PROJECT MANAGEMENT IN PHARMACEUTICAL INDUSTRY

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Abstract: Driving a product to the market safely, quickly, and cheaply is the best way for a pharmaceutical company to be successful. In the era of an increased consumer demand for pharmaceutical products, the complex process of new product development has to be shortened as much as possible without damaging the overall quality and efficacy of the new product. The pharmaceutical industry is booming, and the race in delivering new products to the market is speeding up. Pharmaceutical companies encounter enormous challenges during the long and extremely complex product-development process. From the initial research in the early laboratory stages until the ultimate product market launch, this long process includes management in a number of different business processes, such as technical development using quality by design, regulatory strategy, clinical studies, and supply chain. To be able to find the most cost-effective ways of speeding up the process of development of new products, and particularly of the clinical trial phase, pharmaceutical companies faced up the need of introducing and implementing project management, which in other manufacturing industries was done a long time ago. Identification of risks of each of the phases in the process and an effective risk mitigation plan became key factors for success for these companies, both from financial and technical perspective. However, implementation of effective project management in launching new products does not only support the success and profitability of pharmaceutical companies. Effective project management in the pharmaceutical industry also makes available new medical discoveries for patients in need sooner and at lower costs, and by enabling a treatment for a certain disease supports maintenance of human health and improves the quality of life worldwide. The article begins with introduction, continues with the interconnection between the new product development and the need of implementing project management in the pharmaceutical industry, refers to the planning of clinical trials of new products as a very important phase of the business life cycle in this industry, explains the basic definition of project management in the pharmaceutical industry and its specifics, and ends with a conclusion.
Keywords: pharmaceutical industry, pharmaceutical companies, project management, drug development.

1. INTRODUCTION

Project management is a well-established practice being implemented in different manufacturing industries for many decades, regardless of a product or a service they are designed to deliver. Yet, the pharmaceutical industry started its intensive implementation recently, just about three decades ago and it became of a great value for supporting successful launch of new pharmaceutical products on the market. In this industry, the implementation of project management is especially important in the phase of research and development (R&D) of new products, as it plays a big role in managing a complex context due to unique regulatory, compliance and quality related issues in the area

(Shah, 2017). Although global healthcare demands that the pharmaceutical industry develops medicines that save and improve the lives of millions of people at a low cost, costs permanently increase. Costs of developing a single drug reached over one billion US dollars compared to 138 million US dollars in 1975 (International Federation of Pharmaceutical Manufacturers & Associations, 2012). According to data from the member companies of the Pharmaceutical Research and the Manufacturers of America (PhRMA) research and development costs (R&D) reached about 83 billion US dollars in 2019, comparing to 5 billion US dollars in 1980 and 38 billion of US dollars in 2000 (Pharmaceutical Research and Manufacturers of America, 2020).

Costs in the pharmaceutical industry are also increasing because of the always changing regulatory policies, introducing stricter regulatory and compliance rules on new products development, impacting the development phase, and manufacturing and registration strategies. The time needed for authorization of a product launch has being significantly prolonged, affecting the product development economics. This also puts additional pressure upon the pharmaceutical industry to accelerate the drug-development stage in order to compensate the prolonged time of regulatory approval (New Drug Product Exclusivity, 2020).

With access to many innovative ideas, companies often try to develop many products in parallel, which might lower management's capability to focus separately on any of them. At the same time, the management has to coordinate not only all the processes, but also internal functional groups (such as R&D, regulatory, legal, finance, supply chain, sales, and marketing) and all the external partners. Dealing with all these challenges, the pharmaceutical industry learns the importance of focusing on a single product while developing multiple products in parallel, comprehending the importance of using project management strategies. Project management becomes even more popular in this industry as it helps mitigating inherent risks of every stage of product development, which is confirmed to be crucial for reducing time and costs of new product development (Thomsett, R. 2002; Engval et al., 2003). This article begins with presenting the facts on the interconnection between the development of a new product and the need of project management in the pharmaceutical industry, referring to the planning of clinical trials of new products as a very important phase of the business life cycle in this industry, explaining the basic definition of project management in the pharmaceutical industry and its specifics and at the end presents the conclusion.

2. THE INTERCONECTTION BETWEEN THE DEVELOPMENT OF A NEW PRODUCT AND PROJECT MANAGEMENT IN THE PHARMACEUTICAL INDUSTRY

"*Drug development can be described as a continuous undertaking of tests, experiments, and studies to determine, define, and document the safety, efficacy, and quality of a particular chemical or biological compound with the ultimate goal to obtain approval from regulatory authorities to market the drug*" (Raemdonck&Burns, 2018).

R&D projects in pharmaceutical industry face significantly bigger uncertainty than those in other industries. In this industry the relation of unknown and unforeseeable risks overcomes known and foreseeable risks to a much greater extent in comparison with other manufacturing industries. Most of the new molecules and drugs development start based on untested hypothesis that might reveal some threats due to unacceptable aspects of their profile which usually cannot be rectified once the development phase is started, despite the money and the time already spent their development. Scientists design experiments based on assumptions to obtain data that verify models and theories. Often, these assumptions are based on limited historical knowledge. As new information becomes available, the assumption changes, and this impacts the original hypothesis. The fact that there is also a certain extent of inaccuracy in using human factor, measurement instruments and statistical analysis in testing the hypothesis, increases the risk of obtaining inconclusive results. Since the 90's, the vast amount of investment in R&D of new pharmaceutical products is not reflected accordingly in the number of newly registered products. The causes for the low rate of new registrations of pharmaceutical products are presented as follows (A CBO Study, 2006):

- **Significant increment of opportunity costs**. These costs appear in R&D in all industries, yet their amount is especially high in the pharmaceutical industry. In this industry total R&D costs on development of new products might be twice as big as direct costs. At the same time, indirect financial costs from investing capital in pharmaceutical R&D projects might equal total R&D expenditure of a pharmaceutical company. This has a negative impact on the return of the assets if the company decides to make other investment out of the process of development of new products;
- **Parallel testing of different molecules**. The laboratory testing of a new molecule is a time consuming process which creates high costs. From the many parallel projects on development of new molecules, only one or two would result in new products that would be successful on the market. All other projects would be terminated as unsuccessful, thus creating substantial costs for the pharmaceutical company;
- **Prolonged duration of the clinical testing phase**. This is a result of the involvement of pharmaceutical companies in clinical research of products for chronical deceases. The application of the product takes long time, i.e. the research has to be conducted for many years in order to obtain relevant statistical data which

would confirm or exclude the possibility of existence of side effects. Also, companies are due to conduct additional testing for most of their products after putting the product on the market to provide information on the differences of the efficacy and quality of their product in comparison to the products provided by their competitors (Pharma Figures Report, 2018).

The length of the project itself also raises the probability of encountering unknown and unforeseeable risks that can result in turbulence in the project that can be incontrollable. Changes in regulatory requirements impact product development as well, causing changes in direction of the project and significant delays in its accomplishment or even project failure (Pattanaik 2014). Many challenges arise while approaching a new project in R&D, thus some strategic considerations need to be addressed at the very beginning of its undertaking. Besides the potential therapeutic utility of the new drug, the project must also have commercial value and fit within the overall R&D strategy (Raemdonck & Burns, 2018; IQVIA Institute for Human Data Science, 2019). Thus, the shortening of the duration of each phase of the development of a new pharmaceutical product until its final placement on the market depends on a strong interconnection between strategic decision making and project management.

3. PLANNING AND MANAGEMENT OF CLINICAL TRIALS OF NEW PRODUCTS

The strategy of the development of a new product has to be based on clearly defined goals, which could be achieved only by thorough planning and management of clinical research. It is a time consuming and very expensive process, as it includes research of approximately 10,000 substances of which only 250 pass to the preclinical development phase; 10 out of the last group pass into the clinical research phase, while finally just one is placed on the market (Drug Discovery & Development, 2007). In order to provide efficient planning and management of clinical research of new products most of the pharmaceutical companies, especially those with a high rating on the world market, developed their own project management systems. However, some of the companies use already ready planning systems on commercial terms that help them manage development projects and follow their progress. For all of them the most difficult decision to make, regarding the time and the investment spent in the development of a new product, is whether to continue or terminate a project when its economic logic becomes jeopardized. It seems that the best way to make a decision whether to continue or to terminate such project is provided by a creation of the so called *target product profile (TPP)* (Blomquist & Muller, 2006). The creation of TPP includes (Roberts,1999):

- Development formulation code:
- Therapeutic indications;
- Acceptable safety of the pharmaceutical profile, as well as of the safety for the organism;
- Acceptable stability of the clinical and final formulation included in an acceptable manufacturing process of a product for commercial purposes;
- Minimal requirements for effective ways of application;
- Estimation of the risk-benefit ratio by including references on possible unwanted effects or certain contraindications, thus excluding the so called therapeutic window;
- Easiness of application and dosage;
- Innovation – new type of molecule substantially different from those already created by the competition, first of its kind.

Once the creation of the TPP is finalized and thoroughly analyzed, the creation of the development plan for a new product may begin. The development plan is based on four groups of key activities: preclinical development, clinical development, production and regulatory issues (Parikh, 2001; Brown and Grundy, 2004).

Preclinical development of a new product includes toxicology studies which test and estimate: acute toxicity; subacute toxicity by testing on animals in a period of 2-4 weeks; sub chronic toxicity by testing on two different kinds of animals in a period of 3 months; chronic toxicity by testing on 2 kinds of animals for a period of 6 months; reproductive toxicity by testing embryonal toxicity, fertility and prenatal toxicity, followed by testing for malignant and its eventual mutagenic potential; providing pharmacokinetic studies; and finally, absorption, distribution, metabolism, and excretion by testing again on two different animal models.

Clinical development of the new product is conducted in four phases:

1. Human pharmacology which includes application of one or multiple doses; bioequivalent studies; interaction studies; and testing on specially defined population, for example, children, adults, females, men, patients with certain disease, etc.;
2. Therapeutic exploitation which includes definition of the dosage regime;
3. Therapeutic confirmation by conducting risk-benefit studies (efficacy and safety);
4. Beginning of therapeutic application (post marketing period).

Production of a new product comprises:

- Production of testing doses;

- Formulation of the drug;
- Completing the total manufacturing of a commercial product;
- Testing the stability of the drug;
- Characteristics of substances and of the drug formulation.

Regulatory issues are related to issuing various licenses by authorized institutions and agencies according national, as well as international regulative (Rang et al., 2003).

4. PROJECT MANAGEMENT IN PHARMACEUTICAL INDUSTRY

The previous two chapters present a clear overview of the inherent pressure that pharmaceutical companies face in development of new products and their placing on the market. Except internal challenges, they also have to deal with an increased external pressure imposed by rising healthcare costs which derive from the increased number of aging population with chronical deceases, on the one hand, and from the monopoly imposed by healthcare providers, on the other. To keep up with the severe competition on the market, pharmaceutical companies have to develop new molecules and products and to be able to place them on the market safely, quickly and at low cost. Although applied efforts are huge, the hit rate of creating a new product is rather low - estimated to be around 0.02% to 0.01% at annual level (Pharmaceutical Research and Manufacturers of America, 2005). The very high rate of unpredictability in development of new products combined with all inherent difficulties and potential problems that have to be solved for a project to be successfully completed imposes the need for proper project management implementation. Project management in the pharmaceutical industry is a complex undertaking which should follow the full business lifecycle form definition and justification of the project till delivering clear and demonstrable benefits for the business. This means that project management in the pharmaceutical industry has to cover the entire project procedure beginning with active ingredient discovery and concluding with compound development. It has to plan the entire R&D process, to monitor its execution and to evaluate the results thereof. It should also plan all critical dates, milestones and resources, as well as the needed budget. The effective project management as usual should provide cost effective planning, optimized business procedures, efficient allocation and usage of resources, and at the same time it has to bring all cross-functional project members together in achieving the project goal. The process of management of pharmaceutical projects has five key phases, which are also practiced while executing projects in all other industries (Brown & Grundy, 2004):

1. Project definition;
2. Strategy creation;
3. Detailed planning;
4. Implementation and control;
5. Revision and learning.

However, project management in the pharmaceutical industry has one specificity more. Because of the very high rate of uncertainty within the pharmaceutical industry, it should also enable an effective method of comparison of a significant number of different projects in order to quickly identify those which are worthwhile to proceed with. In order to mitigate possible difficulties in full implementation in all of the project phases, project management in this industry applies the so-called *portfolio management*. Portfolio management is defined as a systematic comparison of a project with a set of different criteria which helps the decision making process and facilitates full implementation of the project by linking it with the R&D strategies. Portfolio management might be based on various techniques, but the most implemented one in the pharmaceutical industry is the so called *AID analysis (analysis of the level of attractiveness- difficulties in implementation)* (Brown & Grundy, 2004). The AID analysis enables defining the economic attractiveness of a project and estimates the real probability of its full realization. The economic attractiveness analysis has to take in consideration the real economic potential of the project; to evaluate the market share and its consumption potential; to determine the competitiveness of already existing similar products on the market; to evaluate the present non-met medical needs; to define the scope of the population of targeted patients; to define the duration of the treatment with the new product; to confirm the competitiveness of quality, expected efficiency and the safe profile of the new product; to define marketing costs and competitiveness when entering the market; to provide patent protection and its exclusivity within the industry. Yet, the positive results from the analysis of the economic attractiveness of a project are not enough for its final selection and execution. There is also another set of criteria that a project has to meet, which confirm that it might be fully realized. These criteria are dictated not only by the market, but also by the available technical possibilities for its successful completion and regulative requirements on registration of new products. Projects with clearly defined goals and well designated timing on meeting market needs, as well as those which are well technically supported and for which precise regulatory procedures are in place, have advantage to be finally chosen, executed and fully realized. The second set of criteria besides all technical possibilities, takes into consideration the clarity of clinical goals; appropriate timing

for accomplishment of project tasks; appropriate timing for registration of the new product and its placement on the market. By analyzing both of the criteria sets, portfolio management enables project management in the pharmaceutical industry to have a clear view upon many different opportunities, thus providing a real possibility to make the most convenient option within a given time framework and limited recourses within a changing environment (Brown & Grundy, 2004). It not only helps project management to choose the best projects that would enable realization of research, as well as of business goals, but it also enables achievement of the best results from each project with wise allocation of resources, rationally defined priorities and complete commitment to the organization.

5. CONCLUSION

Project management has been a well-established practice in manufacturing production, however it started to be implemented in the pharmaceutical industry about three decades ago. The pharmaceutical industry was excluded from the traditional competitive pressure present in other industries, which is the main cause for the very late implementation of real project management in this industry. Lately, however, pharmaceutical companies started to face significant pressure by the presence of many similar pharmaceutical products on the market, fast changes of the regulative in the area, health innovations, as well as a strong wave of mergers which began at the turn of the 21st century. As the competitive pressure increased and the need for shortening the time for creating and delivering a new pharmaceutical product to the market increased, implementation of project management became crucial for the success and survival of pharmaceutical companies. Implementation of project management became the main factor for speeding up development of new pharmaceutical products, and especially of the phase of clinical trials. The functioning of the traditional model of management of pharmaceutical projects based upon standardized uniform processes is very difficult in the contemporary reality, as this model makes the full realization of projects completely unpredictable within a complex organizational framework, burdened with too many uncertainties, interconnections, and challenges with regard of strategic allocation of resources. The contemporary model of project management is directly interconnected with the business strategy, enabling flexibility and creativity of projects, putting due attention to all details in order to accomplish all crucial goals by keeping on mind the complete picture of all defined and analyzed stakeholders' needs, thus providing mutual trust and openness of the project. Therefore, project management in the pharmaceutical industry helps mitigating the uncertainty, which makes planning possible. New developments of modern societies make it essential to also consider more subtle management aspects, such as: choosing a certain project instead of deciding in favor of another; making an overview of the global picture in which the project is imbedded and considering and defining many variations and possibilities of its full implementation. The main aim of project management in the pharmaceutical industry is not to neglect indebt analyses of different activities, but to become fully aware of the direction of the activity flow and the outcomes thereof, thus enabling real expectations from the return value from all the project undertakings while helping successful by-passing of the most important treats.

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