STRATEGIC OUTSOURCING IN PHARMACEUTICAL INDUSTRY

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Abstract: The pharmaceutical industry is facing a tremendous challenge from the current global economic crisis. Enormous earnings from new "blockbuster" drugs are perishing and old drug targets are leading to limited profits. Despite substantial investment in research and development of new drugs, the return thereof is disappointing. New targets including biologic, biomarker, as well as studies of the genome, as well of drugs for treatment of chronic diseases, have much longer duration of the development phase. Therefore, companies are focused on shortening duration, lowering costs, enhancing efficiency and minimizing usage of resources. All these challenges are forcing the pharmaceutical industry to change its drug development model from a model relying on internal capacities to an open model that embodies aid from a Contract Research Organization (CRO) experienced in understanding regulatory standards, equipped with adequate infrastructure, qualified and competent staff in pharmacy, and experienced in dealing with regional issues. Outsourcing has great importance for pharmaceutical companies. Manufacturers of original pharmaceuticals may opt for outsourcing of different phases of drug development, while generic companies confide the clinical trial – the last phase of drug development – to selected CROs which meet high standards of expertise in performing the studies, using highly reliable analytical methods, located in attractive geographic locations and have competitive pricing.
This paper is inspired by the challenges with which the pharmaceutical industry has to cope in the new globalized world. At the beginning the authors provide short introduction to the significance of outsourcing in the case of the pharmaceutical industry; than differentiate Big Pharma from generic pharmaceutical companies; define benefits and risks from outsourcing in the pharmaceutical industry; stress the significance of project management as a key prerequisite of planned and executed outsourced activities; and finally present concluding remarks.
Keywords: pharmaceutical industry, outsourcing, Contract Research Organization (CRO), Big Pharma, generic companies, project management, drug development.

1. INTRODUCTION

Life sciences refer to a number of companies involved in the health care of human population and of animals, as well as companies involved in agricultural biosciences. All of these companies vary in terms of their size and organizational aspects. Among them are large multinational pharmaceutical corporations, several small and medium-sized biotechnology companies, but also several large companies that produce medical devices and medical equipment. Some of them specialize exclusively in one area, but most are engaged in several different areas. Pharmaceutical industry is an economic activity that constantly faces rapid changes of its business practice and which needs a competitive strategy for survival on the global market. Therefore, many pharmaceutical companies are facing the challenge of choosing the right direction of further development. Until recently, during the long, arduous and expensive way of creating new drugs and their production, pharmaceutical companies relied solely on their internal potentials. The traditional model that they used not so long ago is known as a profit alone path - self-generating profit. The implementation of this model largely depended on the launch of entirely new drug molecules, and given the real picture in a sector where objectively at present there are significantly less new syntheses than in the past, this model is doomed to failure. Moreover, it is assumed that this model would not be efficient enough to meet the needs of the market (Sachs, 2004). Estimations point out that the full time-length of a new drug development might reach up to 20 years and cost over 1 billion American dollars. The traditional model was in general mostly used by the so-called Big Pharma - the 10 biggest pharmaceutical companies in the world. Due to the

rapid rise of discovery and production of new antibiotics in the Golden Age of the industry (since World War II), these companies recorded a high percentage of research and development, market launching and commercializing of new drugs. Several decades later, however, the volume of investment in new research continued to grow, which did not result in the same pace of development and marketing of new drugs. At the beginning of the 21st century the number of studies in this area grew by more than ten-fold - from 500 to more than 5,000. At the same time their funding reached over 100 billion American dollars per year (Cockburn, 2004). Despite the huge amount of investment, the results were quite disappointing. Thus, in a period of almost four decades, no new broad-spectrum antibiotic has been discovered, and for much more serious diseases, such as various forms of malignancy, diabetes, Alzheimer's disease, Parkinson's disease or schizophrenia, there is still no effective and, at the same time, well-tolerated therapy. Over-investment followed by poor research results, as well as the inability to make a profit, are clear indicators of inappropriate allocation of finances and inadequate resource allocation, as well as mispricing which is a clear indication that this industry is facing a productivity crisis. In order to ensure profitable operations, even the most powerful pharmaceutical companies had to cooperate with external specialized organizations, known in the modern terminology as Contract Research Organizations (CROs) that enabled them achieving better economic performance. In near future the certainty of change in the method of payment for the drugs according to their efficiency and to their safety profile, should also be taken into account. In the coming era, the rules of the game in this sector may change dramatically, which will inevitably affect the change of the pharmaceutical industry structure, reflected not only through the prism "who does", but also through the prism "who takes". Therefore, pharmaceutical companies instead of acting into a business environment of making a profit on their own, have to adapt to an environment of generating profit in cooperation with a wide range of other, external organizations - academic institutions, hospitals, institutes and the like. Two other important factors - the significant progress in the field of information technology, and the concept dictated by the health sector based on the principle paid for received – should also be paid due attention. Under current circumstances of increasing market pressure, tightening of medicines registration regulative, needs of increasing profit, and reducing costs, are becoming more and more evident. The clinical assessment of new drugs characteristics becomes a prerequisite for obtaining approval of their placing on the global market. All this is an increasing burden that even the most powerful world pharmaceutical companies have to face in terms of globalization of the world economy,. Further in this paper authors provide information on differences between Big Pharma and generic pharmaceutical companies; define benefits and risks from outsourcing in the pharmaceutical industry; stress the significance of project management as a key prerequisite of planned and executed outsourced activities; and finally present concluding remarks.

2. BIG PHARMA COMPANIES VS GENERIC COMPANIES

As far as most people are concerned, the pharmaceutical industry consists of a small number of very large multinational corporations with household names such as AstraZeneca, GlaxoSmithKline (GSK), Eli Lilly, Merck, Novartis, Roche and Pfizer. Apart from the Big Pharma companies, there are numerous pharmaceutical companies working in the field of production of the so called generic medicines. For example, Teva which is the biggest generic drug manufacturer is the 11th largest pharmaceutical company in the world (Noor, 2013). The pharmaceutical industry in some ways resembles an iceberg. The worldwide well-known companies, which are loosely defined as research-based pharma companies, represent about 40% of the market in terms of finance (Noor, 2013). However, they correspond to only a small fraction of the industry as a whole, with less than 90% of the total number of pharmaceutical companies known as generic companies, being largely invisible to the general public. At the same time, generic companies produce the vast majority of all pharmaceuticals sold worldwide. In 2013, 84% of the 4,000 million prescriptions issued in the USA were filled by generics (Boehm, 2013); (Kesselheim, 2016). The asymmetric relation between Big Pharma, on the one hand, and the generic companies, on the other hand, is caused by the patent system, as large research pharmaceutical companies invest many billions of dollars in the search for new drugs (Boehm, 2013); (DiMasi, 2003). The majority of candidate drugs never make it to the market place, as during development the drug might be found not to work or to have serious side effects and might never be used on patients. However, a small number of new pharmaceuticals do enter the market each year and the patent system ensures, for a limited period of time that the innovating company retains exclusive rights to sell the pharmaceutical. A successful pharmaceutical, once approved by medicines regulators, such as the FDA in the United States and the EMA in the European Community, may be sold afterwards. The innovating company patents the drug, thus gaining exclusive rights to sell the product until the patent expires. However, although patents in developed countries are usually granted for 20 years, the window-time of exclusivity of sales is significantly shorter, being in most of the cases no longer than 10 years. This derives from the need for the innovating company to patent the drug well before its first launch in order to protect its intellectual property. During this short period of ten years or less, the innovating company has to recoup all the R&D costs of both the drugs being sold and of all the other drugs that failed during

the development process, comprising manufacturing and marketing costs, as well. The instant that the patent expires, generic competition leads to a dramatic reduction of the price and major loss of market share. Since patent life is one of the key determinants of the income that can be generated from a product, it is not surprising that research companies try to extend patent life as much as possible. This "patent ever-greening" might sometimes be done simply by patenting the manufacturing process or the drug formulation or, in some cases, the drug delivery system, all of which can be implemented much closer to the launch date (Boehm, 2013). At the same time, generic companies put additional effort to set patents aside or to find ingenious ways to get around the patents. When the patent expires anyone is free to manufacture and sell what is now named as generic pharmaceuticals. The majority of pharmaceuticals, i.e. those that face patent expiration, are therefore manufactured and sold by generic pharmaceutical companies. These companies never have an unsuccessful product, whereas the research pharmaceutical companies rarely have a successful one. This has a major effect on the profile of the business, the way in which companies are structured and the way in which they operate. Generic pharmaceutical companies are low-cost, low-margin and low-risk businesses. The products that they choose to manufacture and sell have already been confirmed to be valuable and commercially successful on the market. They also do not need to incur any research and development costs, although some of the larger companies do undertake process-orientated R&D in order to introduce more efficient and low cost manufacturing. Marketing costs are very low as well, since products are already well established on the marketplace and the demand is well understood. In many ways, generic pharmaceutical companies are in commodity markets where competitive differentiation is based on cost of goods and profitability is determined by the market share.

3. OUTSOURCING - BENEFITS AND RISKS

Pharmaceutical companies are forced to conduct thorough trials that should demonstrate the quality, safety and efficacy of drugs during a comprehensive, lengthy process, respecting strict principles defined by legal provisions. These trials are conducted under specified time constraints and deadlines, as well as precisely defined budgets. The coordination of project activities and management of projects that take place simultaneously have a key strategic role in the efforts on time-cuts until tested drugs are placed on the market. Contract Research Organizations (CROs) have an important place and role in these activities. They aim to meet the requirements of their clients, i.e. the high standards in terms of fulfilling tight deadlines, quality of performance of required activities and costs of services. It is estimated that the delay of only one day past the deadline for placing the drug on the market might cost companies on average 1.3 million American dollars. In case of a single original drug on the market, the financial loss may be ten times greater, having on mind that it directly affects the observance of the planned deadlines for the launch of the new drug on the market (Zboralski, 2001). Pharmaceutical companies try to reduce growing costs of different phases of drug development as much as possible by reducing the so-called empty gaps in the process that occur as a consequence of certain omissions in the performance of various project activities. The need to reduce the growing costs in this highly scientific and specialized field forces all entities to rationalize their operations without affecting the quality of their products. This applies both to Big Pharma and for generic drug companies.

The practice of engaging and cooperating with CROs is not a novelty in the field, yet it has been especially intensified in the last 30 years. The role of CROs may be undertaken by scientific research organizations, academic medical centers and university hospitals, laboratory analysis centers, affiliated management organizations and institutions strictly specialized in a specific market segment. All these institutions might be outsourced in the pharmaceutical industry to accomplish a particular segment of client needs in regard of the project. Given the fact that the guaranteed period of enjoying monopolistic benefits of patent registration is significantly shortened, and regarding the huge increment of administrative costs per drug, as well as the rising level of protection of intellectual property rights by WTO rules, pharmaceutical companies started to transfer certain phases of drug development to hired CROs for a fee. Such organizations may be negotiated on their own national markets, but also may be found on foreign markets. Thus, a significant reduction in administrative costs of management and of full implementation of the project, including costs for all required permits, is provided. Additional pressure to optimizing costs, derives from rising competition from market entry of Chinese and Indian pharmaceutical companies (Maiti, 2007). Therefore, emergence of new markets in the world, where it is possible to obtain services from well-equipped scientific research and medical centers that dispose with highly qualified staff, is of high importance. Thus, separate phases of drug development may be organized and perfectly executed whit minimum operating costs, while the company in charge simultaneously manages to rationalize the use of its own resources, to remove the empty drains and to provide maximum rationalization of the duration of each phase while optimizing operating costs. The strategy of pharmaceutical companies from developed countries is dominated by determination to undertake intensive activities in scientific research work and development of a growing number of new generic drugs. Companies rarely decide to transfer all phases of scientific research work to centers outside their headquarters and prefer to carry out

the initial development phases relying on their internal resources and potentials. Once the initial phases of drug development have been set up and completed, companies prefer to leave some of the development phases to a hired CRO. For generic drug manufacturers this mainly refers to the final phase of development known as pharmacokinetic study which provides final conclusions and proves for bioavailability/bioequivalence of tested products in comparison to the original ones. Usually this phase is transferred to CROs recruited from less developed countries (OECD, 2008). The benefits of hiring outsourced organizations in the final phases of generic drugs development are multifold, as different studies may be executed in different centers simultaneously which shortens the time of drug development and, at the same time, saves costs of engaging additional recourses and time in the parent pharmaceutical company's facilities. Finding potential outsourcing partners is a complex process in itself, especially given the number of more than 2,000 CROs offered on the global market. Even lesser is the number of CROs that provide a one-stop shop to provide a whole list of diverse services, thus their engagement avoids the need of additional engagement of other CROs in performing specific type of services (Goldenberg, 2011). The selection of a CRO is based on certain parameters such as: 1. Assessment of experience and level of quality of provided services; 2. Potential for organization, execution and management of larger volume of projects; 3. Quality in organizing and storing databases of completed projects; 4. Financial strength and stability; 5.Price of services (Zboralski, 2001). The complexity of the selection process and proper choice of a competent CRO is executed in three consecutive phases. The first phase of the process takes place in five steps: planning, data collection, initial evaluation, bids and selection of specialized CROs. The second phase is the compilation of a list of potential specialized CROs. For this purpose it is necessary to make: current evaluation of the work of each engaged CRO; revision of CROs systems and conditions; identification of future outsourcing needs; and finally, structured evaluation of new specialized service providers for the needs of the sponsor of the clinical trial and their adding to the list. The last, third phase, should enable the selection of the most appropriate CROs under a long-term partnership development agreement (Bhatt, 2011). Specialized CROs with good communication, joint planning of activities, sharing responsibility and commitment to work and economy in operation, are being always preferred. The final list of long-term partnerships should not include specialized CROs for which there is insufficient data or a complete analysis and evaluation on cooperation, or with which the relationship is not sufficiently mature and there is no long-term mutual benefit which prevents future cooperation. Having all this in mind, it becomes clear that outsourcing strategy does not create only advantages, but also carries certain risks. Barthelemy identified seven critical mistakes that managers make in defining and implementing an outsourcing strategy. These are as follows: wrong choice of outsourced activities; wrong choice of an external executor; inadequate coverage of risks with the provisions in the concluded contract; elimination of subjectivity in perception of a situation, while losing the big picture in the company; loss of control over outsourced activities and not comprehending hidden costs of outsourcing and; failure to develop an alternative strategy (Barthelemy, 2003). Despite the stated omissions and risks, however, opting for an outsourcing strategy creates new opportunities for pharmaceutical companies.

4. PROJECT MANAGEMENT AS A KEY FOR WELL PLANNED AND EXECUTED OUTSOURCED ACTIVITIES

Project management is the key element of delivering and planning a strategy, including the outsourcing strategy. Project management was introduced into practice in the business world about three decades ago. From the mid '90s of the 20th century and the beginning of the new millennium, given the rapid expansion of legislation in the field of pharmacy, the performance of pharmaceutical activities became unthinkable without the application of project management. The need of project management in pharmacy was created by the necessity to get drug development in time and place the drug on the market as soon as possible. This especially applies to the part of planning and performance of clinical studies in the final stage of drug development. As drugs are developed for treatment of various diseases, the design of the project and other important features for its successful implementation vary depending on the type of the tested drug. The individual specifics of the work arise from the phase of the examination; from the population that should be included in it; from the correct selection of respondents according to given criteria with the examination plan; from duration of the examination in order to obtain valid results; from the monitoring of given parameters with the examination plan; from the organization of the examination (Thomsett, 2002). Therefore, the quality of research results depends on the perception of all necessary factors upon which strategic management of drug development projects in the pharmacy is based. Project management happens to be a well-established technique in the industrial production and lately also became especially important for the pharmaceutical industry. Traditionally, the pharmaceutical industry was isolated from the competitive pressure present in other industries where the project management approach was mainly based on application of standardized and uniform processes. Competition is the main reason for increasing the pressure on faster delivery of new products and time-cuts until the final product enters the market. Therefore, an appropriate project management is a major

factor in accelerating the development of new drugs, especially in the clinical research phase. Nevertheless, it has to be stressed that this is very difficult to be achieved in the real economy, as project execution is quite uncertain under the influence of an interdependent environment burdened with challenges of strategic allocation of funds within the context of a complex organizational framework.

5. CONCLUSION

Research in the field of pharmacy remains beset with many challenges of which most do not appear to have obvious solutions. Despite exclusive rights of a new drug sales through its patent life, increasing regulation in the pharmaceutical industry is leading to additional costs and prolonged molecule development phase, as well as shortening of the patent expiry period. Increasing risk aversion by executive management teams is contributing to a slowdown in the appearance of new drug molecules. In the meanwhile, the risk tolerance in patient populations decreases significantly, thus weakening success rate of regulatory bodies' marketing authorization approvals. Cost pressures within national health services are leading to a progressive downward movement of prices while market penetration by generics is facing a rapid increase. Most of the experts in life sciences consider that the current pharmaceutical business & research model is no longer sustainable. However, no-one has yet come up with a better model. The new model of "higher achievements with lower prices" contributes to switching the focus of many companies to the possibility of outsourcing operational activities in the process of drug development. They see greater opportunity in doing business with developing countries, where services in the area are offered at lower prices. In recent past these countries were perceived only as a market for final pharmaceutical products. However, the financial crisis in developed countries opened new opportunities in areas such as development and production of new drug molecules. Many countries with growing economies are attractive in terms of having talented, educated and competent staff, as well as technical facilities of high quality able to meet the high standards in this area with significantly lower prices. Therefore, pharmaceutical companies enter into partnership agreements with CROs from less developed countries. At the same time, large pharmaceutical companies are investing heavily in emerging economies in terms of upgrading existing facilities, building partnerships, or acquiring local service providers. Even the largest pharmaceutical companies are facing the pressure of finding new opportunities instead of using their specific well-known and well-established expensive drugs to serve smaller populations of patients meeting their specific needs by finding and using new cheaper drugs. In this regard, developing countries are seeking continued support to meet the needs for medicines with significantly lower prices. Thus, within the globalized world the pharmaceutical industry faces a strong challenge to appear with a dual role: as innovator of products and as producer with lower costs. A new development - the so-called virtual development and research - rapidly overtakes traditional way of effectuating tasks in more academic institutions and specialized bioinformatics companies. They all start to introduce semantic technology and computer simulation models which contribute to the elimination of differences such as geographical distance. The actual changes and processes within the modern society - social, economic, scientific and technological - lead to the inevitable development of multinational development networks without which the success of pharmaceutical companies on the global market is no longer possible.

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