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Key Aspects of Pharmaceutical Engineering in Engineering Companies' Activity

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Abstract: This article covers the key aspects of pharmaceutical engineering in activity of engineering companies involved in pharmaceutical plants design. We determined that the main part of the project engineering activity in pharmaceutical manufacturing should take regulated companies or engineering departments. The core units are infrastructure development, value engineering, planning and monitoring, designing, project analysis, introduction to the construction activities, Statutory and GxP compliance, commissioning and qualification and the project turnover to the client. We reviewed every aspect of the section separately.

Key words: Pharmaceutical Engineering · Project · Regulated Companies · Value Engineering · Project Analysis

INTRODUCTION

Project engineering is a technical support of the process of creating a new object, such as design development and construction. It contains of technical consulting, development of technological systems, decision optimization (choice of the best solutions) and control functions execution. For instance, construction and project engineering provides coordination and project review, permits obtaining and commissioning team preparation [1].

Project engineering includes:

- Capital project development;
- Client functions performance at all stages of the investment process;
- Coordination of project documentation composition for construction and modernization;
- Investment intentions development and construction expediency evaluation;
- Normative-technical design review;
- Design decisions review, alternative solutions production;
- Risk calculations and risk review;
- Project documentation implementation;
- Collection and process of data at all stages of the project [2].

MATERIALS AND METHODS

To define the key aspects of project engineering in the regulated pharmaceutical company activities we used: system review, comparative analysis, post evaluation, investment research, continuous sampling, expert evaluation and decision theory. Thus I have arrived to the following results.

RESULTS

The main part of the project engineering activity in pharmaceutical manufacturing should take regulated companies or engineering departments that perform the functions of project engineering mentioned above. In its turn regulated company should organize the project engineering activity in accordance with the defined procedures and processes included in the project infrastructure (Fig. 1). It is necessary to establish the project engineering organization structure.

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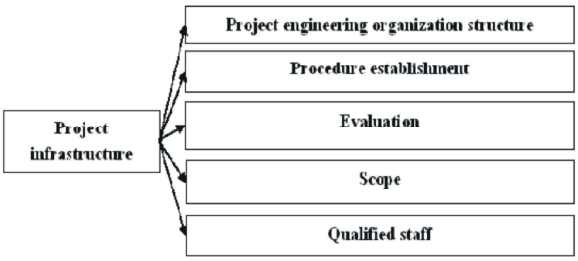

Fig. 1: Components of the project infrastructure

For each project regulated companies should have the defined groups responsible for the projects assigned to them, each group should have the assigned area of responsibility for making decisions and financial issues. Also key stakeholders involved in the project and financially responsible for the project and its outcome should be defined.

After that it is necessary to establish the project engineering procedures. To do that regulated companies should have the defined procedures that cover the intended number of projects including the established control procedures in general and in a single project. These procedures should define the project group structure, type of records and should include the documentation maintenance strategy that defines:

- Information retention criteria and information;
- Planning, progress, expenditure report;
- Change control (relevant to each stage and activity);
- Project evaluation;
- Quality control.

Further it is necessary to evaluate project engineering. In this case regulated companies should ensure that project objectives system (such objectives as process, product and equipment) is defined at the early stages of the project and subsequent methods and procedures are established for risk assessment and contribution assessment to identify and mitigate risks of the project objectives.

When defining a scope of the project engineering, regulated company should guarantee that project groups, procedures and responsibilities correspond to its scope, modification and contribution to the GxP regulated system. When forming a qualified project engineering staff, regulated companies should ensure that personnel involved into project development is properly qualified and trained and has the resources and support complied with the technical specifications and number of activities, their types and scope.

As it was stated earlier, the main part of the project engineering activity in pharmaceutical manufacturing should take regulated companies or engineering departments. Regulated company (project organization) should have a concerted and determined activities defined by the eagerness to minimize costs and improve quality (Fig. 2).

When generating a project, regulated companies should have a mechanism for regular analysis of current and future demands for the current possibilities and accessible technologies. This information should be used to define the requirements and as a foundation for change implementation. Also, while developing a project, regulated companies should have a mechanism of analyzing proposed changes and methods for work scope definition (user requirements specification).

During the project review regulated companies should ensure that the appropriate decisions, such as risk assessment and environmental impact, are used to establish the effective project approach. The established approach should consider the full life cycle and possible risks, for instance: possibility of minimal cost could be non-optimal due to high operating costs or other significant risk exposure factors.

In extension project such decisions should be reassessed according to pre-defined schedule.

Besides that regulated companies should have means of definition of the most appropriate project realization methods according to budget and schedule.

Within the limits of resource provision for project management, regulated companies should provide the project with the access to the adequate resources including qualified personnel, means of communication, funding, offices and systems.

Value engineering is the key aspect of project engineering as it guarantees the confidence in reasonable investment in any activity, its evaluation and organization for optimal value derivation. Value is defined by costs, quality and scope [3]. Meanwhile regulated company should have defined methods of efficient decisions-making relative to project execution based on the project's revenue capability. Within the limits of project engineering activities, regulated companies define the investment risks and review them (Fig. 3). To perform that review they should adequately assess the investment risks and take into account all possible consequences and advantages of project viability and the means of its execution. The necessity of the timely execution and risks connected impossibility to do that should be clear to stakeholders.

Regulated companies should ensure that appropriate supplier assessment and selection methods of are established and they are based on project set terms complying with:

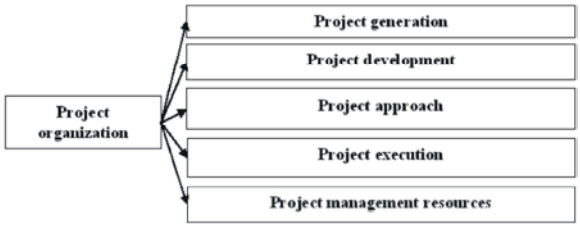

Fig. 2: Project organization components

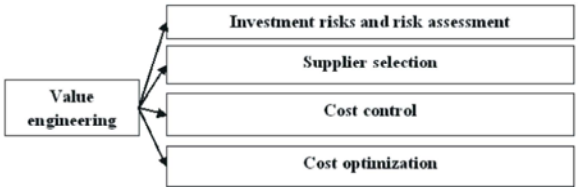

Fig. 3: Value engineering components

- Quality; low costs; work experience in this area; technical support; scope of work; project schedule.

While performing cost control procedures, regulated companies should be able to assess the project cost assumptions, review and manage them during the project execution on the regular basis. Not only should they assess and control but they should also optimize the cost of the project. Regulated company should also have a review system for the proposed solutions to the specific project requirements to ensure proper quality for the best price. The complete life cycle of any proposed solutions should be considered in this review.

Planning and monitoring is one of the parts of the project engineering. With planning and monitoring of project engineering regulated company should have long-term business strategy, which may include a formal organizational structure and a plan of the facility. It should also have a formal method of the project plan development to achieve specific goals considered in accordance with the formal organizational structure and program of action to compare the progress of the project with the project plan.

For planning and monitoring of the project engineering activity it is necessary to perform such operations as: long-term strategy development; project planning; level of project quality planning; monitoring; change control.

Let us consider the planning and monitoring operations of project engineering mentioned above individually.

When developing a long-term strategy, regulated companies should consider formal master plan of the territory. Such strategies should be reviewed and tested to ensure that they reflect the commercial and political environment.

When planning a project, regulated company should have a project plan development system that includes:

- Timing;
- Functions;
- Methodology;
- Correlation;
- Resource requirement.

When planning a project quality level, regulated companies should ensure that plans to ensure project quality are available and are suitable for the proposed project and organized in accordance with the agreed project schedule. Plan to ensure project quality should determine the standards of acceptable quality and ways to achieve them and evaluation, for example: inclusion of analytical stages, approval and quality control of suppliers.

Project quality plan should cover the following aspects of the plan:

- Control process of change implementation and commissioning;
- Risk management strategy implementation (how to manage risks and how to assess them);
- Document inspection, review and validation before release on preliminary stages (such as conception approved for design and construction (approved for execution)); document number assignment and versioning; equipment and instruments identification numbers assignment; project and progress review; Document flow.

During monitoring regulated companies should have a system of determination of the most appropriate means to t rack progress in accordance with the project plan (the current operating costs, the progress of work, completed operations) and a system for forecasting the final cost and completion date of the project. This information should be regularly communicated to the key stakeholders (i.e., users, senior management and financial department).

Besides that regulated companies should have the amending recognition system in project activity.

Change control system should use a system of a regular review of the possibilities of change implementation and determination of the appropriate course of action. This system should process and improve scope, schedule and budget to reflect a certain result. Change and its potential contribution should be conveyed to key stakeholders (i.e., users, members of the project quality division, cost management and senior

management). Change control system and related methods of the review and approval should be adapted for the stage of the project and the effect of regulation, allowing effective and rapid change control.

The important aspect of the project engineering is design. Design refers to the most important processes for the project as a result of its implementation is the development of a unique object, goods or services [4]. Regulated company should have an ordered design technology to achieve optimal value with respect to the size of the project and scope of work. According to this project engineering in design consists of: user requirement specifications; project development; Result of the project (final product).

Consider the above components of the design within the regulated company project engineering implementation.

Regulated companies should have established methods for the design and review of formal user requirement specifications that cover the fundamental aspects and scope of user requirements. Users should be involved in this activity as much as possible. At a minimum, users are required to perform a review of these requirements and approve them.

The requirements should be set objectively so that they could be confirmed during testing and commissioning. Agreement with the objectives of any strategy or master plan should be confirmed.

Requirements should be focused on the product and technological needs as well and, as much as possible, leave engineering aspects open for further definition.

Besides that user requirements should be written in layman's terms and should be used as a basis for development of the project, project specifications and drawings. Users and developers should determine the allowable repetitive design steps with increasing degree of elaboration of the project on which it can be considered. This process should make it possible to maintain the quality and more accurate assessment of cost and schedule.

The stage, at which the development of the project should be considered, will vary according to the type, scale and risk. Each stage usually needs no further contractual obligations of the owner to the agent.

Usually the stages include: start-up (definition of project objectives and user requirement specifications of the original project); collaboration (acknowledgment of the economic model with the definition of eligible project costs); GxP compliance and risk assessment (understanding the amount of additional effort required for formal verification system); construction admission; Execution (development of the up to product drawing reception issued for construction and specification).

The structure and level of detail as a result of the project (product to be turned over) should be defined by the chosen contract strategy, an acceptable level of risk and the size and nature of the support of the project.

For each stage of the project certain results are defined and may include:

- Conceptual information: section, materials flow pattern, dynamics of staff and sequence of the production;
- Intermediate step: the development process flow diagram and layout of instrumentation, preliminary specifications for equipment, sketches, architectural drawings;
- Final stage: the specification of drawings and purchase orders;
- Certain results of internal documentation for compliance with the standards (e.g., sanitary standards, voltage regulation) and reception of confirmations.

Planned, implemented and executed investments take the form of capital (investment) projects. But the projects should be chosen, calculated, executed and most importantly, evaluated for their effectiveness, especially on the basis of comparing the costs of the project and the results of its implementation. That is what project analysis (analysis of investment projects) is for.

Design analysis is an analysis of financial rate of return of a capital project. In other words, it is a cost comparison of capital project investments and the benefits to be derived from the project [5- 9].

For the implementation of project analysis regulated company should have a formal system for the review of the project in accordance with the objectives to make sure that quality meets the requirements and is obtained with the optimal cost. Design review consists of:

- Product quality control;
- Project review stages;
- Project review mechanism;
- Project review final result.

When carrying out the construction quality control, users should collaborate with the developer quality control system of the drawings, specifications and pricing, which are generally defined in terms of project Quality Assurance plan.

Each project should be reviewed in the preliminary stages, as well as in the review stage of the project and documented properly at the design stage, aimed at addressing the following points:

- Does the construction meet the user requirements;
- Does the concept of the project take into account the specifications and compliance with the implementation intentions, the object's location, available materials, local technical level, local skills;
- Laws, including local and international standards, corporate codes;
- Risk control and safety analysis, including: building materials, design strategies for highly protected risks, the risk of fires and explosions, natural disasters, security; ergonomics; environmental review; energy efficiency and cost of ownership; cost optimization to ensure the proper performance of costly objectives; analysis of monitoring of the implementation of activities in accordance with the schedule; consideration of constructability (i.e., coordination of services, transportation routes, contract strategy); technical possibility of maintenance (i.e. access and space, transport of materials); The possibility of commissioning (i.e. sewage, availability of adjustment and measurement).

Regulated companies should define the methods of analysis of the project design in accordance with the type and level of risk, use of suitably qualified personnel to check the project requirements. Besides that methods should comply with all codes, regulations, technical norms and standards, which should be followed.

Regulated company should ensure that the review includes all the factors that are most likely to be important at this stage.

In carrying out the final result of the analysis of the project regulated companies should have appropriate methods of recording and disseminating the results of analysis of the project, as well as amendment management techniques. The results should confirm the compliance with the current requirements of the project.

Construction produced by regulated company should have adequate methods for selecting a method of these construction works and management. In project engineering they consist of:

- Management system;
- Quality standards;
- Construction works.

With the control system regulated company should have established methods of review of contract strategy construction capabilities, suitable for the type, scope and risk. They should take into account local customs and practices and should be directed to:

- Drawings and specifications compliance (quality control);
- Reporting on progress and emerging problems/issues;
- Management of the objects built outside the boundaries of the site;
- Productive interaction between supplier quality management system and internal quality control system of the organization, i.e., the use of project change control on monitoring changes in the facility;
- Direct access to on-site production facilities and personnel management while working on the premises of the organization (including a site visit to clarify the needs of the project);
- Operation and safety;
- Creation and approval of the work plan of production;
- Creation of proper documentation and records, i.e., recording the assembly system;
- Maintenance of a list of defects and deficiencies, as well as the definition of completion;
- Commissioning;
- Managing contractors;
- Training contractors.

In setting standards regulated companies should have proper ways to determine achievement of quality standards.

Quality management system should include:

- Risk assessment;
- Sample review and approval;
- Ways of defining quality standards, for example, construction of a sample facility;
- Management of materials and equipment delivered to the object;
- Quality control of construction works – maintenance of the cleanliness of the pipeline, sewer, intermediate inspection, testing phased project;
- Product quality tests;
- Standards for documentation and delivery records during construction.

Construction work at the site and outside it should be based on realistic assessment of suitable local practices to achieve project objectives.

Regulated company should have mechanism to determine and ensure compliance with all applicable rules and GxP regulations to allow a legal and complying with the rules construction.

Project procedures should provide assurance that the responsibility for the formal definition of the responsibilities and enforcement actions do not contain a non-GxP regulations and standards (rejections or amendments). It can be applied to the practice of building the facility, test structures and records, as well as to the technical requirements (e.g., pressure control, electrical codes and the CE mark (according to EU product safety)).

Requirements for various permits required for construction, leasing and approval of the project should be identified and responsibility for their implementation should be clearly assigned.

Local documentation features should be defined for the official record, as well as responsibilities for creating, updating and filling the accounts should be clearly assigned.

Regulated company should have a system to ensure commissioning in compliance and qualification (validation) for projects consisting of:

- System description;
- System risk assessment;
- Commissioning;
- Qualification (validation).

For description of the systems and subsystems regulated companies should have established methods for their use in the operation and administration skills. They should be divided into logical units and, where possible, into systems complying with GxP and non-GxP systems to reduce qualification costs of GxP acts.

With systematic risk assessment regulated companies should have established methods of risk assessment systems and determine the level of risk to product quality and patient safety.

While ensuring effective commissioning of project, regulated company should have a system that not only works but is also effectively documented, especially in the case of systems with a high level of risk. Commissioning should refer to the user requirements and testing should confirm that these requirements have been satisfied. The team engaged in commissioning should have methods of acquiring products intended for human consumption, maintenance management and requirement standardization and support logbook from starting of the project to the stage of its turnover.

Besides that during qualification (validation) regulated companies should have risk assessment techniques to ensure that the undertaken qualification based on the critical quality characteristics and critical process parameters corresponds to the respective level.

Final design engineering procedure is to turn the project over to the customer. At the same time the regulated company should have the described system of turnover of the completed project to the user.

Turnover to the user should include the documentation that confirms the function and the ability to objectively facilitate future support, for example:

- Construction drawings and records of "building de facto";
- Reports of initial commissioning period and records of the content and maintenance;
- Spare parts, workshops and technical instructions (procedures);
- The login information for the proper maintenance and system maintenance and calibration;
- Proper training and related documentation;
- Full package data for certification (validation).

The project should be completed and the following system records should be released (to ensure entry status of "building de facto").

Regulated company should prepare the policy, standard operating procedures, scheduled maintenance work and other plans, in accordance with necessity, required to operate and maintain the system. Operators and maintenance personnel should be trained to work in the system before the turnover.

A phased turnover of large or time-dependent projects can consider a valid phased turnover system. In this case, the methodology and the division of responsibilities should be described. Deviations (exceptions and list of work in progress), which may require further work in the later stages should be clearly documented in reports to ensure continuity.

DISCUSSIONS

As a conclusion we can state that we have reviewed the key aspects of the project engineering in compliance with GxP. We determined that the main part of the project engineering activity in pharmaceutical manufacturing should take regulated companies or engineering departments. The core units are infrastructure development, value engineering, planning and monitoring, designing, project analysis, introduction to the construction activities, Statutory and GxP compliance, commissioning and qualification and the project turnover to the client. We reviewed every aspect of the section separately. At the same time we found out that, while creating the project infrastructure, we should establish a

procedure to evaluate the project to determine the scope, the selection of the project, project review, project execution, project resource management of the regulated company. When analyzing the cost of the project of the project engineering in the regulated companies, we have defined the investment risks and risk review, set appropriate methods for evaluating and selecting suppliers, cost control, cost optimization. Planning and monitoring consists of a long-term strategy, project planning and project level of quality planning, monitoring and change control. We found that the design relates to the most important processes for the project and regulated company should have an ordered design technology, consisting of user requirements, project development and the result of the project (final product). We also defined design review as cost-benefit analysis of the capital project that is performed to control the construction quality, cost-benefit analysis contains of design review stages, design review tools and the final result of design review. Apart from that it is necessary to take into account a management system and quality standards of regulated company construction activities. Commissioning in compliance with statutory and design qualification contains of system description, system risk assessment, commissioning and qualification. Therefore it is possible to provide maintenance of the new product creation using the project engineering instructions mentioned above.

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