THE PHARMACEUTICAL INDUSTRY AND PRODUCT LIABILITY EXPOSURES

By
Johannes Klose, Reg. Pharm, ARM, PhD
Allianz Global Corporate & Specialty
PharmChem Solutions
Lavaterstrasse 67
CH-8002 Zurich
Switzerland
johannes.klose@art-allianz.com

1. A Snapshot of the Pharmaceutical Industry and Future Trends

1.1 Overview

In the broadest sense, the Pharmaceutical Industry comprises various different business models which cover all or only some parts of the pharmaceutical product life cycle. Traditionally, the pharmaceutical industry segment was constituted by research-based pharmaceutical companies which had an integrated business model from the research laboratory to distribution, meaning they developed, manufactured and distributed medicinal products.

A pharmaceutical product is defined in the term *medicinal products* within the European Union in Article 1 of Directive 2001/83/EEC as follows:

Proprietary medicinal product:

> Any ready-prepared medicinal product placed on the market under a special name and in a special pack

Medicinal Product:

> Any substance or combination of substances presented for treating or preventing diseases in human beings. Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product.

Substance:

Any matter, irrespective of origin, which may be:

- human, e.g. human blood and human products
- animal, e.g. micro-organisms, whole animals, parts or organs, animal secretions, toxins, extracts, blood products
- vegetable, e.g. micro-organisms, plants, parts of plants,vegetable secretions, extracts;
- chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical modification or synthesis

The classic pharmaceutical product life cycle can be depicted as follows:

Research/Discovery -> Development -> Manufacturing -> Marketing -> Distribution -> Surveillance (-> Withdrawal)

Research/Discovery

Research/Discovery represents the earliest R&D stage and comprises 'untargeted' research (basis for important scientific discoveries) as well as 'targeted' drug discovery. This early R&D stage is lengthy, complex and risky and it needs a significant proportion of the total R&D budget. Especially at this early stage the pharmaceutical industry cooperates with the public research sector and specialized smaller pharmaceutical companies (R&D licenses).

Development

Substances from Research and Discovery undergo a preclinical (toxicity, pharmacology) as well as clinical (Phase I to III) development. Between 1 in 5000 to 1 in 10.0000 substances are necessary to produce 1 new substance which becomes a marketable medicinal product. Unsuccessful research accounts for 80% of the cost and 25% of the time. This high failure rate implies significant cost which requires a strong cash flow to be financed. Failure rates are much higher in Research/Discovery than in late development stages.

Research/Discovery and Development is usually referred to as R&D. The R&D stage without administrative procedures for registration and market launch takes about 10 years. Development of a New Molecular Entity (NME) has now reached US$ 800 Million, which is a 250% increase from a decade ago (Source: The Tufts Center for the Study of Drugs Development, Nov. 2001). However, average pharmaceutical R&D expenditure as percentage of sales has always been in the range of roughly 17 to 20% in the last 15 years in Europe and has even declined from more than 20% in 2000 to 17 % in 2005 (Source: EFPIA).

Manufacturing

Traditionally, manufacturing is part of the integrated business model. Pharmaceutical companies produce and / or buy raw materials to synthesize Active Pharmaceutical Ingredients (API's). API's are incorporated into the final dosage forms which are packaged.

There have been tremendous changes in the global manufacturing and distribution patterns of the pharmaceutical industry. Production of raw material and API's as well as packaging and formulation services by toll manufacturers have become more and more important in the last decade.

Marketing

The pharmaceutical industry uses a variety of marketing instruments and has accomplished a high level of sophistication in the targeted use of these instruments. Apart from phone calls, journal ads and direct to consumer advertisements (DTC's), sales reps play a crucial role in attracting physicians awareness and in influencing their prescribing habits. The top 30 pharmaceutical companies use almost 100.000 sales reps in the US.

Diminished growth has driven promotional spend and size of sales forces down.

Maintaining huge numbers of sales reps in many markets is only possible for the very big pharmaceutical companies. Medium sized and smaller pharmaceutical companies rely very much on the cooperation with marketing and distribution partners (licenses).

Distribution

The pharmaceutical supply chain depicts how medicinal products are delivered to patients. According to the basic supply chain model for prescription drugs, pharmaceutical companies distribute the products to wholesalers, which sell it to pharmacies. Pharmacies represent in most cases the ultimate contact to the patient / consumer.

Players and their relationships in the supply chain vary depending on product type (e.g. prescription / OTC; drug / medical device; hospital product / pharmacy product), regulatory environment and other factors. Numerous pharmaceutical supply chain variations result in significant price variability across different types of consumers and markets.

Generics

As soon as a pharmaceutical product comes off patent the originator company looses its marketing and distribution monopoly and another pharmaceutical company (generic manufacturer) is now able to file approval for, manufacture, market and distribute a essentially similar product (generic product) without a marketing license from the originator company.

Essentially similar means that the generic product has the same amount of the active ingredient in the same dosage form as the originator product and has been shown to be bioequivalent to the originator product. Essentially similar products are supposed to be therapeutically equivalent and interchangeable.

Patent protection lasts for 20 years and can be extended up to 5 years through a Supplementary Protection Certificate (SPC). Originators apply for many different patents around a single pharmaceutical product (lifecycle maximization). These additional patents refer to many different product properties as for example new uses, indications, dosages, changes in formulation, color or markings and create many different 20-year protection periods for one single product. The complexity of patent coverage of pharmaceutical products results in substantial litigation due to patent infringement.

An originator company may derive additional protection for a pharmaceutical product from data exclusivity. Several countries introduced principles of data exclusivity in the

late 80ies to compensate for insufficient patent protection. During the period of data exclusivity, health regulatory agencies are not allowed to process applications for generic products.

1.2 Current Situation of the Pharmaceutical Industry

Especially in the last two decades, changing markets, limitations in healthcare budgets and rising cost as well as complexity in R&D processes and regulations have increased pressure on all segments of the classic value chain. This created opportunities for new business models and resulted in the formation of service providers with specialized activities as for example basic research laboratories, Contract Research Organizations (CRO's) for clinical trials, toll manufacturers and contract sales services. Growth perspectives and market opportunities depend on the business model as well as political, regulatory and market environments.

Global Market

Growth of the global pharmaceutical market did not achieve the double digit rate of recent years and decreased to about 7% in 2005. The 2005 sales figure of the global pharmaceutical market is roughly US$ 550 billion. Almost half of the worldwide market sales derive from North America (mainly US) and about one third derive from Europe. (Source: DrKW Equity Research).

Pricing pressure from generic competition and limited healthcare budgets, declining R&D productivity and increased regulatory hurdles altogether result in slower long-term growth.

Domestic Markets

USA

The US has been one of the fastest growing markets. Growth of US prescription drug sales exhibited a significant slowdown in recent years due to very intense generic competition, increased patient co-pays and a decreased number of approved new molecular entities. Medicare reform in 2005 resulted in new prescription drug coverage

for recipients of Medicare and is likely to increase US prescription drug growth, primarily by means of volume growth but could be partially offset by price reductions.

Europe

Growth was also reduced in the European pharmaceutical market in recent years. Major drivers for deceleration have been price cuts, generic competition and cost-effectiveness evaluations. In contrast to the US, the majority of prescribed drugs are paid from governmental healthcare budgets and the European market is highly fragmented. For this reason, governmental cost-containment programs have a major influence on pharmaceutical prices and sales growth.

Significant differences in pricing levels throughout the European Union provide the basis for parallel trade (pharmaceuticals are exported from low-price countries into high-price countries). Parallel trade leads to a loss of pricing power and sales growth for the pharmaceutical industry. Parallel trade in the EU pharmaceutical market was estimated to amount to more than € 4 billion (value at ex-factory prices) in 2004 (EFPIA). Due to intensive supply chain management by major pharmaceutical companies, the extent of parallel trade in Europe has dropped in 2005.

Europe's Biopharmaceutical sector is by far smaller than the US counterpart. Revenues in the European Biopharmaceutical sector in 2005 amounted to roughly € 8 billion in contrast to € 38 billion in the US.

Japan

Japan is the second largest national domestic market for pharmaceutical sales, partly because Japan has the highest level of drug prices in the world. Low-single digit growth characterized the Japanese pharmaceutical market for many years. On a constant dollar basis, the Japanese pharmaceutical market exhibited almost 7% growth in 2005 which is one of the highest year-on-year growth rates in the last decade. Growth drivers included increased prescription in cardiovascular, CNS, oncology and innovative products as well as the absence of governmental periodic price cuts (every 2 years).

Flat sum reimbursement and increased patient co-pays represent inhibitors of sales growth in the Japanese market. Incentives for Japanese doctors dispensing drugs have decreased in recent years which resulted in more drugs being dispensed by pharmacies and a change in prescribing decisions. Prescribing habits are more and more shifted from financial motivations towards therapeutic decisions (Source: DrKW Equity Research).
From a domestic pharmaceutical company perspective, 2005 was a year of significant consolidation (four big M&A's).

Growth Markets

Form a global perspective Asia (especially China and India), South America (especially Brazil and Mexico) and Middle East are examples for pharmaceutical markets which exhibit above average growth.
Apart from growth which is driven by economic and demographic factors, there are growth opportunities from breaking up the integrated value chain. Indian pharmaceutical companies for example established themselves as reliable lowest-cost contract manufacturers of API's and finished dosage forms, especially for generics. Cost squeeze is forcing Indian companies further east to China to drive down costs. Big Indian pharmaceutical companies increasingly accomplish strong positions on generics in the US market. Due to lower cost, China is competing with India in manufacturing of API's and finished dosage forms. Many pharmaceutical companies are setting up R&D centers and local R&D co-operations in China due to low cost and speed of recruitment. The Chinese pharmaceutical market had more than 20% growth in 2005 and is assumed to exhibit double-digit long term growth.

Generics

The average European and North American market share of generics in 2005 was about 15% in value and about 20% in volume with significant differences from country to country. Generics had a low market share (ex-factory prices) in countries like Spain, Portugal, Switzerland, Ireland and Belgium and a comparatively high market share in Latvia, Slovenia, Hungary, Germany, UK and Denmark. (Source: EFPIA, EGA).

Generic attack typically occurs for commodity products (used for large numbers of patients) in chronic indications (sustained cash flow) and is facilitated if active ingredients and dosage forms do not imply too complex and costly manufacturing procedures. Additionally, bioequivalence is often more difficult (cost and time) to demonstrate for sophisticated dosage forms.

As with any other product, generics gain market share depending on the length of time on the market because it takes time to create awareness and penetrate the market. The dynamics of market penetration varies to a large extent and is usually faster if a large number of generic manufacturers simultaneously attack an originator product.

Biopharmaceuticals with high sales figures (peptide hormones such as insulin and protein hormones such as erythropoietin) are a future growth opportunity for generic manufacturers as soon as regulators have paved the way for biosimilars (essentially similar biopharmaceuticals).

It is in some respects paradox that the generic business model relies to a large extent on R&D productivity but at the same time threatens R&D budgets of originator companies by reducing their cash flows. It remains to be seen how this affects generic growth in the long term.

1.3 Trends and Developments in the Pharmaceutical Industry

Changing Market Dynamics

The traditional dominating pharmaceutical markets North America and Europe which accounted for almost 80% of worldwide sales in 2005 have ceased to exhibit double digit growth. European pharmaceutical markets are more and more dominated by cost-containment policies which aim at diminishing product prices and thereby limit pharmaceutical product sales growth. It is likely that rewards for innovation (attractive product prices) will decline also in the US.

Double digit growth rates in pharmaceutical markets can now be observed in Asian, South American and Middle East Markets, which are in many cases part of overall economic double digit growth.

Health Economy: Pricing pressure and Cost Containment

Increasing average life expectancy as well as the growing number of elderly people in relation to working age citizens contributing to social funds is both putting enormous pressure on publicly funded healthcare budgets. If unemployment rates are rising, this situation is worsened due to fewer contributors of premiums and more recipients of benefits. Demographics will be and unemployment rates currently are more favorable in the US compared to Europe. Additionally, less than 50% of the healthcare spending in the US is publicly funded (Source: OECD).

Growth of expenses for pharmaceuticals exceeded total healthcare growth expenditure in many European countries in the last 10 years. Compared to the enforcement of fundamental changes of structures and processes in the healthcare sector, cutting back prices of pharmaceuticals is a much easier way to control healthcare budgets. This approach necessarily entails discussions about the therapeutic and economic value of medicines. In the past, governmental control of the therapeutic value of medicines was accomplished to a large extent by drug regulatory authorities that approved new medicines on the basis of efficacy, safety and quality.

The increasing need for control of healthcare budgets in Europe resulted on the one hand in the creation of organizations that evaluate cost-effectiveness of drugs (e.g. NICE in the UK and IQWiG in Germany) and on the other hand in an enlargement of duties and responsibilities of some drug regulatory authorities.

New drugs, which are structurally very similar to already known drugs and exhibit only minor differences in terms of efficacy, safety and quality, represent one of the hot spots in the discussions about the economic value of innovative medicines.

In addition to governmental efforts to control healthcare budgets, pricing pressure arises from generic competition. Drug sales at risk from generic competition between 2006 - 2010 are estimated at roughly US$ 100 billion, which equals almost 20% of 2005 global pharmaceutical sales (Source DrKW Equity research). European governments and also Medicare/Medicaid in the US are enforcing increased utilization of generic medicines.

Drug Regulatory Authorities – rising therapeutic standards

Currently, many diseases that affect larger parts of the population can be treated quite effectively with reasonably priced and well investigated medicines. New drug therapies for these diseases have to meet the high standards for efficacy, quality and safety of already existing and thoroughly tested drug therapies. The situation may be different for diseases with none or few drug therapies.

Standards for efficacy, safety and quality as well as cost-benefit regarding new medicines for the treatment of theses diseases are higher than in the past. Every single new piece of medical evidence and especially every major drug withdrawal for safety reasons increase the pressure on drug regulatory authorities to demand more detailed clinical evidence, more long-term safety trials and more post-marketing studies.

The developments mentioned above resulted also in the evolution of a broader risk management concept for pharmaceutical products, i.e. interventions that improve the safety of how pharmaceuticals are prescribed, dispensed and used. Drug regulatory authorities have recently issued guidance documents on risk management interventions for pharmaceutical products.

Detection of risks in preclinical and early clinical development as well as post-marketing surveillance of adverse events (pharmacovigilance) represent the classic cornerstones of pharmaceutical product safety apart form Good Manufacturing Practice (GMP) to ensure high quality of medicinal products. Risks which are associated with prescription, dispensing and use have traditionally not been subject to intense monitoring and intervention because influence on the behavior of doctors, pharmacists and patients was deemed a much more difficult task than control of a pharmaceutical product's quality, properties and information.

R&D

There have been fundamental changes in the health economic as well as drug regulatory environment in the last decade which have induced and are going to lead to significant changes affecting pharmaceutical R&D.

R&D investment in the US grew 4.6 times while in Europe it only grew 2.8 times in the last 15 years. This resulted in a process of concentration of R&D in North America and at the same time the European research based pharmaceutical industry lost competitiveness. This development was partially driven by a greater reward for investment (attractive product price) in the US compared to Europe.

Today, rapid growth of R&D investment is occurring in China and India (Source: EFPIA).

Pipelines of pharmaceutical companies are nowadays dominated by specialist products because commodity product markets are saturated and more prone to price erosions.

Biopharmaceuticals, personalized targeted medicine and nanomedicine are just a few examples of new and promising areas of research. Genomics and proteomics and the availability of many new technological platforms opened the doors to new R&D opportunities but have also increased the complexity, length and cost of early stage R&D considerably. Similarly, rising regulatory standards increased the complexity, length and size of clinical trials. Post-marketing studies which are imposed by drug-regulatory authorities further increase the total R&D cost of a drug. Recently, an increased failure rate in late stage developments has been observed. Late stage failures imply extraordinary high cost, which are very difficult to compensate, because the number of promising drug candidates which are taken down the road of clinical development is very limited due to budgetary reasons.

Analysis of recent years reveals that R&D output (number of new molecular entities filed for approval) is declining. At the same time the estimated cost of bringing a NME to the market has more than doubled in the last fifteen years, but this is also true for sales which results in a net effect of quite stable R&D expenditure as percentage of sales. In Europe for example, the R&D expenditure as percentage of sales has been about 16% in 1985 and about 17% in 2005 (Source: EFPIA). This puts the issue of rising R&D cost in a different perspective. However, declining R&D productivity in recent years (number of NME's launched for approval) is a matter of fact and is worrying with respect to opportunities from new areas of research as well as from new technologies such as genomics and proteomics. Although biopharmaceuticals represent today about 20% of NME's launched on the world each year, they have not been able to compensate for

declining R&D output so far. The issue of complex, costly and lengthy research and development with high failure rates applies also – and perhaps even more – to biopharmaceuticals. This is a lesson learned from capital markets by investing in biotech companies.

Extrinsic increase of complexity, cost and time in pharmaceutical R&D processes are drivers for outsourcing, break up the traditional integrated value chain and create business opportunities for smaller specialized companies.

Decreasing R&D output is an extremely important issue for pharmaceutical companies because pipeline valuation represents a key driver of the share price. To sustain shareholder value, pharmaceutical companies are forced to respond to decreased R&D productivity. One type of strategic response is consolidation which can be a means to acquire attractive pipelines and promising future growth perspectives. Consolidation may occur along the integrated value chain with or without focus on therapeutic areas or it may occur around specialized activities of the value chain.

Another response pattern is cooperation, for example in-licensing of new compounds in different stages of development as well as the formation of research alliances with other companies (especially biotech companies) and the public research sector. This type of response would generally imply that pharmaceutical companies keep R&D activities but restructure it. In some cases, it could also result in pharmaceutical companies completely abandoning R&D activities, which would then be performed by specialized R&D companies.

Apart from consolidation and co-operation responses may also imply an increase of proportional R&D expenditure.

Whatever the response is, R&D driven companies have to stop declining R&D output to ensure sustained growth and shareholder value.

Manufacturing

The break up of the traditional integrated value chain affects also the manufacturing of pharmaceutical products. Production of raw material and API's as well as packaging and formulation services by toll manufacturers have become more and more important in the last decade. The global outsourcing market for pharmaceutical toll manufacturing

services is estimated at about US$ 8 billion and growing at 10% annually (Scrip Magazine October 2000).

Manufacturing of API's for generics is very much price-driven and is nowadays performed to a large extent in India, China and Eastern Europe. Manufacturing of API's and final dosage forms in these markets is growing at double digit rates.

Biopharmaceuticals are structurally much more complicated than most chemical entities. The production and dosage formulation of biopharmaceuticals (e.g. insulin for inhalation) requires completely different high-tech manufacturing processes and facilities compared to traditional dosage forms. New production plants and complicated processes have to be set up.

Complicated and costly manufacturing is likely to prevent generic competition for biopharmaceuticals to a certain extent. However, generic companies have years ago started to plan and develop production of biosimilars to be able to act quickly when biopharmaceuticals come off patent. Comparability of biopharmaceuticals (standards and requirements for biosimilars) is currently a hot topic for drug regulatory authorities.

Marketing / Sales

Even Marketing & Sales is affected by changes in the integrated value chain. Nowadays, it is quite usual that companies access a new market without setting up their own sales force. Contractual sales services and co-operation with marketing / distribution partners have gained a lot of importance.

The size of sales force is flattening or even decreasing in established markets. The increased proportion of specialty products entails different targets (specialist doctors) and sales models. Marketing is getting more individualized and focuses increasingly on attitudes, behavior, influence and volume of the prescribing doctor to accomplish sustainable relationships. High frequency contacts with common messages are replaced by fewer contacts with high quality and tailor-made medical scientific information.

Due to negative perceptions of aggressive and incentive-driven marketing, pharmaceutical industry associations and their members developed and adopted codes of practice on the promotion of medicine.

Distribution

Globalization and the internet pose new risks to the pharmaceutical supply chain. Maintaining supply chain integrity is an important issue nowadays for pharmaceutical companies.

Re-import from lower price markets into higher price markets (e.g. Canada or Mexico into the US or cross-border trade in Europe) is a topic which is getting a lot of attention from pharmaceutical companies because it threatens companies' margins and gives rise to new risks associated with repackaging and transport such as defective labels, inadequate storage and transport conditions, diversion or counterfeit.

Patients and consumers are purchasing drugs in the internet and are at risk to buy drugs from criminal and health endangering distribution channels because it is difficult for them to verify the identity and trustworthiness of the sellers.

Players in the downstream supply chain (wholesalers and pharmacies) are put under pressure by governmental provisions to control healthcare expenditures. The traditional role model and added value of pharmacies and wholesalers is increasingly put into question and their established position in the supply chain is threatened and starting to be bypassed to decrease the distribution cost of pharmaceutical products. Hospitals, pharmacies and managed care organizations are beginning to purchase directly from manufacturers.

Manufacturers, wholesalers, re-importers and pharmacies will face substantial changes with regard to their role and position in the pharmaceutical supply chain. The extent and impact of changes depends on the respective political, economic and regulatory market conditions.

1.4 Fundamental Changes in the Pharmaceutical Industry – Chasing the Future, caught in the Past?

The pharmaceutical industry is facing fundamental changes which are going to result in diminished returns as well as increased cost.

Diminished returns are primarily driven by cost containment (cut back of prices and negative impact on reimbursement of products), generic competition and declined R&D output.

The reasons for decreased R&D productivity may be manifold: increased regulatory standards, increased complexity of R&D technologies and processes, inefficient R&D structures or insufficient R&D investments.

Increased cost result from rising regulatory standards (pre-approval and post-marketing) which increase complexity and length of R&D processes and may also increase the failure rate of late stage R&D. Additionally, cost may increase due to new and complex technologies in R&D and manufacturing.

Diminished returns and increased cost foster a breakup of the traditional integrated value chain. Strategic options for pharmaceutical companies are:

- striving for growth through consolidation and maintaining the established business model of the integrated value chain
- restructuring and outsourcing parts of or all R&D processes by means of cooperation with third parties and formation of research alliances

Time will tell which companies have made the right strategic decisions. The others may get caught in the past and chasing the future.

2. Assessing and Managing Pharmaceutical Product Liability Exposures

2.1 Risks for Pharmaceutical Companies

Pharmaceutical companies are exposed to a variety of different risks such as for example product liability, business interruption, patent infringement, R&D risks, product recall, natural catastrophes, fire, political risks and currency risks. There are many more risks which constitute a pharmaceutical company's risk map and these risks vary from company to company. Insurers as well as pharmaceutical risk managers perceive product liability risks as greatest threat to the pharmaceutical industry. This perception is supported by a number of very large pharmaceutical product (drug) liability losses in the past.

2.2 Description of Pharmaceutical Product Liability Exposures

Pharmaceutical product liability exposures differ in many respects from other product liability risks as far as drugs are concerned. Due to their mechanisms of action in the human body and their inherent properties, almost every drug causes adverse drug reactions. It is impossible to eliminate all adverse drug related effects by modifying the design. This implies that a drug cannot be 100% safe despite perfect and appropriate manufacturing, warning and use. Pharmaceutical products are to a certain and limited extent "unavoidably unsafe" in that they cause adverse drug reactions. The acceptability of these adverse drug reactions (risks) is judged during approval of a drug by regulatory authorities that perform a complicated risk / benefit analysis. When drugs are placed on the market they are considered to be "safe" for their intended and ordinary use and based on the instructions and warnings which are provided with the product at a certain point in time. The safety and thereby the risk / benefit ratio of a drug depend on the state of the medical scientific knowledge at a given point in time. Accruing research and medical evidence is constantly changing the state of medical scientific knowledge which may impact the safety of a pharmaceutical product due to a different outcome in the risk / benefit assessment. For this reasons it is necessary to monitor the safety of pharmaceutical products after market launch as well as the new medical evidence which could impact the risk / benefit ratio of a pharmaceutical product.

Medical Dimension of Pharmaceutical Product Liability Exposures

New medicinal products are tested in human beings for safety and efficacy in clinical trials before they get approval by a drug regulatory authority. Due to economic reasons, clinical trials can only be conducted in a limited number of patients ranging from a dozen up to a few thousands. Adverse drug reactions which occur in a frequency of less than 1 in 5000 cannot be detected. After market launch, the number of patients exposed to a drug increases over time and rare adverse drug reactions (up to 1 in 10.000.000) can be detected. Moreover, the selected patients for clinical trials and the control of correct information and use of investigational pharmaceutical products in clinical trials are quite different from "real life" conditions after market launch. This is taken into account by

post-marketing surveillance (spontaneous adverse event reporting system, periodic safety update reports including risk / benefit assessments).

Psychological and Societal Dimension of Pharmaceutical Product Liability Exposures

The psychological and societal dimension of pharmaceutical product liability exposures is often ignored or neglected because psychological and societal aspects tend to get daffed aside by purely medical – scientific discussions. Communication, perception and acceptance of risks may influence litigation and numbers of claimants. Individual and societal values determine risk perception and risk acceptance. Trust plays a very important role with respect to risk perception and risk acceptance. From an individual point of view it is very important that a patient has the option to choose if he wants to take certain drug related risks. Additionally, intensity and tenor of media coverage are key drivers in risk perception and risk acceptance.

Facts get easily mixed with assumptions and hypotheses and this new mixture can lead to severe misinterpretations and misperceptions. Especially the crucial point of causality is often inappropriately addressed in mass media coverage of pharmaceutical product safety issues. 'Fear of claims', questionable jury awards, loss of revenue and reputation can occur despite credible evidence for causality and even in cases where a causal link has been ruled out.

Legal Dimension of Pharmaceutical Product Liability Exposures

Medical-scientific, psychological and societal product safety contexts have different financial impacts depending on the legal environment. Especially the US tort system represents a legal environment that is able to transform critical pharmaceutical product contexts into multibillion dollar lawsuits. Multi-plaintiff lawsuits or class actions represent an attractive 'investment opportunity' for US litigation lawyers. Campaigning for plaintiffs by US lawyers, attractive risk / return prospects for plaintiffs and a compensation culture mentality drive the US 'tort machine'. Corporations with large profits are considered as 'deep pockets'. Even in the absence of credible evidence for

causality, defense cost and administration expenses can amount to hundreds of millions of dollars.

US annual tort costs reached US$ 260 billion in 2004 and are by far outreaching those of any other country. Since 1950, US tort costs have grown much faster than GDP. About 50% of the money spent on US torts goes to injured parties, 30% to the lawyers and 20% to administration (Source: Tillinghast Towers Perrin).

From a global perspective, the US legal system represents the biggest legal threat for pharmaceutical product liability exposures. At the same time, the US pharmaceutical market is the biggest and most important market in the world.

Financial Dimension of Pharmaceutical Product Liability Exposures

Medical-scientific, psychological, societal and legal pharmaceutical product contexts are ultimately transformed into financial numbers which impact pharmaceutical companies and their insurers. Pharmaceutical companies face additional financial exposures such as loss of market share, revenue, brand value and shareholder value. The above description of pharmaceutical product liability exposures demonstrates that it is not sufficient to consider only the medical-scientific dimension in order to estimate financial impacts of pharmaceutical product liability exposures. Qualitative and quantitative assessment of pharmaceutical product liability exposures has to take this into account

2.3 Identification and Assessment of Pharmaceutical Product Liability Exposures

Identification, evaluation and assessment of pharmaceutical product liability exposures depend on the perspective and strategic objectives. Moreover structure, resolution and process of the risk assessment depend also on financial and personnel resources. Perspective and objectives differ in some respects between pharmaceutical company and insurer. Portfolio control and management of accumulation are important tasks for insurers and usually not of significant interest to an individual pharmaceutical company.

There are different approaches possible to analyze pharmaceutical product liability exposures.

A generic product liability assessment approach would make use of assessment criteria such as product classification, design, raw material, manufacturing, quality control, marketing, sales distribution, usage, disposal/recycling, claims experience, legal parameters and soft factors. Performing such an analysis for all products and locations can be extremely time-consuming in the case of large corporations.

Another option is to eliminate the assessment of individual products and locations and apply the assessment criteria to the entire product portfolio and the entire company. This approach is much more feasible but involves a significant loss of resolution, because individual products are not analyzed.

A third option is the use of filters to generate subsets of products which are representative for the exposure of the total product portfolio. This results in a limited number of products which can be assessed using the above mentioned assessment criteria. Generic assessment criteria from pharmaceutical product liability approaches are usually not specific enough to measure the complex contexts which are outlined in section 2.2.
A variety of risk assessment criteria can be used for qualitative analysis of individual products taking into account the different dimensions of pharmaceutical product liability exposures. For example development risk, risk / benefit ratio, lawyer activities and patient exposure could be used for the assessment of individual products.
Quantitative assessment and risk modeling can be accomplished by using surrogate parameters for severity and probability.

Whatever approach is used, an important objective is to ensure consistency and transparency by defining a systematic approach for pharmaceutical product liability exposure assessment. A defined approach aims at describing risks in a clear and consistent way for underwriters and is not intended to predict the occurrence of a particular loss. The quality and feasibility of any risk assessment approach depends on the quality of data available for the process as well as on the complexity of the liability exposure under examination.

2.4 Managing Pharmaceutical Product Liability Exposures

There is a huge variety of potential measures to control and manage pharmaceutical product liability exposures in the pharmaceutical industry. Most of them are not any more voluntary but part of regulatory requirements. All the International Standards such as for example GMP (good manufacturing practice), GLP (good laboratory practice), GCP (good clinical practice), GPP (good pharmacovigilance practice) and many other international guidelines and papers such as ICH, CIOMS as well as guidelines from drug regulatory authorities are describing risk management processes and measures. In addition to these already existing quality standards, guidelines and regulations, there have been recent developments in the drug regulatory area which resulted in the evolution of a broader risk management concept for pharmaceutical products. Risk Management of Pharmaceuticals got a new dimension by setting up interventions that improve the safety of how pharmaceuticals are prescribed, dispensed and used for certain drugs. Risk Management in pharmaceutical R&D has meanwhile also developed into a huge field.

Improvement of product safety is usually not feasible by modifications of the chemical structure, because this results in a completely new product. Improvements of the dosage form as well as timely, complete and adequate warnings represent important risk management measures which are directly linked to the product. This is now supplemented by risk minimization action programs that influence prescribing, dispensing and use.

Timely, proactive and transparent communication of risks to doctors, patients, the scientific community, stakeholders, shareholders and regulators are important measures to manage the societal and psychological dimension of pharmaceutical product liability risks. Building trust in the public is a very important risk management measure if critical product safety issues arise.

There are many legal risks associated with pharmaceutical product liability exposures. Awareness and adequate assessment of consequences in litigious legal systems is elementary to set up adequate measures of risk control. These could include for example monitoring of public news and internet forums, legal developments and activities (plaintiffs, lawyers, legislation) as well as frequency and tenor of media coverage.

From an Insurers' perspective, pharmaceutical product liability exposures represent quite complex risks. This is partly due to the intricate medical-scientific product safety contexts and partly due to the various dimensions of pharmaceutical product liability risks. A specialized know-how which is closely linked to business processes supports the insurers risk management.

Apart from qualitative analysis of pharmaceutical product liability exposures, the quantification of pharmaceutical product liability risks represents a challenging task for an insurer. Quantification of risks is also an area, where an insurer can probably add most value to the pharmaceutical industry by means of services and support.

Pricing, accumulation control and portfolio control of pharmaceutical product liability exposures is closely linked to profound qualitative and quantitative assessment.

3. Conclusions

Changing markets, limitations in healthcare budgets and rising cost as well as complexity in R&D processes and regulations have increased pressure on all segments of the classic value chain. Future perspectives of growth and market opportunities of the pharmaceutical industry will depend on the strategic responses to the new challenges in the pharmaceutical value chain. The success of new and modified business models will also depend on political, regulatory and market environments.

An optimistic outlook for the pharmaceutical segment could be as follows:

Research in the Biotech area is resulting in many new therapeutic approaches and innovative products. Economic growth enables health-care systems to pay for innovative medicines. Medical genetics and pharmaco-genetics foster safety and efficacy of drugs.

Distorted financial impacts from the US tort system are reduced. The pharmaceutical industry as well as regulatory authorities successfully develop and implement risk minimization action plans to increase patient safety and reduce the number of product withdrawals. It will be interesting to observe how all these optimistic developments are going to affect pharmaceutical product liability exposures and their financial impact.