialized countries of Asia (NIC) (such as Singapore, South Korea, Taiwan and Thailand) and many economies of Latin America (Argentina, Brazil, Mexico and Venezuela) have made remarkable improvements on this field (ACC 2010). The advanced feedstock nations in the Middle East have been gradually expanding their advantageous position, meanwhile working on new investment strategies in order to reduce their dependence on oil and gas exports. Their amassed funds have been invested, among other industries, to chemical downstream production (refineries, petro-chemical plants and chemical end-products) (DBR 2008). The economic reforms in China started in the late 1970s. In 2001 joining WTO, China has been fully integrated in the world market. Since then only the international trade participation of China and the inflows of foreign direct investment have higher rates than the rapid economic

[4] Gartner conducted a research study of 100 US-based chemical companies through online surveys in February 2010.

growth (Greaney and Li 2009). Also India kept up with the developments. In 2010 India was on place eight among the countries with top chemical sales.

The direct impact of the rise of emerging markets can be reflected either from the demand or the supply side. The demand for chemical products has been strongly shifted to emerging countries, namely due to three interacting factors. The companies from matured markets recognized early the expanding opportunities and the benefits from low costs production. While the structural changes towards service oriented economy limited the growth opportunities on the matured markets, the emerging markets just entered the path. Despite of relatively high risk, the companies started to invest in the emerging countries and even to move their whole production in that area. This is true for chemical companies and for their customer industries, such as construction, textile, and electronics. Following the customer, even more manufacturers moved or opened their subsidiaries in emerging countries. And finally the demand for chemical products there increased through the growth of countries own manufacturing industries, facilitated by legal reforms and booming economy. Changes in the structure modify also the demand. For instance, China attracted investments in basic chemicals first. Today being a world major exporter for basic chemicals, China starts supporting programs for the specialties. The share of specialty chemicals in the chemical export increased from 6.2 % in 2006 to 12.5 % in 2010 (CPCIF 2011).

This strong expansion of chemistry and its customer industries, especially in China, cannot be caught up by production. For some chemical substances, there are still supply shortfalls, e.g. ethylene (DBR 2008). Since many chemical substances are used as preliminary products for further chemical processing, the chemical companies themselves have to face the shortage too. The supply disruptions are reflected in the prices. The same applies for the raw materials themselves.

In the globalized chemical market volatile prices of raw materials, energy, and end products became the common concern. Customers do not easily accept any price increase, thus margin pressures follow.

One another serious issue—the supply chain disruptions—is also clearly related to the growing dynamics. Apart from the supply shortfalls and relocations or bankruptcies of the business partners, the companies themselves have to look for better contracts consistently in order to win the competition, since the pressure has increased.

Changing competitive landscape

The price and margin pressures are the traditional drivers for change. In the globalized world with export oriented emerging countries, these pressures are stronger. However, this is not only because of the low-cost advantages in the emerging markets. The intense competition is fostering increasing technological dynamism, commoditization,[5] and decreasing product life cycles (Eisberg 2010).

[5] Commoditization is the process by which a product reaches a point in its development where one brand has no features that differentiate it from other brands and consumers buy on price alone.

The companies are forced to use all options they have, to stand the competitive pressure. The fast orientation on the markets, as well as continual search for hidden potential in companies businesses is essential.

Field research shows, that the following three areas became more and more important: meeting customer needs, fast reaction time through more flexible business models and portfolio consolidation. The anticipation of customer needs has been stepped up notably due to the crisis. Especially the customer driven innovation became much more important (Morawietz et al. 2009). However, the first steps such as bundling products with services or total quality management have been made already before the crisis as a reaction on the increased competition.

The second area: flexible business models, involves changes in internal organization and new forms of cooperation between companies. For instance integrated companies should consider how many different business models are able to coexist (CHEMIE.DE 2010). Examples for extended forms of cooperation are new partnerships regarding market, collaborations for development, joint ventures to penetrate new markets or to gain new technology. For example, Dow Corning was established as a joint venture equally owned by The Dow Chemical Company and Corning Inc. in 1943 specifically to explore and develop the potential of silicones. Today, there are many examples for joint ventures in order to provide synergies by vertical downstream integration between chemical and oil and gas industries. Crack products from crude oil refining are used for synthesis of polyolefines for instance, at the same time, the supply of energy for chemical manufacturing can be ensured. As examples, LyondellBasell, formerly Basell, originally arose from a joint venture between BASF and Royal Dutch Shell. The Dow Chemical Company and the Saudi Arabian Oil Company (Saudi Aramco) are currently establishing the worldscale Sadara Chemical Company joint venture.

Mergers and Acquisitions, as long as carried out properly, enable to follow the strategic goals more quickly or make changes more rapidly. The learning process of a company required to catch up with new technologies, new processes, and new products can be also reduced (Siu 1999). For example, DuPont acquired the Danish niche chemical company Danisco in order to gain access to Dansico's enzyme technology as well as its strength in cellulosic ethanol research. Both technologies can enrich DuPont's product range (Cassidy et al. 2011).

In the last twenty years, the portfolio consolidation has been one of the most important goals among the global chemical players. In consequence, the industry's competitive landscape has been extremely restructured. The traditional oil and gas players (such as Shell or BP) have largely sold their chemical businesses. The large integrated chemical players (BASF, Dow or Akzo Nobel) have dramatically changed their portfolios. Some of them have strengthened their main business with buyouts of similar businesses, for instance the disaggregation of former Hoechst. Its pharmaceutical business has been absorbed into Sanofi Aventis, the agrochemical business has been sold off to Bayer Crop Science and Celanese took over its basic chemicals and Clariant the specialty chemicals division. Other companies, such as BASF, Dow and Akzo Nobel, have enhanced their value chain by acquiring specialty producers. Additionally, new large players formed themselves through "buy-

and-build" strategies (Ineos, Hexion, Lyondell Basell), often using access to private equity. In the emerging countries, the fast growth was the stepping stone for the strong competitive position of the new global players, such as Saudi Arabia's SABIC and Sipchem or China's Bluestar (Morawietz et al. 2009).

The world financial crisis has reduced the Investment- and M&A–Activities to a minimum. On the other hand the companies facing an economic crisis are much more sensitized for their improvement capabilities. As soon as credit was available again, strategic investments became more important than ever. The producers of specialties are trying to sharpen the portfolio, basic chemical companies aim to downsize their overcapacities, private-equity-companies are looking for acquirers and investors from financial sector are ready to enter the market (Delloitte 2010).

In the medium term, the process of concentration in the global chemicals industry particularly in the basic chemicals sector continues, where the production costs per unit fall. A.T. Kearney estimates, in the future, there will be only one to three Western players per customer segment (DBR 2008). In the specialty chemicals segment the M&A activities may reach beyond the own industry to come closer to the end-customer or to extend the own know how (CHEMIE.DE 2010).

1.2.2.2 Technological Market Environment

In the context of technological environment the prime topic is the research and development (R&D) activity in the chemical industry. However, two other issues should also be discussed here: the infrastructure and the trend towards alternative feedstock, since nowadays these have a strong influence on the use of technologies.

A winning innovation is a critical factor for success in the R&D-driven industries, like chemicals. Successful innovations can produce 25–35 % return. For instance, according to the study of the Council of Chemical Research, in the US for public chemical companies every dollar invested in R&D returns as 2$ in operating income over six years (17 % return). However, the research intensity (R&D expenses as a proportion of sales revenues) in the industry has fallen, despite of the constantly rising R&D spending. According to the US-based consultancy Kline the research intensity achieved its maximum in 2004.[6] Considering the segments, the research intensity of specialty chemicals companies was 2.8 %, investments of basic chemical companies were 1.1 % and the diversified companies lay in between with 2 %. Kline also analyzed the geographical division. The research intensity was highest in Europe, corresponding with high representation of specialty and diversified companies in the region (Challenger 2008).

As the companies from matured markets move their activities to the markets with strong growing demand and lower costs, whole R&D sites are being relocated. In Asia centers of excellence arise, partly by foreign investments, partly by strong governmental support. Furthermore in China the steering of foreign

[6] Kline analyzed the R&D spending of the top 50 global chemical companies.

investments moves rapidly towards high tech production. However the relocation of the R&D sites does not match the relocation of the production. Since 2008 only high tech companies can take part on support benefits (Abele 2010). Since the scientifically relevant infrastructure and human resources as well as own scientific networks provide the basis for R&D allocation plans, the early developed countries still provide a favorable environment. BASF, for instance, still allocates its R&D investments as follows: 80 % in Europe, 17 % in USA and 3 % in Asia (Challenger 2008).

The traditional R&D with focus on product and technology innovation is increasingly been complemented by developing new ways of marketing, branding, cooperation and searching for new business models or targets. In 2007 BASF used 63 % of its R&D spending on product innovation, 19 % on process optimization, 16 % on new methods and 2 % on new applications (Challenger 2008).

However, it is not only the R&D spending by chemical companies, which reflects the image of technological improvement. The more the technology is advanced the cooperation between different academic fields appears necessary (CHEMIE.DE 2010). This can for example be seen in the area of bionic science and chemistry.

Another point is that in the Asia, the research sponsored by government is traditionally much stronger than in matured markets. A study on nanotech patents carried out by University of Muenster (Germany) shows the high importance of universities and research institutes in nanopatenting in China. As the governmental sponsorship decreases, universities begin to cooperate with industry, to set up science parks and spin-offs. The applied research in China is booming since the reforms of the national research system. The growing number of patents in nanotechnology since 2000 confirms this. In 2005 China ranked first ahead of the US and Japan, the generally perceived leaders in nanotechnology (Preschitschek and Bresser 2010).

The main targets of research within the chemical industry are the improvements of product features ("smart" materials and advanced composites) and alternative feedstock to oil-based products. The technologies in focus are bio-based processes, novel catalysts, sustainable chemistry and energy efficiency. BASF, for instance, has 5 areas with the highest attention: energy management, raw material change, nanotechnology, plant biotechnology, and white (industrial) biotechnology.[7] These clusters are expected to bring in annual sales between $2.6 and $5.2 billion by 2015 (Challenger 2008).

The infrastructure is crucial for the success of the chemical companies. The essential business activities such as communication, supply chain operations, funding, staffing, or sales all depend on a functioning infrastructure. Despite of high growth rates on the emerging markets, the infrastructure there does not

[7] White biotechnology uses biocatalytic processes (enzyme, cells and microorganisms) in the industrial production of chemicals. These can replace the conventional production processes as well as raw materials or energy sources.

Table 1.2 Quality of overall infrastructure (2011, weighted average) (WEF 2011)

Country	Rank	Score	Country	Rank	Score
Hong Kong SAR	1	6.71	Canada	11	5.88
Germany	2	6.35	Japan	15	5.69
Singapore	3	6.33	United States	16	5.68
France	4	6.30	Taiwan	20	5.62
Switzerland	5	6.15	Saudi Arabia	25	5.31
United Kingdom	6	6.09	Italy	32	5.01
Netherlands	7	6.02	China	44	4.63
United Arab Emirates	8	5.97	Brazil	64	3.99
Korea, Republic	9	5.94	Mexico	66	3.98
Denmark	10	5.89	India	89	3.60

achieve the level of matured markets. It implies the high level of risk, the companies have to anticipate. For instance, in the latest survey Banomyong shows, that the infrastructure in Asia is not improving quickly enough to enable a successful supply chain management (Banomyong 2010).

The World Economic Forum issues yearly the global competitiveness index[8] (GCI) for 133 countries. Infrastructure is one of the nine pillars for the evaluation. The Executive Opinion Survey shows how the infrastructure in the country meets the needs of the companies inside the country. The matured chemical markets and the Newly Industrialized Nations (Hong Kong, Singapore) approached the top positions in the ranking (Table. 1.2). China (44) and India (89) ended up rather poor. In contrast, the oil-rich Gulf States ranked in the first third (WEF 2011).

1.2.2.3 The Political and Legal Market Environment

Chemical companies have to act in a highly regulated market environment. Indeed dealing with many and various regulations is one of the characteristics of the chemical industry. It is essential for the success to follow the latest changes, because of the immediate consequences for the competitive position. The direct economical sanctions (fees, competitive disadvantages) are not the only reason for the efforts. The chemical industry has had strong public attention for the past

[8] The World Economic Forum postulates that as a nation is developing, the wages tent to increase, so the labor productivity must improve for the nation to stay competitive. As the productivity drivers differ depending on the stage of development the nation is in, the GCI distinguishes between three types of stages: factor-driven, efficiency-driven and innovation-driven. Thus the pillars are given different weights depending on the per capita income of the nation. The twelve considered pillars are: institutions (public and private), infrastructure, stable macroeconomic framework, good health and primary education, higher education and training, efficient good and labor markets, financial market development, technological readiness, market size, business sophistication, innovation. Approximately two thirds of the variables are identified through the Executive Opinion Survey and one third comes from statistical sources.

30 years. Pollution caused by technological defects, risks caused by low quality products or non-legal practices quickly become subject for the media. Particularly the goal of sustainability receives increasing attention.

In addition to common market regulations (e.g. laws against unfair competition), there are three areas of matter crucial for the chemical industry: human health and safety, environmental compliance and intellectual property rights.

However, the protection standards and compliance with the norms differ strongly between countries. Europe and the US have typically high levels of regulation. They have been confronted early on with the challenges of protecting human health and the environment as well as making the necessary investments to prevent accidents and increase safety measures.[9] Over the years, the regulations got intensified. Since the EU and the US are strongly innovation oriented, they took on the pioneering role in the protection of intellectual property rights too. The emerging markets despite of the pressure from matured markets can only slowly catch up with the standards.

On the field of environmental compliance, health and safety the latest challenge faced by chemical companies is the European REACH legislation (Nr. 1907/2006). It constitutes an entirely new approach of compliance addressing the production and use of chemical substances and affects also companies outside the EU to a large extend. REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) came into force on the 1st of June 2007. It is a volume-based legislation which is being carried out in three phases. During the registration all substances (over 1 t/a) produced in the EU or imported have to attain a registration number. For the registration the proof of harmlessness and safety has to be provided by an in-depth description and evaluation of substance properties and usages. In the evaluation phase the danger status will be officially approved. The substances labeled as SVHC (Substances of Very High Concern) are subject to authorization or restriction procedures. The expected social profits of REACH are: an extensive monitoring of chemical substances, pressure to substitute dangerous substances and approach to the goal of establishing one international standard.

The significant differences to other similar regulations (e.g. TSCA in the US) are: the shift of burden of proof to manufacturer or importer of chemicals, the principle 'no data no market', as well as the compulsory data exchange along the value chain with suppliers and users. The sharing of data between the producers of the same substances attempts to reduce the testing effort. However, the additional communication presents a grave effort itself.

Indeed the most serious charge against REACH is the enormous effort the companies have to render. The costs of the required safety analysis can be critical for small and medium companies. On the other hand the international companies have to register various substances and intermediates from subsidiaries abroad as soon as imported for further proceeding. These costs can have a negative impact

[9] In the 1970s and 1980s a number of chemical accidents (such as Seveso, Bhopal and Schweizerhalle) put pressure on the chemical industry and politicians.

on the competitive position. A global relocation of specific production sites to less regulated countries might follow. If REACH as a quality feature can compensate the disadvantage, the further development will show.

Another point is that the producers abroad consider the regulation as a technical barrier for the market entry. As a result, the companies (local or importing), for which the legal procedures are too expensive, might decide to no longer supply the European market. However, the European Chemical Agency (ECHA) provides support for producers or importers outside the EU. And outside the EU are institutions being established, to help the producers to handle the requirements (e.g. REACH 24 h China).

In parallel to REACH another globally important legislation is being introduced: the GHS (Globally Harmonized System of Classification and Labeling of Chemicals). It has been initiated by United Nations and aims a globally standardized labeling system for chemicals. In the EU, the GHS for substances came into effect since 2010 and the GHS for procedures is set for 2015. In the US the GHS is scheduled for 2011. In China it has been implemented into three compulsory standards in 2010 and China is currently working on system coordinating the GHS adoption.

Next to REACH and GHS, there are some other legislations with single purposes the companies have to comply with: RoHS/WEEE and China RoHS legislation, TSCA (Toxic Substances Control Act), American Food and Drug Administration (FDA) and Clean Air/Water Act. Particularly for international companies, the complexity of legal environment covers a large part of the overall complexity problem.

A second challenge regarding the legal environment is the management and protection of intellectual property. For the chemical industry as one of the most innovative industries, a strong protection of knowledge is crucial. Therefore, an intelligent patent strategy is an important key success factor, not only to protect and defend the innovation itself, but also to build market entry barriers excluding new market players and to hinder competitors in their business.

Basically, a company tries to file patents for all products or methods, which shall be protected against imitators, thereby achieving technical, economical or salable advantages. The alternative strategy is to keep an invention protected by simple non-disclosure (company secret), however, there is always a risk of disclosure due to fluctuating employees for instance.

In very competitive research areas a large quantity of patent coverage enables a company to cross-license their patents with competitors, i.e. two companies allow each other to use specific inventions.

According to this strategy companies try to file as many as possible ‘blocking patents’, which either can be cross-licensed with other companies, or, which hinder competitors to file patents for a specific area of research. The economic usability of reserve patents is often not visible at the point in time, when they are filed.

Another intellectual property strategy is to publish an invention as ‘defensive disclosure’, so that it enters the public domain and becomes prior art. This prevents another party from obtaining a patent.

A critical challenge is the geographical range of protection as there does not exist any fully working global patent protection system yet. Regions like Russia, Latin America, the Middle East, and Asia (except Japan) still have gaps to close.

The OECD has worked on pursuing the worldwide attention to data protection for many years. In 1983 the economic value of certain data on chemicals has been introduced in broad terms in three resolutions. Apart from the OECD efforts, the WIPO (World Intellectual Property Organization) was established in 1967. Since 1974 WIPO belongs to the UN. Its aim is the worldwide guarantee of intellectual property rights. Among others the responsibility of WIPO is the enforcement of the PCT (Patent Cooperation Treaty) from 1970. Each patent approved to the company of one PCT member state is effective in all member states. Currently 145[10] states ratified the treaty (China in 1994, India 1998), but important chemical producers like Argentina, Saudi Arabia, Taiwan or Venezuela are not among them. In 1994 within the framework of GATT the TRIPS (Agreement on Trade-Related Aspects of Intellectual Property Rights) has been concluded. TRIPS is a set of requirements on member states, which can be enforced by WTO sanctions. However, TRIPS includes only minimal requirements, it lacks on the proper interpretation, which is often necessary.

One another important topic among the political and legal environment is the political stability as well as the reliability of the public institutions and the legal system. The investments into new assets in chemical industry are comparatively high, thus they are designed for long periods. The additional costs in disadvantageous political environment can increase rapidly. Therefore, the political situation must be taken into account in each choice of new location.

The World Economic Forum issues yearly a report on private and public institutions for 139 countries. The attributes of public institutions being examined are: property rights, ethics and corruption, undue influence, government inefficiency, and national security. In the category private institutions corporate ethics and accountability are being reviewed. Table 1.3 shows which position the major chemical players have attained (WEF 2011).

Table 1.3 Quality of institutions (2011, weighted average) (WEF 2011)

Country	Rank	Score	Country	Rank	Score
Singapore	1	6.11	France	28	5.00
Switzerland	6	5.78	Taiwan	31	4.94
Netherlands	10	5.61	United States	39	4.64
Canada	11	5.57	China	48	4.32
Saudi Arabia	12	5.47	Spain	49	4.27
United Kingdom	15	5.34	Korea, Rep.	65	3.89
Germany	19	5.27	India	69	3.84
United Arab Emirates	22	5.21	Brazil	77	3.72
Japan	24	5.18	Italy	88	3.61
Belgium	27	5.03	Mexico	103	3.44

[10] July 15th, 2011.

1.2.2.4 The Demographic Market Environment

The reflection of the demographic environment is essential for chemical companies, since various strong interdependencies exist. The chemical industry has a great social responsibility. First, many of the products have a direct positive or negative impact on health and safety of beings and their environment. Second, the chemical industry is an important employer. For example, more than 34 million people in the EU are working in the chemical industry. On the field of social standards for the employees, the chemical industry serves as a benchmark for other European industries (VCI 2010).

On the other hand, the chemical industry depends on skilled labor. Ageing of the world population, the quality of education, and the mobility of labor are serious issues for chemical companies. Population ageing is a result of two demographic trends: decreasing of fertility rates and rising of life expectancy. Most of the nations follow these trends. Still there are differences in the speed of the ageing process between the countries. There are great differences even within the industrialized countries. The population of the US is much younger than the European or Japanese are. And within the EU: France and Great Britain are ageing slower than Germany and Italy. However, in some countries, the changes are so dramatic, that their future labor, capital, and goods markets will be strongly affected (Börsch-Supan and Ludwig 2009). For example the rapid ageing in Asia causes the median age rise well above the world average in 2050 (Asher 2010). Since the ageing of the population is spread in both developed and developing countries, the consequences for the industry are inevitable. The shortage of labor force can lead to the increase of its price and more capital intensive production. Large international flows of labor, capital, and goods from the faster ageing countries to the slower ageing countries may follow (Börsch-Supan and Ludwig 2009). Ageing pushes the human resources strategies of the companies higher in the priority list. Considering this, new strategies including employment of older people and new approach in human resources development can be just as important as the right choice of the location and technology.

The level of education and the international mobility of labor have to be considered additionally to the ageing issue. Since only unskilled workforce has unlimited surplus, the surplus on skilled workers must be obtained. The activities a company itself must take depend strongly on the coverage the public sector provides. Table 1.4 shows the state of the higher education in the main chemical nations. The ranking is based on secondary and tertiary enrollment rates and the evaluation through the management representatives of the home industries (WEF 2011).

Table 1.4 Quality of higher education and training (2011, weighted average) (WEF 2011)

Country	Rank	Score	Country	Rank	Score
Switzerland	3	5.80	Japan	19	5.27
Singapore	4	5.77	France	20	2.24
Belgium	5	5.75	Spain	32	4.90
Germany	7	5.73	United Arab Emirates	33	4.84
Netherlands	8	5.66	Saudi Arabia	36	4.81
Taiwan	10	5.64	Italy	41	4.69
Canada	12	5.59	Brazil	57	4.35
United States	13	5.57	China	58	4.34
United Kingdom	16	5.47	Mexico	72	4.07
Korea, Republic	17	5.44	India	87	3.88

1.3 The Global Pharmaceutical Market

1.3.1 Key Figures

Global Pharmaceutical Sales and Production

One of the differences between the chemical and pharmaceutical market is the global market share. Asia plays rather an inferior role in the global pharmaceutical industry. From the 597,043 million euro (in ex-factory prices) worldwide sales in 2010, the three early industrialized regions North America, Europe, and Japan account for more than 80 %. Asia (excluding Japan) together with Australia and Africa come up to only 12.4 % market share (Fig. 1.13). On the production side the numbers look very similar. In 2007 the US accounted for 38.1 % of the world pharmaceutical production and Europe was the second largest producer with 36.1 % (Fig. 1.14). Considering individual countries, Japan ranks second with some distance to the US, followed by China, Germany, and France (Fig. 1.15) (EFPIA 2011). Within the Europe the largest sales volumes in 2010 were in France, Germany, Italy, and Great Britain (BPI 2011).

Global Pharmaceutical Growth

The pharmaceutical industry is becoming increasingly important all over the world. In the last ten years the pharmaceutical sales more than doubled (increase of 234 %). Figure 1.16 shows the year-to-year growth of the worldwide sales. The two strongest years were 2003 and 2010, where the growth exceeded 13 %. Even in the years of the financial crisis the pharmaceutical industry achieved positive growth rates (ACC 2011).

However, there are grave differences between the world regions regarding the growth rate. Figure 1.17 shows the growth in world regions for three consecutive years (2008, 2009, and 2010). The pharmaceutical market in North America, which already operates on a high level, grew in 2008 only by 1.7 %. One year later, even despite of the crisis, the growth rate there was more than doubled. This is attributed to the increased demand and launch of several innovative products on the US market

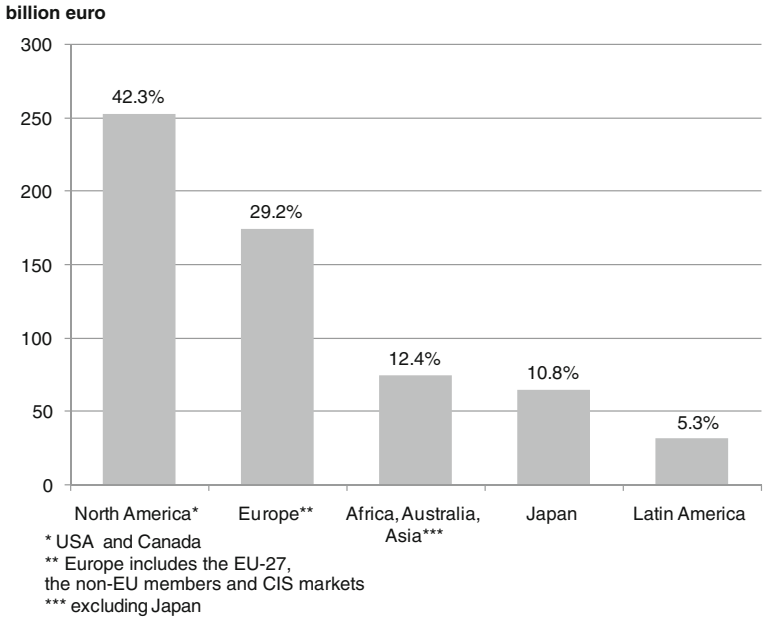
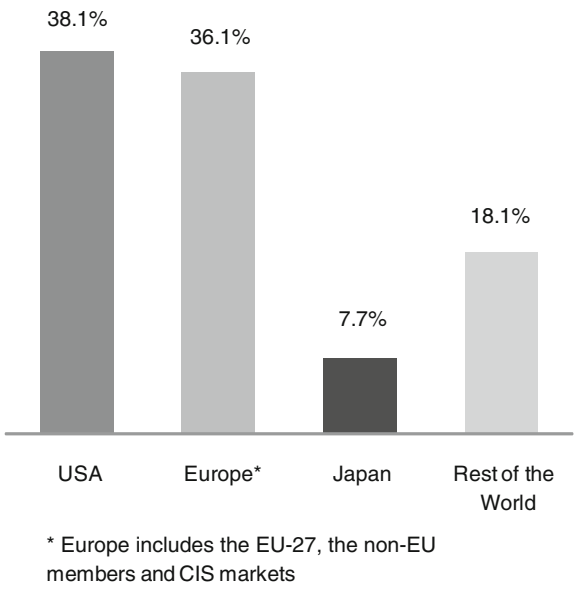


Fig. 1.13 The world pharmaceutical sales and market share (2010, billion euro and percentage) (EFPIA 2011)

Fig. 1.14 Regional breakdown of the pharmaceutical production (2007, percentage) (EFPIA 2010)



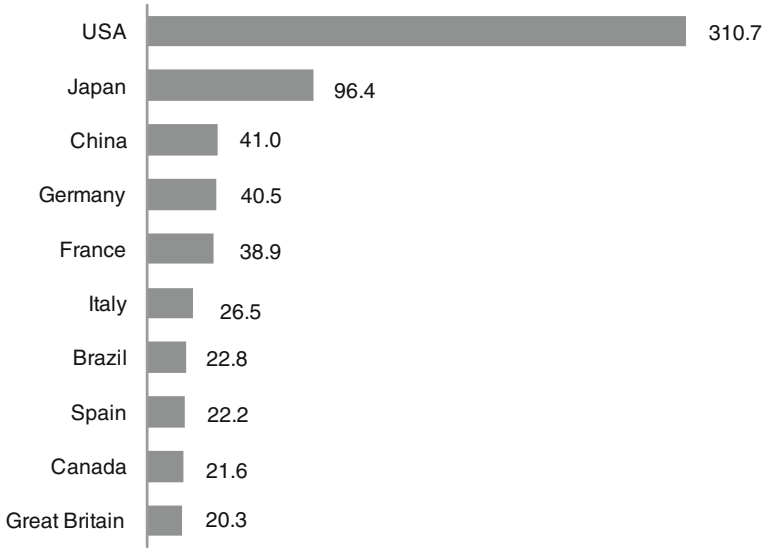


Fig. 1.15 The top ten pharmaceutical markets (2010, billion US dollar) (BPI 2011)

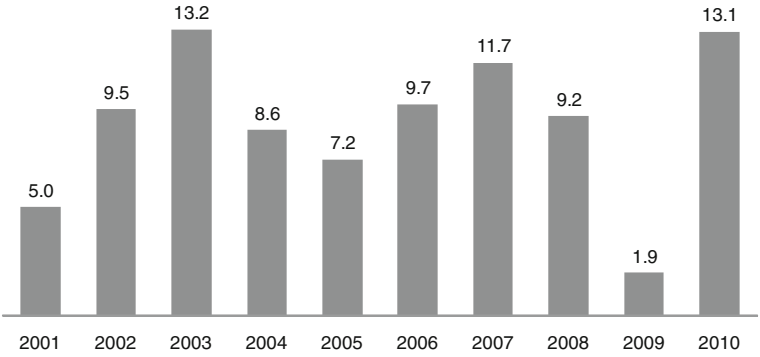


Fig. 1.16 The growth of global pharmaceutical sales (2001–2010, percentage) (ACC 2011)

(for diseases like thrombosis, cancer, and arterial fibrillation) (RNCOS 2010). In contrast the EU market increased by 10.5 % in 2008 and fell to negative rates in the two following years. The Japanese market could hold strong growth rates in 2008 and 2009 and decreased only in 2010. This shows clearly that the pharmaceutical markets in different regions develop differently and independently from each other. Furthermore the pharmaceutical industry sales are mostly independent from the general economic situation. Emerging regions of Asia and Latin America achieve high growth rates. The crisis strongly stressed the market in Latin America in 2009, but one year later the growth rates rose to a new record high. The growth rates in Asia remained high over the three years. This is attributed to the high growth rates in

the booming regions of Asia. The growth rates in China were at 27 % in 2008 and 2009 and 22 % in 2010 (BPI 2009, 2010, 2011).

Following the trend in the five year period (between 2004 and 2009) the region which includes Asia, Australia, and Africa shows the highest growth of 13.9 % (Fig. 1.18). On the second place is Latin America with 10.9 %. The well developed regions are not able to keep up with these rates. Europe had slightly higher growth rates than the US and Japan in this period (EFPIA 2010). However, the figures of the year-to-year growth in 2009 and 2010 show that Europe experienced an upturn lately (Fig. 1.17).

Figure 1.19 shows the growth rates in the top ten countries. There it is obvious that the high growth rates in Asia and Latin America are caused by a few countries only, like China or Brazil. Within the EU the highest growth rates were achieved by the new EU members, thus not among the top players either (BPI 2011).

Global Pharmaceutical Market Share

The differences in the growth rates between the world regions have an impact on the pharmaceutical market share (Fig. 1.20). In the last five years the traditional market leaders, the US and Europe, slightly lost their shares to the emerging regions in Asia and Latin America. Japan could hold its position. In 2009 the high growth rate brought Japan even to 11.2 % market share (EFPIA 2006, 2010, 2011).

Global Pharmaceutical Trade

The pharmaceutical trade is clearly dominated by the EU (Fig. 1.21). With exports summing up to 308 billion US dollar and imports by 247 billion US dollar in 2010, the EU broadly overtakes the countries on the following positions. Even if the intra-European trade is excluded, the EU keeps the top position for exports. The extra-European exports account for 27 % of the worldwide exports. The imports slide to the second place with 13.3 % close behind the US. The US

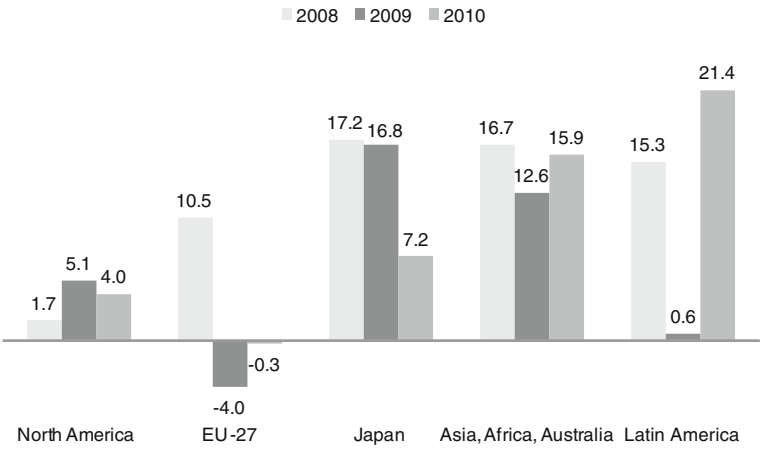


Fig. 1.17 Growth of pharmaceutical sales in world regions (2008–2010, percentage) (BPI 2009, 2010, 2011)

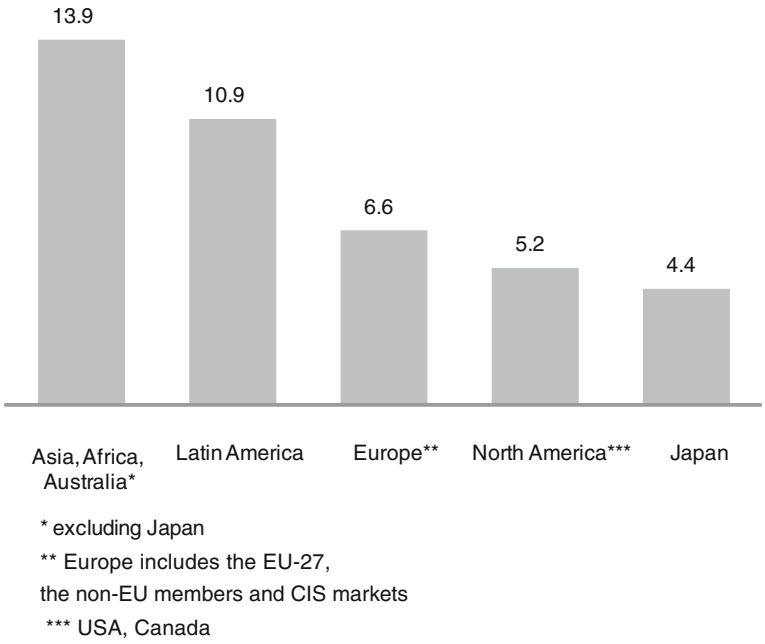


Fig. 1.18 Growth of pharmaceutical sales in the world regions (2004–2009, percentage) (EFPIA 2010)

account for 13.9 % of the worldwide pharmaceutical imports with the value of 66 billion US dollar. On the export-side the US are on the third position with 45 billion US dollar. The second largest exporter is Switzerland with 50 billion US dollar and an export share of 10.8 %. The fourth position on the export side gains China with 11 billion US dollar and the fifth India with 7 billion US dollar. As for the imports—with 19 billion US dollar Switzerland is on the third position followed by Japan with 17 billion US dollar (WTO 2011).

Global Pharmaceutical Companies

The structure of the pharmaceutical industry is shaped by national medical traditions, intellectual property protection standards, and industrial policy (EFPIA 2010). Since these differ from country to country, the global structure appears rather heterogeneous. For instance, there are many small companies in China that are mostly specialized on generic drugs. The top 3 companies in China occupy only 5 % of the pharmaceutical market there. For comparison, the top 3 companies worldwide account for more than 16 % of the global pharmaceutical market. Furthermore, there are more than 2,000 applications for approval of generic drugs registered yearly in China and only about 40 approvals for drugs, which have never been launched before (Achema 2010). In India, the business is also primarily oriented on generics, but India has more large producers of generics with a strong lobby position in the Indian government (Cipla, Ranbaxy, Hetero Drugs, Nacto Pharma).

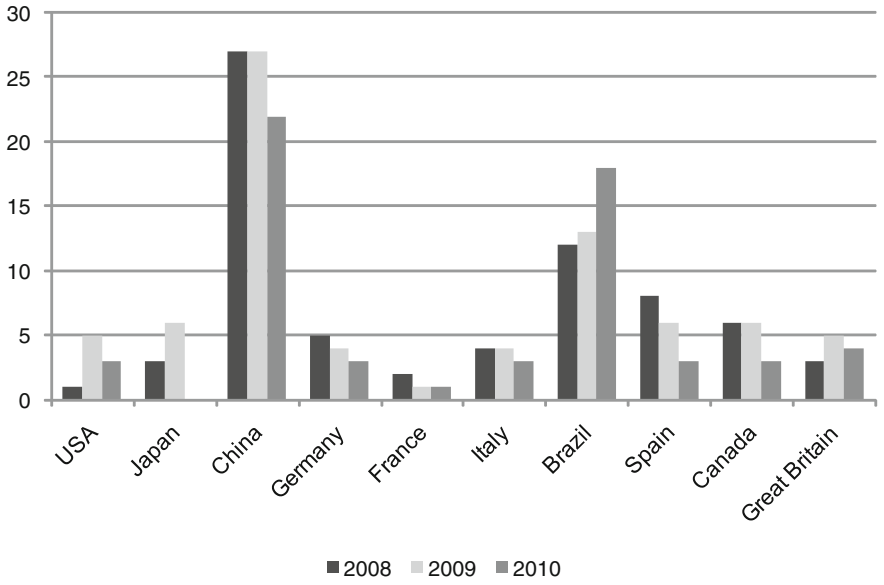


Fig. 1.19 The growth of pharmaceutical sales in the top ten countries (2008–2010, percentage to local currency dollar that is the currency fluctuations are not considered) (BPI 2009, 2010, 2011)

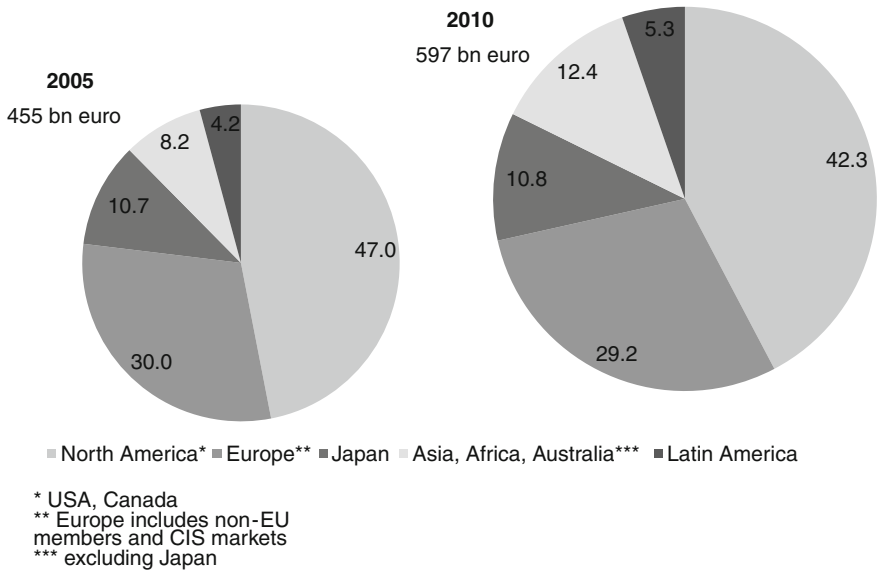


Fig. 1.20 Regional breakdown of the pharmaceutical sales (2005 and 2010, percentage) (EFPIA 2006, 2011)

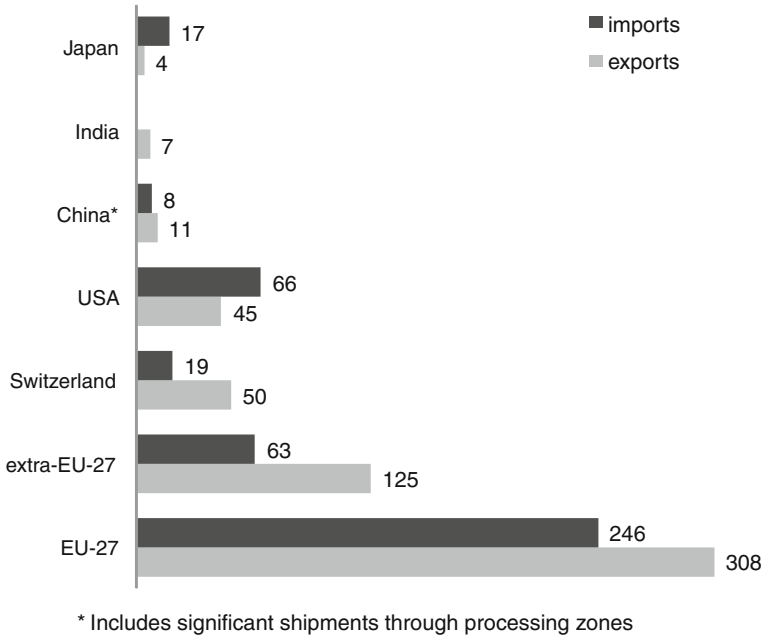


Fig. 1.21 Leading exporters and importers of pharmaceuticals (2010, billion US dollar) (WTO 2011)

The origin of the companies dominating the world market is almost exclusively in the US and Europe (Fig. 1.22). 7 of the top 15 companies come from the US, 4 from the EU and 2 from Switzerland (Cacciotti and Clinton 2011).

1.3.2 The Market Environment of the Pharmaceutical Industry

1.3.2.1 The Economic Market Environment

The pharmaceutical industry is one of the fastest growing industries with a high level of resilience to the volatility on world markets. Consequently it is one of the most important growing markets worldwide (PWC 2008a). On the other hand, the industry has to cope with particular economical issues which are attributed to the specific nature of healthcare products. This chapter gives an overview on the prospects for growth and the main economical threats the pharmaceutical companies are facing.

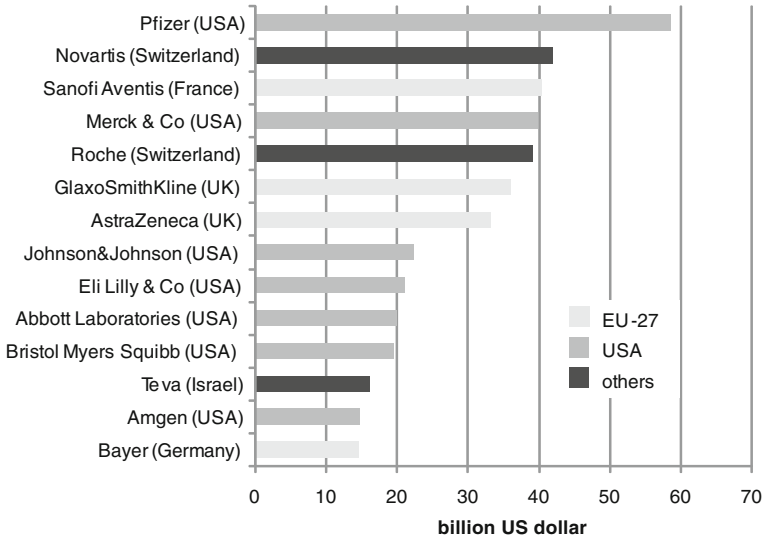


Fig. 1.22 The top 15 pharmaceutical companies worldwide according to the sales volume (2010, billion US dollar) (Cacciotti and Clinton 2011)

Growth Prospects

The growth perspectives are facilitated on both supply and demand side. The crucial importance of innovation in the pharmaceutical industry is a significant growth promoting factor. New technologies and product-innovations generally enable increase of production or profits. The production of drugs is also positively affected by the feature of many healthcare products to induce a supply-driven demand, i.e. the demand emerges only after the market introduction of the product. Pharmaceutical producers benefit less than others from new production facilities in low income countries and cheaper precursors due to the approval requirements, but indeed they derive the advantages. For example, the less sophisticated operations like packing are being often moved to low income countries. Their admission is requested right at the beginning of the pharmaceutical's registration. The advantages of globalization among the well established producers are rather on the side of the originators. The threat of new competitors from emerging markets is delayed in the in-patent sector, because of the high R&D investments and the know-how needed for the entry. The producers of biosimilars have often alike advantages as the originators, because imitation of the complex production process of biopharmaceuticals is much more difficult and thereby generates a higher barrier for the potential competitors. In contrast, the producers of generics have to anticipate a quick expanding of new competitors from low cost countries (PWC 2008a).

The growth on the demand side is attributed to even more factors. The worldwide improving of the income situation and opening up of the markets are very important opportunities for the pharmaceutical industry. Particularly in the

emerging countries, the improving income has a stronger effect because there the elasticity of demand for pharmaceuticals is higher than one brackets. The growth in the matured markets is induced less due to quantitative than to the qualitative demand. New medication and product differentiation are the keys for the success there. The incipient trend towards individualization in diagnostics and therapy facilitates the differentiation. Also the growing public awareness towards health issues favors the development. Whole new therapeutic areas occur due to the intensified search for more quality of life and the broadening of the definition of health. It can be concluded, that especially the private spending will continuously increase on matured markets (PWC 2007).

Another trend positively affecting the demand for pharmaceutical products is the ageing and growth of the world population. The population is growing, if the birthrate exceeds the mortality rate. Despite of the fact that the birthrate in all industrialized and emerging countries is dropping, the world population is growing by about 78 million each year (PRB 2011). This is caused by remaining high birthrates in some parts of the world (Central and South Africa, South and East Asia) and growing life expectancy due to improved healthcare in most world regions.

The population ageing means that the proportion of the elderly population is increasing. It is a result of low birthrates in industrialized and emerging countries and high life expectancy. In more developed regions, the number of elderly people exceeded the number of children first in 1998. It is expected that after 2045 this will occur worldwide. In terms of figures, the population aged over 60 developed as follows: 200 million in 1950, 600 million in 2000, 700 million in 2009 and 2 billion are projected for 2050. Ageing applies to nearly all countries in the world. In more developed countries the elderly people account for 20 % and by 2050, the share will rise to one third. In less developed world regions the share is currently 8 %, but will increase to 20 % in 2050. Yet, the demographic change in the developing regions is faster. The countries have to face the changes on lower development stage and the time left for adjusting on the new demographic structure is shorter (UN 2010). Without appropriate programs, this might cause macroeconomic problems and have also consequences for funding of the health-care system. Thus the pharmaceutical companies might have to face the negative consequences of the demographic change, if the funding of the healthcare system will not be adjusted.

Apart from the opening of new markets and advantageous demographic trends, the growth perspectives for pharmaceutical industry include also the development of the diseases. Particularly in the emerging countries, the changes are grave. Along with the economic progress, the civilization or lifestyle diseases (cancer, diabetes, high blood pressure, allergies, asthma) spread. Meanwhile the disease burden there resembles the one of the developed world (PWC 2007). Moreover, the extremely swift urbanization and mobility increases the risk of the infectious diseases. The nature of strains to build up a drug resistance or mutated forms extends the risk. Another factor is the climate change. The global warming causes the expansion of infectious diseases (e.g. malaria, cholera, diphtheria, dengue fever) to more developed regions. The preventive measures in North America and

Western Europe are expected to be sufficient. The impact of global warming there involves rather worsening of respiratory illnesses, since the production of pollens and other common allergens increases. Another point is that, there are still diseases, which do not have therapy yet and also that new diseases can emerge. To find a new effective medication, especially for diseases like cancer, means to gain a large head start for pharmaceutical company (PWC 2007).

Thus the new fast growing purchasing power in emerging countries and the demand for new medicines in both matured and emerging markets as well as the anti-infectives markets represent enormous potential for pharmaceutical producers. The matured markets have much higher purchasing power but low growth rates. The pharmaceutical market in the emerging countries has huge growth prospects, particularly because of the fast growing economies, high ageing rates and social changes. China is predicted to be the second or third largest pharmaceutical market by 2020. India and Turkey might be upon the top ten. The decisive factor in less developed regions is the pricing due to the still low purchasing power. However, all the markets have one thing in common: the driving factor will be the innovation which is able to meet the various upcoming conditions (PWC 2007).

Figures confirm the positive trend. As already stated the healthcare expenditures grow with increasing GDP and also as proportion of the GDP. Consequently the increase occurs in most of the countries of the world. Figure 1.23 shows the growth of healthcare expenditures in Europe, the US, and Japan, presented as percentage of GDP. Since 1960 the proportion of expenditures has been tripled. The forecast for 2020 predicts even faster growth. In the US the expenses are expected to reach more than 20 % and the OECD-average shall rise from 9 to 15 %. In 2004 the worldwide healthcare expenses amounted to 4 billion US dollar, which is in average 639 US dollar per capita. The healthcare-expenses of the nation ranking first, the US, were 6,103 US dollar per capita. The average in the OECD[11] countries was 2,716 US dollar, indicating that the differences are huge. For instance the per capita expenses in Germany were 3,521 US dollar, whereas in China 70 and in India only 31 US dollar (PWC 2008a).

Considering only the prescriptive drugs, the E7[12] countries spent in average 0.94 % of their GDP in 2004 and accounted for 8 % of the world market. The G7[13] countries spent 1.31 % of their GDP accounted for 79 %. Even if all 14 countries spend the same proportion of their GDP for prescriptive drugs in 2020 the market would be, only due to the growth of GDP, worth 800 billion US dollar. The data of the whole pharmaceutical sales confirm this development. In 2010 the sales worldwide increased to 812 billion US dollar compared with 643 billion US

[11] The average is based on data from 30 OECD Members in 2007: Australia, Canada, Czech Republic, the EU-14 (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, and United Kingdom), Hungary, Iceland, Japan, South Korea, Mexico, New Zealand, Norway, Poland, Slovakia, Switzerland, Turkey, United States.

[12] The seven major emerging countries: China, India, Brazil, Mexico, Russia, Indonesia, Turkey.

[13] France, Germany, Italy, Japan, United Kingdom, Unites States, Canada.

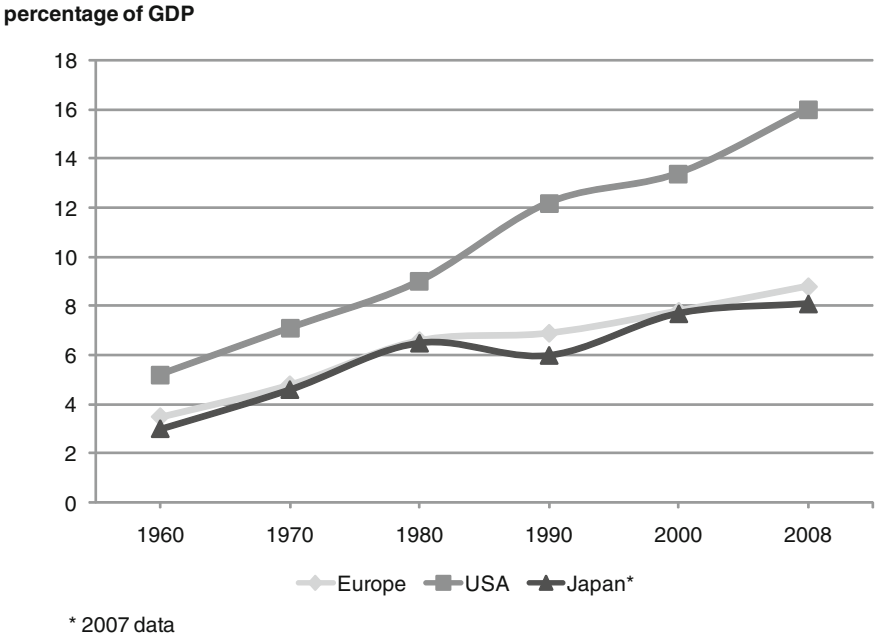


Fig. 1.23 Total spending (public and private) on healthcare as a percentage of GDP at market prices in Europe, the US & Japan (1960–2008, percentage) (EFPIA 2011)

dollar in 2006. The forecast for 2015 is 1.1 billion US dollar and for 2020 1.7 billion US dollar (PWC 2008a).

The Specific Challenges of the Pharmaceutical Industry

One of the crucial issues the top-pharmaceutical producers are facing is a lack of productivity in the lab. The originators are spending far more for R&D and produce far less molecules than 20 years ago. In 2007 Price Waterhouse Coopers indicated following reasons: (1) the targeted diseases need more complex medicines, (2) the demands for financial resources are higher but funding is more difficult due to higher risk and competition from other sectors like biotech, (3) many companies run a disadvantageous research-practice by concentrating on new molecules without sufficient knowledge of the disease, which is often responsible for late and expensive breakups (PWC 2007).

On the account of lack of sufficient innovation new problems occur: the financial situation is worsening, sales and marketing expenditures are rising, and the battered reputation does not improve. The bad reputation is a problem the pharmaceutical producers have been dealing with ever since. It refers to both the response of the medicines and the possible side effects of it. Specific sales practices (e.g. payments to medical practitioners for the preference of own products) in the recent years has also left its marks. Since improvement is not fast enough and public regard towards health is rising, the reputation is rather worsening.

The rising sales and marketing expenses were supposed to improve the financial performance, however, they had a negative impact eventually. Meanwhile sales and marketing costs are the biggest corporate expense. For instance, in 2005 R&D accounted for 17 % and sales for 33 % of the total corporate spending. There are several reasons for the growth of sales expenditures. Mostly it is due to the specific conditions for sales and distribution. In the matured markets the medical practitioners and the health insurance systems have a strong bargaining power. Also the complex healthcare system forced the companies to extend the sales channels. Through the fast expansion there are processes left which needs to be optimized. Lack of product improvements and bad reputation are contributive factors for difficulties. And last but not least the doubtful marketing practices towards healthcare practitioners do not cost only money but undermines the trust in the healthcare system. Many governments in the US and EU have already passed laws for more transparency in the promotion of medicines (PWC 2007).

Funding of pharmaceutical companies is a cyclical problem—adverse rating due to bad financial performance implies less money for further research. The deteriorated financial performance is caused by various reasons: (1) higher costs for R&D and higher break-offs, due to the higher complexity of the R&D process, (2) the absence of new TOP-sellers, (3) rising costs of market entry due to the difficult approval procedures, (4) high sales and marketing expenditures, (5) bad bargaining position with well organized customers and with highly specialized certificated suppliers, (6) overcapacity, (7) battered reputation.

For the big pharmaceutical companies, there is also another serious problem connected to the financial position. In 2006 more than 90 % of the revenues of the top-10 companies came from products which have been on the market for more than five years. Many of these patents are due to expire shortly. The US research company Sanford C. Bernstein has calculated, that the top-10-pharma companies will lose between 2 and 40 % (best and worst company) of the revenues to the producers of generics between 2008 and 2015 (Fig. 1.24). Since these are mostly blockbuster drugs, it makes for the top-10 together about 157 billion US dollar of sales. [e.g. in 2011: Pfizer's Lipitor cholesterol regulator ($9.1 billion), Eli Lilly & Co.'s Zyprexa anti-psychotic ($2.8 billion), Bristol-Myers Squibb Co.'s Plavix blood-thinning agent ($6.6 billion) and AstraZeneca Plc's Seroquel schizophrenia drug ($5.6 billion)]. Moreover, only 4 of them have sufficient pipelines to replace the loss (PWC 2008b). According to Standard and Poors, the expiration loss is unprecedented for both the number of drugs and the amount of sales (S&P 2010). This indicates the end of the blockbuster business model and of course downgrades the financial rating and eventually makes the funding of new R&D more difficult.

In addition to the internal problems, there are also movements happening outside the industry, which have a great impact on the pharmaceutical companies. Two of them should be discussed here: the funding of the healthcare system and globalization.

As the population in both the high developed and the emerging world is ageing, governments are under pressure to adjust the funding of the healthcare systems. One of the steps is to optimize the prescription of the paid medication. The aim is

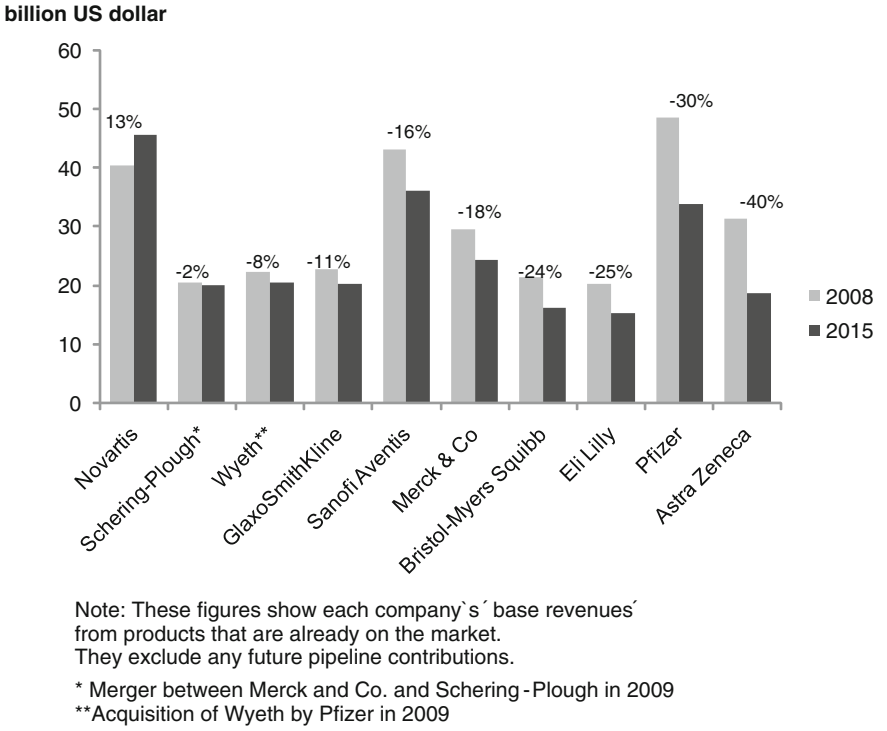


Fig. 1.24 The impact of generic erosion on big pharma revenues (2008–2015, billion US dollar, percentage) (PWC 2008b)

to ensure that prescribed drugs are effective and as low priced as possible. The US and the EU are already building systems for measuring the cost benefit ratios of medicines. The key should be the electronic medical records (EMR)—the data about effects of prescribed drugs gathered by medical practitioners and patients. The outcoming data provide best practice for further drug prescriptions and thus have a great economic impact on the pharmaceutical producers. In future only medicines, which are particularly safe, efficient, and cost-effective, will be included. It is estimated, that about 85 of the 273 big pharma major products might then fail. These make about 82 billion US dollar sales. In addition there is a higher risk in bringing new medicines on the market. On the other hand the EMR is a great data source for the originators too. Since different medicines often work for different people, the detailed records might lead to differentiated products with smaller outputs. This is positive not only for the patients, but also for the companies, since they would spread the risk much better. The clear winners are the producers of successful drugs, because also the prices will depend on the effectiveness.

There are also other ways of optimizing the healthcare system and although it falls to the responsibility of the governments, the pharmaceutical industry must

establish a dialogue with politicians as well as support the finding of solutions to avoid unnecessary pressure on the margins. For instance in the US the administrative costs account for between 20 and 31 % of the healthcare costs. The prevention of the diseases is less expensive than the treatment. Pharma can help to shift the approach towards prevention. Also the legislative requirements on the pharmaceutical companies can be optimized and the costs and therefore the prices can be reduced (PWC 2007).

Globalization has been one of the biggest challenges of recent years. Each industry has to deal with an increasingly complex and a rapidly changing environment. The pharmaceutical industry is no exception there. New markets and wider choices of locations or partners are only one side of the coin. Tough competition, supply chain disruptions, and counterfeiting are the other side. The increasing competition and new markets force pharmaceutical companies to produce more diversified products, to use a differentiated pricing for different markets and cut costs to save the money for innovation (PWC 2007). The innovation involves not only new medicines, but new technologies, business models, and internal processes too (Illert 2009). The traditional supply chains also do not suit the situation anymore. The challenge is to find the best and most reliable suppliers, to coordinate the cooperation between globally spread subsidiaries and research centers, and to update sales strategies. Since the demand in the markets of the developing world rises and the infectious diseases can travel fast, the sales structure must be also globalized. The globalization is expected also to impair the parallel trading and counterfeiting. For instance the re-imports to the EU are worth about 4.2 billion euro and about 10 % of the medicines sold worldwide are counterfeit. The situation is much worse in the developing countries. For example one half of the malaria medicines in Africa are probably fakes (PWC 2007).

In order to meet the challenges pharmaceutical companies have to perform a fundamental transformation of their business. The aim is to change or optimize the business processes in order to fit the new terms as well as to last in the highly dynamic environment. In the course of transformation following stakeholders need to be considered: investors, politicians, and customers. The investors need positive messages about improved productivity in the lab and reduced costs. The governments struggling with funding of healthcare systems would engage the dialog with pharmaceutical representatives, when the reputation improves and the price-healing-ratio is reasonable. In return the pharmaceutical industry would have more influence on legislation, particularly on the expensive approval procedures, international IP-management or cooperation models. Considering the customers, better and cheaper sale structures targeting the end customer rather than the healthcare practitioner as well as differentiated pricing for different markets are recommended (PWC 2007).

Meanwhile most of the major players have taken action towards the recommendations of Price Waterhouse Coopers from 2007. Research is focusing on the specific therapeutic areas in which the company has its strengths and is also advancing by highly rising areas of biopharmaceuticals, vaccines, and in some cases even generics. The revision was accompanied by a boom in the M&A

activity (Most prominent: Merck/Schering-Plough and Pfizer/Wyeth). A strong downsizing of costs has also been started. The leading companies (Pfizer, Merck, GlaxoSmithKline Plc, Bristol-Myers Squibb and Eli Lilly) are all running multi-billion-cost-cutting programs. Sales expenditures have been already cut by 10–15 % from the peak in 2005 and are planned by more than 30 % by 2015. As further sources for cut backs the personnel costs, overcapacities, internal structures, and the R&D approach were addressed. For example, Pfizer was running $2 billion costs saving program and the additional savings of the merger with Wyeth were estimated at further $4 billion. As it seems the companies are again on the way towards a long term profit growth (S&P 2010). However, according to the experts many of the implemented costs saving programs are rather in a manner of a top down approach with only short-term effects thus improper to secure the competitiveness. The search for real internal potentials as well as external synergies (through M&A and partners), and finally the distinction from the competitors has to be the objective (Illert 2009).

1.3.2.2 The Technological Market Environment

R&D Expenditures in the Pharmaceutical Industry

The business of the pharmaceutical industry is strongly R&D oriented. The global average expenditures on R&D among pharmaceutical companies come to 16.5 % of net sales in 2008, which is more than in any other industry. In 2008 the expenditures on pharmaceutical research amounted to 71,409.8 million euro. Thus the pharmaceutical industry accounts for 19 % of global expenditures on R&D. By far the most important driver for innovation are the research based pharmaceutical companies from the US, Europe, and Japan. As Fig. 1.25 shows, their expenditures increase yearly. The US overtook the others in 1995 and expands its lead since then considerably (EFPIA 2010, 2011)

Figure 1.26 shows the differences between these three regions regarding the R&D expenditures in the main industrial sectors. The pharmaceutical sector has a leading position in the US with 25 %. In the EU it ranks second with 17 % and in Japan third with only 8 % (EFPIA 2010).

The leading nations in the pharmaceutical sector have also high levels of national research intensity, calculated as R&D expenditures of all industries as a percentage of GDP (Fig. 1.27). They are surpassed only by Sweden (3.75 %) and Finland (3.73 %). Japan ranks first with (3.44 %). The difference between the US and Switzerland is minimal. Only the average of the EU-27 countries is relatively low. Considering the major European players in the pharmaceutical industry, the differences are rather striking: Germany (2.63 %), France (2.02 %), and Great Britain (1.88 %). Not only economic activities are shifting in the emerging countries, but also research. China has still a moderate R&D investment level (1.34 %), but since the GDP growth rates are immense, China is becoming an important research location (EFPIA 2010).

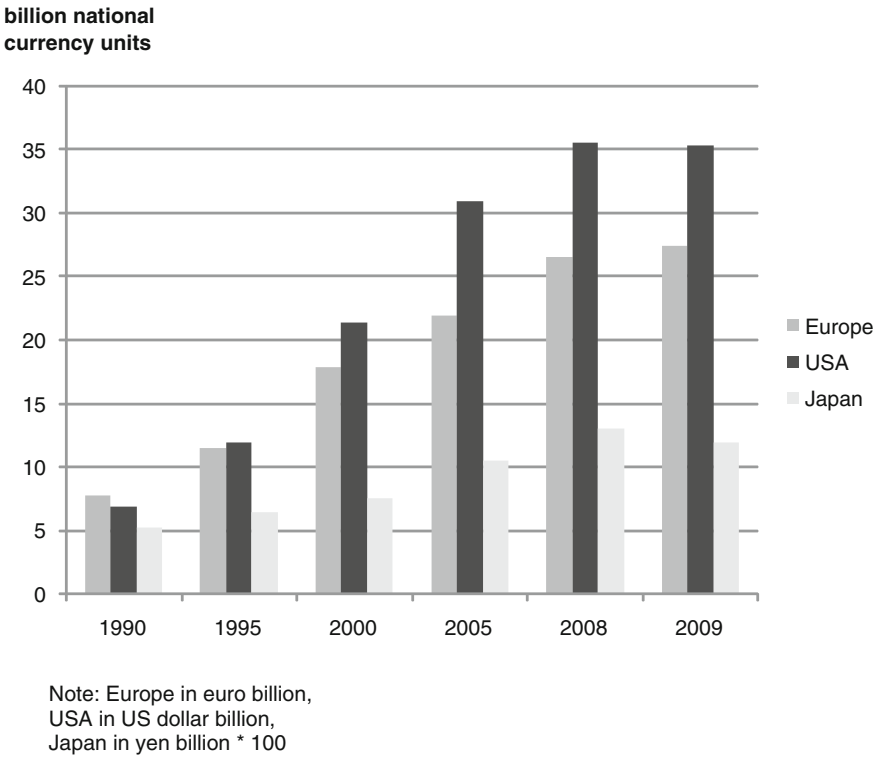


Fig. 1.25 Pharmaceutical spending on R&D in Europe, the US, and Japan (1999–2009, billion of national currency unit) (EFPIA 2010, 2011)

Next to the private research activities of the companies even more important research locations are the Chinese universities. These traditionally are the main resource of innovation in China and work closely with the private sector since the reforms of the education system (Preschitschek and Bresser 2010). The increase of research activities is also expected in other emerging countries like Brazil and India (EFPIA 2010). Considering the pharmaceutical industry, the emerging countries are becoming notably strong in basic research. Furthermore the labor costs there are still lower than in the mature countries. However, the companies from mature markets still do not have sufficient access to these new scientific areas. For the research based companies it is essential to establish a close cooperation or to move own resources there (PWC 2007).

The R&D process in the pharmaceutical industry is highly complex, risky, and expensive. In 2007, the expenses for development of one new chemical or biological entity were more than 1 billion euro, but the success of the medicine is not certain. After 12–13 years of R&D only two or three compounds out of 10,000 reach the market and of these only every fifth achieves the break-even (EFPIA 2009).

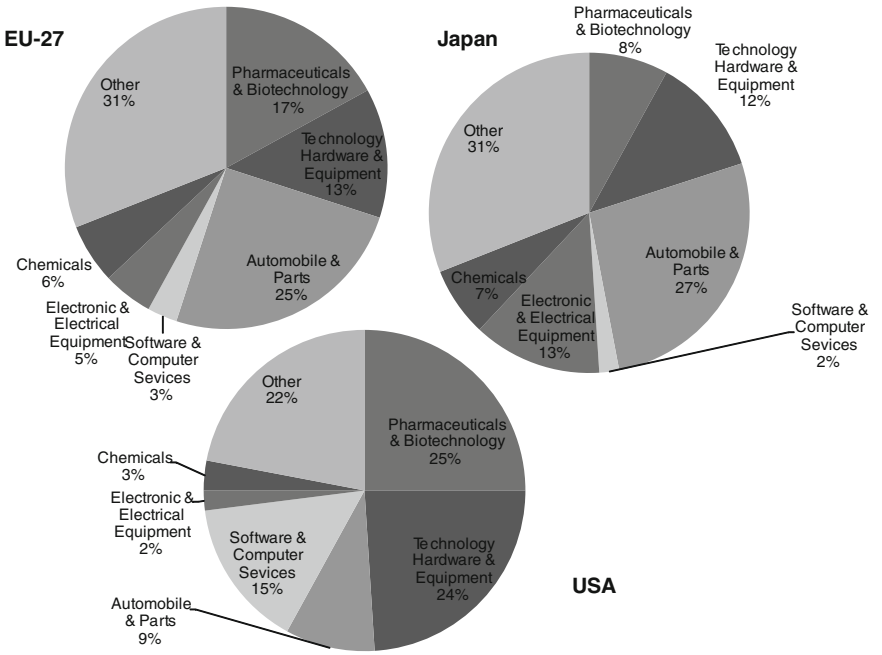


Fig. 1.26 Share of R&D investments in industrial sectors in the three main world regions (2008, percentage) (EFPIA 2010)

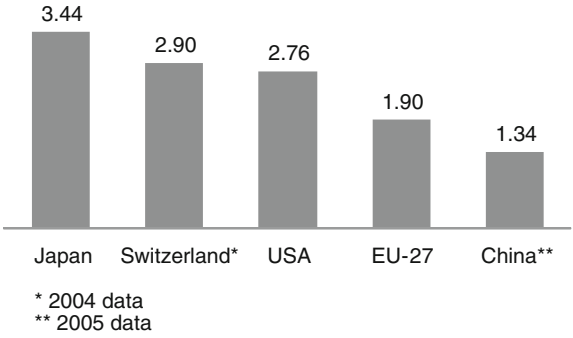


Fig. 1.27 R&D expenditures as a percentage of GDP (2008, percentage) (EFPIA 2010)

Figure 1.28 gives an overview over the process of development and commercial exploitation of new medicine. First the newly discovered compound is subject to the patent application. When granted, the preclinical testing of the chemical, biological and toxicological features, and healing qualities begins. If the results turn out satisfactory the company can start the clinical trials. These are tests on human beings and therefore, follow very strict technical and ethical rules. In phase I between 20 and 100 healthy volunteers receive the new medicine. In the second trials about 100–500 patients are being tested. The compound efficacy (the relation

between dose and effect) and safety (possible side-effects) are the main focus of this phase. In phase III between 1,000 and 5,000 voluntary patients are involved, which allows a much deeper understanding of the effects. Also the comparison with other treatments already in use and the long-term effectiveness are being examined. Finally the marketing authorization can be granted. The monitoring however, still continues. During pharmacovigilance medical practitioners and patients give feedback about the effects of the treatment. It is an important source for further information to effectiveness and long-term safety for a wide range of patient types. Based on these information improvements, new treatments but also withdrawals of the product from the market are possible (EFPIA 2010).

Until the market entry of the new treatment typically already 10–13 years of the patent protection (granted for 20 years) are elapsed. On average the pre-clinical development requires four years, phase I one year, phase II one or two years, phase III between two and four years. The R&D costs are distributed rather unequally. Figure 1.29 depicts results of the survey conducted by The Pharmaceutical Research and Manufacturers of America (PhRMA) among its members. In 2009 the clinical trials required about 59 % (phase I 8.1 %, phase II 15.4 %, phase III 35.1 %) of the R&D budget. The pre-clinical development accounted for

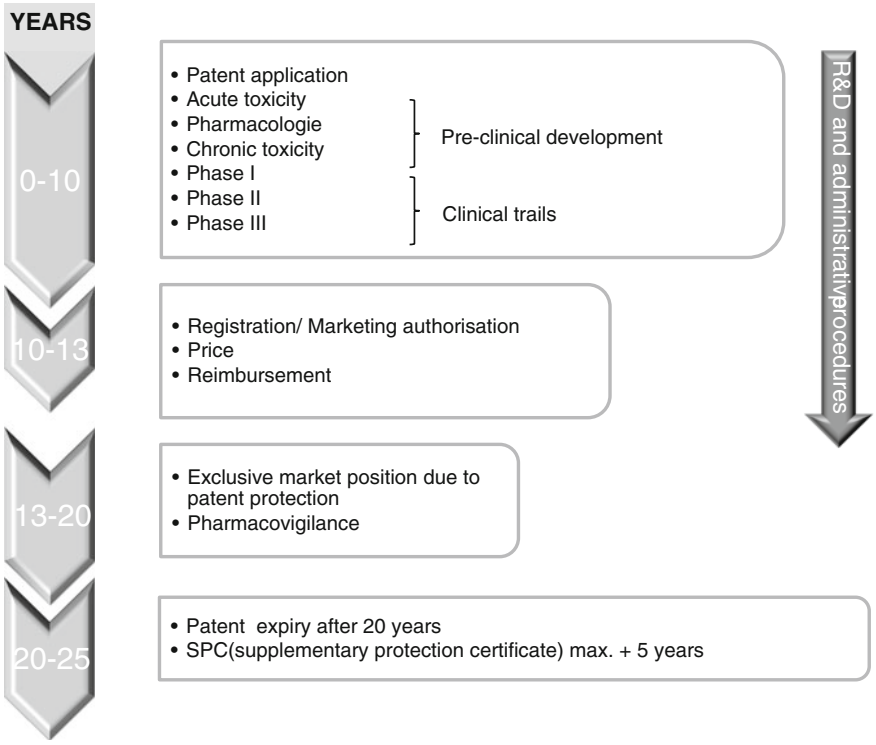


Fig. 1.28 The phases of R&D and sales of new medicine (EFPIA 2010)

25.5 %, the approval 4.4 % and the pharmacovigilance 11.4 % (EFPIA 2011). The costs for clinical trials have a rising trend. In 2008 clinical trials accounted for 53.6 % of the R&D expenditure and a year earlier for 49 % (EFPIA 2010, 2011).

The costs of R&D are rising not only due to more complex diseases, but to a large extend also because of the ever-more demanding legislative requirements. The pharmaceutical industry should engage in a dialog with legislative authorities in order to optimize the requirements for testing and approval procedures (PWC 2007). Figure 1.30 shows the evolution of the R&D costs between 1975 and 2006.

The Compound Crisis

In addition to the sharply rising costs also the number of new compounds reaching the market is sinking. Since the mid-90s the number dropped in all three leading regions (Fig. 1.31). The largest decrease suffered the EU, which has had a leading

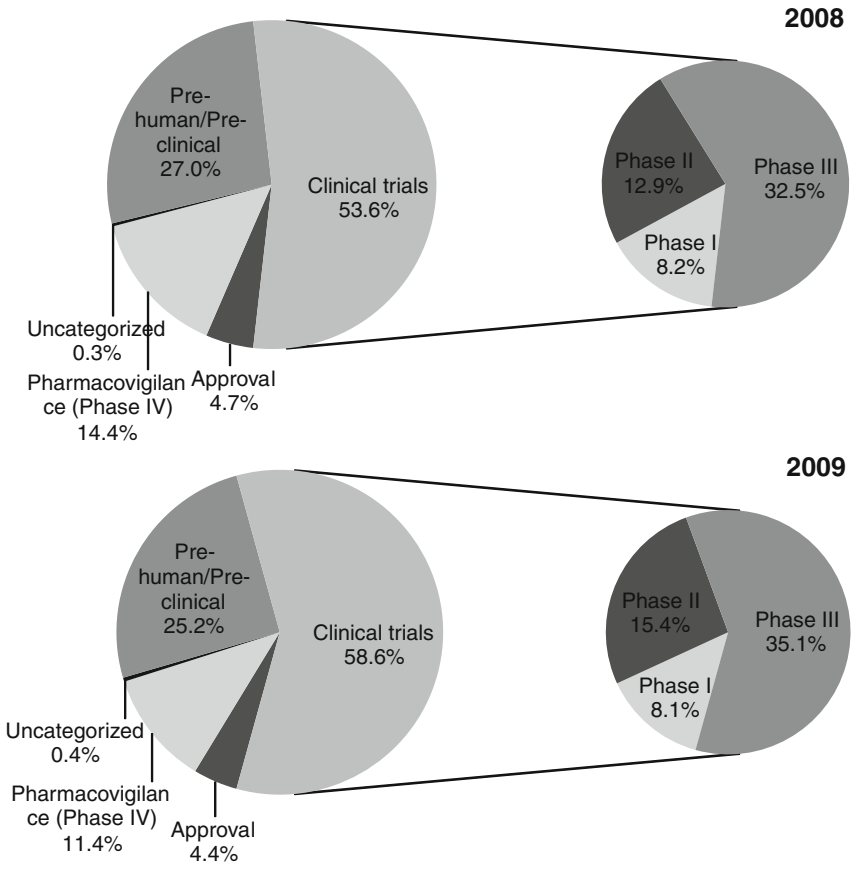


Fig. 1.29 The allocation of R&D investments by function (2008, 2009, percentage) (EFPIA 2010, 2011)

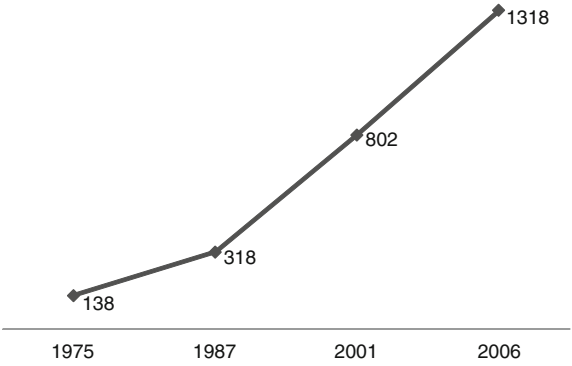


Fig. 1.30 Estimated full costs of bringing new chemical or biological entity to the market (1975–2006, million US dollar) (EFPIA 2010)

position until then. The US have become the major player. Particularly in the fields of biotechnology the EU needs to catch up.

Figure 1.32 shows a deeper insight in the share of new entities which reached the market in the last five-year period. Given the total number of compounds, which were in the trials or waiting for approval, an amount of 2,950 in 2009, the weak chance of any compound to be marketed becomes clear (EFPIA 2010). On the other hand the growth prospects for the industry seem favorable. For comparison, there were only 1,800 compounds in the pipeline in 1999. Many of the recently patented target the most pressing diseases like cancer (750), heart disease and stroke (277), rare diseases including immune system disorders (300), and HIV/AIDS (104) (S&P 2010). Any successful treatment of these would provide high revenues and possibly reach blockbuster rates. This explains the willingness of companies to put high bets in the R&D.

The R&D spending is rising and the amount of new compounds is sinking. In general terms, nowadays only two-fifths of new medicines are produced than ten years ago and the R&D costs are twice as large. The experts speak of a compound crisis. There are several reasons for the rising costs. Besides the increasing legal requirements (approval, trials, and other), many can be found in

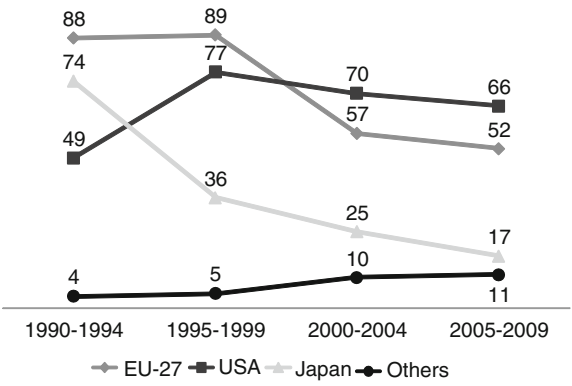


Fig. 1.31 Number of new chemical or biological entities (1990–2009) (EFPIA 2010)

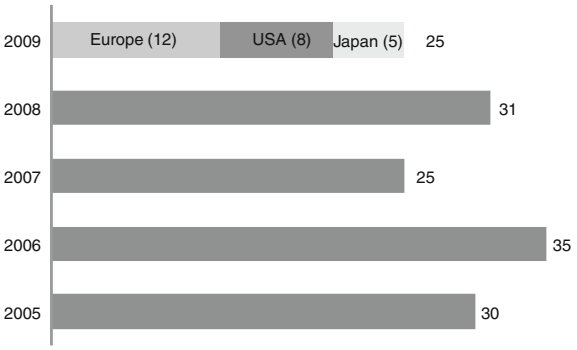


Fig. 1.32 Number of new chemical or biological entities (2005–2009) (EFPIA 2010)

the R&D process itself. In the search for new treatments the biotechnology looks much promising, but the retooling towards the biotech-revolution has also contributed to the increase of costs (EFPIA 2010).

Some of the cost drivers are based rather on the prevailing R&D process and can be optimized by the company itself. First the development of the compound is carried out often without a proper knowledge about the targeted disease. This partly explains the high rate of attrition in advanced stage of development, when already many resources have been spent. This strategy was successful when common diseases ware targeted and a chance for block-buster drugs was much higher. More complex treatments need more resources per se and the risk of dropouts is also higher. Furthermore it is expected that many of the new treatments would be oriented on specific patient subpopulations, thus even if successful, they cannot be turned to blockbusters (PWC 2007).

Since the statistics show that indeed for different groups of patients different medicines are effective and also that there are specific disease subtypes, the idea of targeted medicines seems to be the right approach. However, the strategy of developing new treatments according to specific patient subgroups proves to be more difficult than expected. The human genome is less approachable to mechanistic research than the scientists anticipated. For the past few years a new approach has been developed—the biomarkers. Within the framework of pharmacovigilance supported by databases founded by governments (EMR), better data about effects of the medicines matched with the patient data can be gathered. The evaluation shall help to identify the distinguishing marks of the patient subpopulations. As soon as the biomarkers are defined the patients can get the right treatment without having to try several others first. Also the pharmaceutical producer can save costs, since the number and size of the trials can be reduced and further research can be more targeted. The price of the therapy which has higher expectancy of success can be higher and the marketing costs much lower. The estimated savings of effective biomarkers are 50 %. Another cost saving potential delivers the pervasive healthcare—the monitoring of patients from remote and on real-time basis. With this a part of the clinical trials can be performed outside the clinical setting as well as data with

higher quality can by collected and faster evaluated (PWC 2007). In the recent years the real-time technology is booming (hardware: RFID, software: SAP HANA™), only the legal basis must be established yet.

The low number of new compounds is ascribed also to the cautious R&D strategy. Due to the higher risk whether a compound reaches the market (the approval) or not and then whether or not the new treatment will be eligible for reimbursement (only if there is no other treatment or it proves much better for the therapy than other) the companies try to minimize the risk by 'playing it safe'. Indeed the achievement of minor improvements rather than breaking innovations became a characteristic of pharmaceutical industry in recent years. The standardized 20 years of patent protection, regardless the complexity of the research, facilitate this strategy. Possibly some additional years of patent protection for superior products would bring forward the true innovation. Price Waterhouse Coopers estimates higher cash-flows from truly innovative medicines by 50–100 % if patent protection for them rises from 20 to 25 years (PWC 2007).

Considering the grave organizational and cultural changes the pharmaceutical companies must undertake it might be in many cases more advantageous to buy the research results from small and highly specialized research companies. This reduces the complexity and allows much flexible business strategy (PWC 2007).

Products

The transformations in the pharmaceutical industry have an impact on new medicines. The combination therapies, biomarkers, and identification of disease subtypes imply product diversification. Thus the financial risk in case of failure can be reduced, but more complex technologies and also new manufacturing approaches (the return of economies of scale will drop) are needed first. The new manufacturing process must become more flexible to produce a wider range of products (PWC 2007).

The search for new treatments in order to differentiate own products from competitors resulted in a boom of biological-based medicines. These are more sophisticated than chemical-based medicines and are better suited to fit the individual needs of patients. Examples for the therapeutic areas are cancer, metabolic or immunological disorders. The molecules closely resemble their natural counterparts in the human body. They are also larger than chemical molecules and more complex in terms of manufacturing and administration (the exact function in the human body is difficult to determine). The production is not possible through chemical synthesis but only on biological materials (in bioreactors) (EBE 2008). As for biosimilars (biopharmaceutical generics)—the biopharmaceuticals are difficult to copy, even if the patent application of the process (natural product cannot be patented) is disclosed, because the right conditions in bioreactors are necessary.

The first biopharmaceutical treatment came to market in 1982. Since then over 160 biological drugs and vaccines have been approved and reached ca. 350 million individuals. There are still new products possible, not only among proteins, but

Table 1.5 The key biopharmaceutical companies ranked by sales in 2006

Rank	Company
1	Amgen
2	Genentech[a]
3	Genzyme[b]
4	UCB
5	Gilead sciences
6	Serono
7	Biogen idec
8	CSL
9	Cephalon[c]
10	MedImmune[d]

[a] Acquisition of Genentech by Roche in 2009
[b] Acquisition of Genzyme by Sanofi in 2011
[c] Acquisition of Cephalon by Teva in 2011
[d] Acquisition of MedImmune by AstraZeneca in 2007

also genes (gene-therapy) and tissue-engineering[14] (EBE 2008). In 2001 biopharmaceuticals accounted for 12 % of global market sales, by now they are an estimated 30 %. Among the new molecules launched on the market each year about one-fifth come from biotechnology. Although the sector is fast growing all around the world, the leading position with a sizeable head start has the US. For example among the public traded companies the US accounts for 73.8 % of global biotechnology revenues and 79.6 % global biotechnology R&D expenditures (EFPIA 2009). When having a look at the profitability there are only a few large leading companies. The top 10 companies ranked by sales are listened in Table 1.5. Some of the traditional big pharma companies, like Johnson & Johnson and Merck & Co., also have considerable biotech business areas. However, the market is dominated by small non-profit research companies. These depend on other sources of financing than sales. These include angel investors, venture capital firms, public offerings, partnership deals with big biotech and pharmaceutical companies. M&A plays an important part in this line of business. The big pharma companies made deals with biotech companies in order to improve their pipelines. For instance in 2006 and 2007 Novartis purchased Chiron, Merck & Co. acquired Sirna Therapeutics, and AstraZeneca merged with MedImmune (Hoovers 2010). In 2008 Eli Lilly & Co. purchased ImClone Systems Inc. In 2009 the acquisition of Wyeth by Pfizer and the acquisition of Genentech (remaining 44 %) by Roche also considerably strengthened the biotech lines of these two giants (PWC 2009).

The changes regarding the products are not restricted only to new technologies. Also new uses for long known treatments combined with new technologies are conceivable as vaccines show. As already stated the vaccines sector is growing rapidly (see Sect. 1.3.2.1). One reason is the rising demand, but there is also one

[14] Covers the applications that repair or replace tissues. The tissues are promoted to grow in vivo in bioreactors and than they are implanted into the living body.

other, the broader range of indications the vaccines are developed for. Many of the vaccines in the pipeline differ from the common approach. The largest proportion holds oncology with 90 vaccines in the pipeline (in 2007). Furthermore there are also vaccines for cocaine addiction, diabetes, hypertension, Alzheimer's disease, psoriasis, food allergies, rheumatoid arthritis, and nicotine withdrawal in development. There were traditionally the Big Five players, which dominated the sector (GlaxoSmithKline, Merck & Co., Sanofi-Aventis, Wyeth (now Pfizer), and Novartis via its acquisition of Chiron), but according to the pipelines many smaller pharmaceutical companies might be expanding (PWC 2007).

1.3.2.3 The Legal and Political Market Environment

On this field the pharmaceutical industry faces challenges very similar to those of chemical industry (see Sect. 1.2.2.3). The legal market environment is highly complex since the legislation involves detailed health and safety, intellectual property and approval regulations, which vary from one country to another. However, it is crucial for the success to manage the complexity, because each slip might be disastrous in the fierce competition. For example one gap in the patent application or wrong geographical patent range might lead to the loss of the patent right to a competitor. For pharmaceutical companies this situation is even more difficult than for chemical companies and that for more reasons. Due to higher R&D expenditures the refuse or loss of a patent right hurts more. Second the legislation is more penetrative on the pharmaceutical industry since the medicines are in direct contact with the human body. The R&D-process as well as sales conditions are highly regulated (see Sect. 1.3.2.2). The room for collaboration and the usage of the potential in the emerging countries is also restricted due to regulations. For instance the patent application includes also the suppliers of active ingredients and important auxiliaries. Therefore, the company cannot easily switch to a new supplier. Even the contracts on less important stages of the supply chain (e.g. packing) must fulfill rigorous requirements.

Another important topic is the public attitude towards the pharmaceutical industry and its research. This includes mainly the ethical questions of research (genetic engineering) and the approval of a pharma-promotive legislation among voters (PWC 2008b).

Indeed in the long-term it is expected that companies will relocate in the regions with better conditions—starting with application procedures and approval conditions, further the production and sales conditions, the range of international patent protection, and last but not least the governmental support and political stability. The US have a clear advantage due to the standardized regulations and single language. The EU attempted standardization for this field already in 2001, but it failed because of the different national implementations (PWC 2008b). Among the emerging countries India gained capital importance. The country joined WTO in 2005 and transformed its patent legislation and a huge growth of contract research and manufacturing services (CRAMS) followed. The analysts

estimate that India has potential for 35–40 % of the global pharmaceutical CRAMS market. India has long term experience with R&D and production activities in chemicals as well as advantageous regulations and low labor costs (Goodall 2005).

Still according to the market share the world most important approval authorities are the American Food and Drug Administration (FDA) and the European Medicines Agency (EMEA). The companies evaluate the quality of approval procedures for both comparable, but they criticize the huge differences in the requirements between them. The efforts a company has to supply for the second application are almost double. All previous attempts to harmonize the systems have failed because of the high complexity and costs required (PWC 2008b). The regulators in the emerging countries become more and more important since the manufacturing and R&D activities are shifting away from their traditional locations. The Association of South East Asian Nations (ASEAN) countries, for example, already completely transformed their regulatory systems in order to adjust them to their patient population. The countries also attempt to harmonize the registration and control regulations, which would give them further competitive advantages besides low labor costs (PWC 2007).

Despite of the efforts to harmonize the systems, the pharmaceutical industry will in the future have to deal with more requirements than ever, since the authorities enhance their programs. First the regulators require communication on regular basis at a much earlier development point. For the FDA it is stated within the framework of the Critical Path Initiative with the aim to create new tools for improving safety and efficacy of new medicines. The EMEA intensified a similar goal through its Road Map to 2010. Second in order to improve the risk management, the companies are required to provide information not only on what they know but also what they do not know about the effects of the medicine (European Risk Management Strategy). And third the evidence that the new medicine is better that any comparable medicine becomes increasingly important. Furthermore in order to achieve more transparency all data must be submitted electronically, the prescribing doctors must have access to the evidence on adverse events as well as all business processes must be audited through a third party. The FDA is also running an initiative to improve the manufacturing process and several countries already passed pedigree laws, which apply to every contractor in the supply chain worldwide (PWC 2007). In the US also the Physician Payment Sunshine Act has been adapted. It aims to make the relationship between the pharmaceutical company and the healthcare practitioner transparent. For the pharmaceutical industry it means further reporting requirements and also a dramatic change in the sales process. In order to meet all these new requirements, the companies need to address actively following problem areas: data aggregation and reporting issues as well as process complexities and that in all operations (esp. R&D, finance, sales, and manufacturing).

1.3.2.4 The Demographic Market Environment

The demographic environment of the pharmaceutical industry regards to two strategic issues: the purchasing power of the population and labor market. As already discussed in the Sect. 1.3.2.1 the growth and ageing of the world population favors the pharmaceutical industry. The question on available labor resources and their educational level resembles the situation in chemical industry (see Sect. 1.2.2.4). Since the pharmaceutical industry is even more research oriented than the chemical industry and has also to meet more legislative requirements, its dependence on highly qualified employees is even higher.

On the other hand the research based pharmaceutical industry creates besides the direct employment also indirectly new jobs. Following the studies in different countries the indirect employment (upstream and downstream like wholesalers, pharmacies, pharmaceutical consultants, and suppliers of active ingredients) is three or four times higher than the number of own employees. A significant proportion of them are the positions with high value added. For instance in the EU the industry employs directly more than 633 thousand people and about 113 thousand work in R&D. Since R&D is being done with close cooperation with universities and hospitals, actually more thousand researches are involved (EFPIA 2010).

1.4 Process Areas and Process Groups of Process Manufacturing Companies

Looking at the environment in which the chemical and pharmaceutical industries operate and the market forces to which they are exposed makes clear that both industries are subject to a permanent change process that can only intensify with time. This is forcing existing companies to focus on their core competences and fields of business. In doing so, they must in particular observe, analyze, and describe each of their business processes. The processes that form the focus of these efforts are depending heavily on the company's field of business.

Taking for example in the chemical industry the anticipated changes in products and the resulting resegmentation of the industry, it is apparent that all four segments place different requirements on business processes.

Commodity producers, who are required to supply products reliably at the lowest possible price, must in particular focus on production, quality, warehouse, and delivery processes, while R&D, sales, and marketing processes take more of a back seat. The exact opposite is true for product innovators. As the future developers of new specialist products, they must focus on processes related to research and development as well as sales and marketing of new products. Production and quality management and the distribution of goods are of no concern to them, since these tasks fall under the remit of the product specialists. As subcontractors of the product innovators, the product specialists also have to ensure their planning is as accurate as possible.

The group with the widest range of business processes to manage is that of the portfolio masters. Their core competence lies in the ability to deliver an accurate portfolio management. This is a process that places requirements on both research and development and sales and marketing. Moreover, they must be in a position to produce and ship their product portfolios, which means that over and above production, warehouse, and delivery processes, they must also pay close attention to planning processes.

The pharmaceutical industry too, must focus on a diverse range of different business processes. Research pharmaceutical companies will have to intensify their efforts to ensure their products are on the market for as long as possible before patents expire. This means shortening drug development cycles, which cannot be achieved without closely examining R&D processes. Conversely, generic drug manufacturers in particular must pay greater attention to their production, sales, and delivery processes.

To help chemical and pharmaceutical companies analyze their business processes, SAP Consulting has developed business process maps (BPM), which can be used as a starting point to classify a company's process areas. The company's value chain is examined on the basis of its process areas. In the chemical industry, the process areas are:

- Research and development
- Planning
- Procurement
- Production
- Quality assurance
- Sales and marketing
- Storage and delivery.

The company's process areas are then examined at the next level, namely as process groups. At this point, the first industry-specific play a role. Examples include trading businesses in procurement, batch production and packaging in production, or the management of dangerous goods in storage and delivery. Furthermore, every company has a number of supporting processes that cannot be assigned to a particular process area but that concern the entire value chain. These include industry-specific compliance requirements and financial accounting processes, for example. Figure 1.33 shows the SAP business process map for the chemical industry.

At a first glance, at process area level, the pharmaceutical industry appears to match the chemical industry, the only slight difference being that the production area accounts for the fact that production processes are regulated (Fig. 1.34). However, a look at the process groups soon reveals considerable differences. For instance, the research and development process in pharmaceutical companies is unique, which means the process groups in this area cannot be compared with any other industry. Similarly, the process groups of "active ingredient production", "indirect sales", and "supply chain security" are very particular to the industry.

Nevertheless a certain amount of overlapping with the chemical industry can be identified. The planning process groups are identical, for instance. Both industries

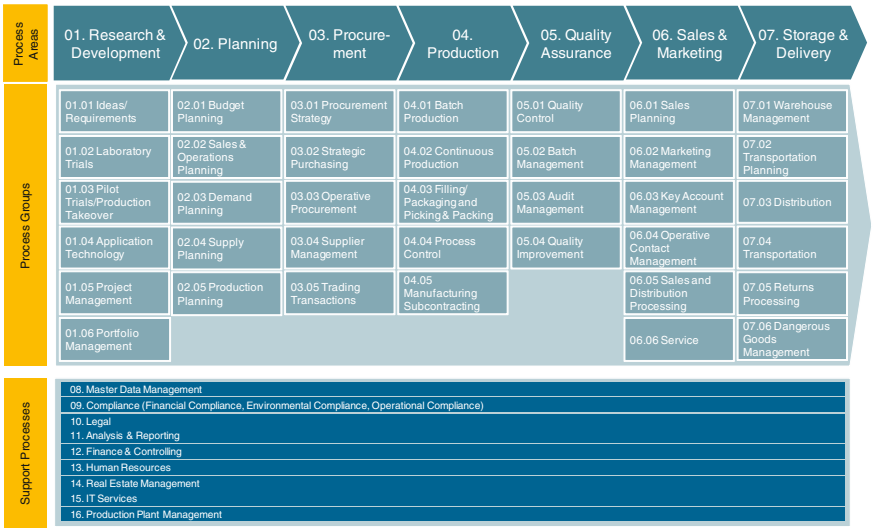


Fig. 1.33 Process areas, process groups and supporting processes in the chemical industry

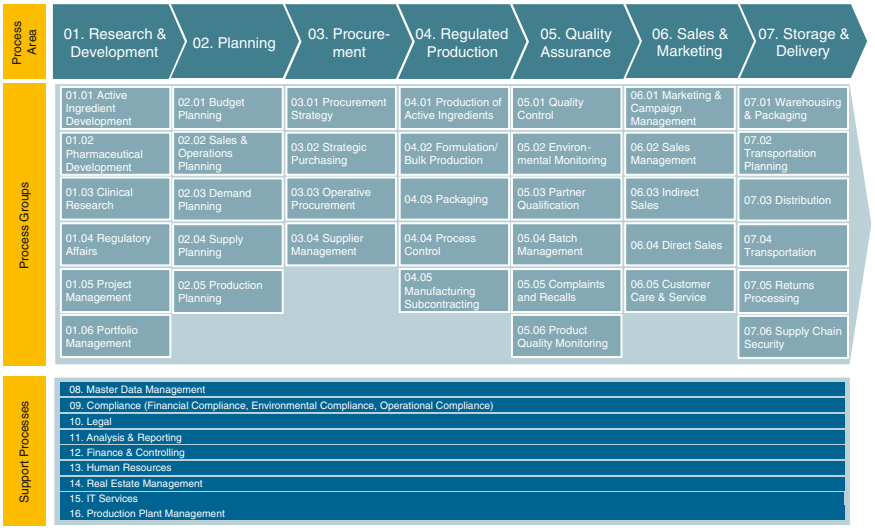


Fig. 1.34 Process areas, process groups and supporting processes in the pharmaceutical industry

also feature manufacturing subcontracting, transportation planning, distribution, and transportation itself. In addition, both industries rely on the same supporting processes. It is important to note, however, that differences may occur in these processes under closer inspection. The compliance process provides one such example. In the pharmaceutical industry, compliance is dictated by validation requirements, while in the chemical industry, REACH is applicable.

Based on the resulting customer-specific business process map, concrete business process management measures can now be taken. The underlying process model for such measures is described in the next chapter.

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