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Conceptual Model for Outsourcing Process in Pharmaceutical Supply Chain

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ABSTRACT

Pharmaceutical companies are regularly being challenged to meet the rising standards of quality, so as to comply with rigorous regulatory requirements. At the same time, the global pharmaceutical market has seen significant changes, forcing pharmaceutical companies to focus more than ever before on customer needs and their own internal efficiencies in order to continue to compete effectively on a local and global arena. Outsourcing services to a third party is a commonly accepted approach to reduce costs and to provide sites of excellence (manufacturing, distribution, research and development, analysis and testing, marketing), but it also holds many hidden risks. The winning formula of outsourcing processes is developing and sustaining a reliable Quality Management System, capable to control efficacy and efficiency of outsourced activities. In this article the conceptual model of outsourcing process has been proposed under the frame of PDCA cycle (Plan, Do, Check, Act). Proposed model has been applied in outsourcing process of transport of medicines, as a case study. Furthermore, this case study has been implemented in the curriculum of postgraduate education in Pharmaceutical management in Faculty of pharmacy on University of Belgrade, as a practical course for understanding the complexity of outsourcing process in pharmaceutical supply chain.

Keywords: Outsourcing, Pharmaceutical supply chain, Quality management

INTRODUCTION

Background of outsourcing process

Over the last few decades numerous processes and activities previously organised inside the company became outsourced. The main reason of delegacy of processes to other companies is cost reduction, but also giving a job to someone who is more specialised, more flexible, where the delegated process is core business. The most common outsource activities today are: cleaning, security, raw materials production, IT services and, recently, more frequent parts of: production processes, quality control, distribution and marketing activities. Outsourcing started with non core processes and is now moving towards more critical applications.[1] Outsourcing offers the opportunity to improve competiveness and provides a path to expanding revenues in new markets.[2] The benefit in outsourcing is also an ability to change supplier more easily, internal headcount reduction, avoidance of internal policies, transfer of risks.[3] The practice of outsourcing is mainly sustainable and outsourcing operations is the trend of the future, and those organisations which already involved with outsourcing are satisfied with the result.[4]

Considering that today critical activities are outsourced, business process outsourcing is one of the main risk fields in modern business.

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Historically, pharmaceutical companies outsourced the activities at the lead optimization stage of drug discovery process, but the rise of acquisitions and merging of pharmaceutical companies changed the structure of world pharmaceutical business.[5,6] Three basic trends are notable: the continuing rise of outsourcing companies in Asia and Eastern Europe, the increase in deals with not-for-profit organizations and, finally, the emergence of a variety of business models under which outsourced work is conducted.[7]

Risk of these operations has directly reflected on product and service quality and indirectly on the business at all, so this problem is recognised in many management and technical standards as a support to manage an outsourcing process.[8-11]

Requirements for managing of outsourcing activities in ISO 9001:2008

Quality dimension in outsourcing processes is discussed in many articles. As a special service provider, business process outsourcing service quality is the degree and direction of variation between the service receiver's expectations and perceptions.[1]

ISO 9000 has achieved its fourth version (ISO 9001:2008) which is the most important version for users because it is used for the certification of QMS.[8] Management of outsourcing processes are explicitly expressed in contrast to the previous versions of the standard.

The type and extent of control to be applied to the outsourced process can be influenced by factors such as:

a) The potential impact of the outsourcing process on the organization's capability to provide product that conforms to requirements,

b) The degree to which the control for the process is shared,

c) The capability of achieving the necessary control.

Fulfilment of requirements referring to these processes can be done this way: it is needed to define a way of contracting business process outsourcing in the way described in chapter 7.4 – Purchasing.[8] It is indicated to start with competence evaluation and selection of suppliers, and develop document(s) where requirements for approval of product, requirements for qualification of personal and requirements of quality management system are strongly demanded. In addition to that, vendor inspection, of the outsourcing company, has to be organized on regular basis. In other words, organizations should coordinate contractor quality plan. In a situation when an organization engages suppliers in order to perform inside the appropriate operations, the above described model must be applied for managing them.

Performance monitoring of the outsourcing process is defined by chapter 8.2.3 - Monitoring and measurement processes. Documents related to outsourcing processes (such as contract) should be dealt in accordance with the standards paragraph 4.2.3. while the records are treated in accordance with 4.2.4. (for examples audits reports from suppliers, shipping records ...). The data are analyzed in accordance with the standards of chapter 8.4. Analysis of data; and continual improvement is expected in accordance with the chapter 8.5. Improvement.

Requirements for management of outsourcing activities in pharmaceutical legislation

Over the last decade, as outsourcing has evolved into the rule rather than the exception in pharmaceutical industry, many lessons have been learned by those involved in the day to day business of contracted operations [12]. Good manufacturing practice from the very beginning considered the contract manufacturing and analysis as a requirement in Chapter 7. Previous version of this Chapter begins with the statements: Contract manufacture and analysis must be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. There must be a written contract between the Contract giver and Contract acceptor which clearly establishes the duty of each party.

Expansion of the pharmaceutical business by increasing the level of compliance, creates "site of excellence" for a particular part of the process, and today, organization for research and drug development (Contract Research Organization - CRO), clinical trials, marketing activities are often outsourced, in addition to production and quality analysis. At the beginning of this millennium, the classical GMP approach, traditionally focused on manufacturing, is coming closer to the business system- Total Quality Management (TQM).[13]

ICH guidelines Q8-Q10 became a revolutionary concept of modern Pharmaceutical Quality System,[14] which provides guidance in all phases of the life cycle of medicinal products - from development to full operation and releasing of products to the market. Paragraph 2.7 of ICH Q10 titled “Management of outsourced activities and purchasing” states: A pharmaceutical company can outsource activities at all stages of the product lifecycle. The pharmaceutical quality system, including the management responsibilities described in this section, extends to the oversight and review of outsourced activities. Normally under contract, the contract giver should be responsible for assessing the suitability and competence of the contract acceptor to carry out of the work required. Responsibilities for quality related activities of the contract giver and contract acceptor should be specified in a written document.

Application of the new ICH guidelines would affect the revision of Chapter 7 of the EU GMP Guide, and the title of Chapter 7, changing from “contract manufacture and analysis” to “outsource activities” and the current changes focus the topic of providing guidance outsourced activities beyond the previous scope of contract manufacture and analysis operations.[15]

This holistic approach to pharmaceutical quality system, reflected in changes to other chapters in the GMP in Chapter 1 (Quality Management) and Chapter 2 (Personnel).[15]

Also the other standardized management systems (ISO 13485:2003, ISO 17025:2007, BS 25999:2006), recognized an organization's need to manage all activities which are part of outsourcing processes, but methods and models are not demonstrated.[9-11]

Certification bodies also do not find enough real evidences through certification cycles about system approach to standard requirement.[16]

Related outsourcing models in the literature

The conceptual basis for outsourcing is Williamson's theory of transaction cost analysis from 1975. Transaction cost analysis combines economic theory with management theory to implement the best relationship of the company should develop in the marketplace.[17]

In order to find an optimal model for managing outsourced activities, Thompson proposes a basic framework within the project will be carried out.[18] In fact, before making a decision, companies should critically examine the expectations and

threats in all phases of the process, and especially before signing the contract. What makes a successful framework for the outsourcing according with Thompson's model?.

Power is the basis of control. Control is based on power and accordingly a company's potential for control of outsourced activities depends on the balance of power between the firm and the provider.

Operational objective of outsourcing is to provide activities, which form an integral part of the company's composite value chain.

The problems to be overcome include: contracts' inevitable incompleteness because all contingencies cannot be anticipated.

The means of achieving control include formal contract and monitoring of delivery.

Andrew Chadwick-Jones, in his publication "Outsourced, But Not out of Mind - Turning contractors into strategic partners" based on research Mercer Management Consulting, gave a model of good practice control of the outsourcing activities.[19] The model consists of several elements, divided into two key phases:

1. Planning and selection, resulting in a formal contract,

2. The development of partnership structures and measurements

Depending on the industry and the specific activities involved, preferred outsourcing model may feature:

- A tactical approach, where supply bases are very competitive and switching costs are low
- A performance manager approach, when switching cost are low but suppliers are not particularly well developed
- "Careful choice" approach, if switching cost are high but processes are simple and well mapped
- A strategic approach when the supply base is generally immature, competition is limited and the concept of outsource has emerged only recently

McIvor in his review research paper gave a practical framework of outsourcing by integrating a value chain perspective, core competency thinking and supply based influences into the decision making process.[17] This framework proposed a four stage analysis to support companies to make an effective outsourcing decision:

1. Defining the core activities of the business

2. Evaluate the relevant value chain activities

3. Total cost analysis of core activities

4. Relationship analysis

Reviewing available literature database, specific model of outsourcing in pharmaceutical supply chain hasn't been developed. Also, QMS framework is not recognized.

The objective of this paper is to develop a conceptual model of outsourcing process implementing the key quality management principles and regulatory requirements, acceptable for global pharmaceutical supply chain. Developed model has to include the risk management tools to facilitate decision making process of outsourcing.

METHODOLOGY

The authors reviewed proposed models of outsourcing published in professional and scientific literature in last two decades about pharmaceutical supply chain. Also, four multinational pharmaceutical companies that have production sites in Serbia has been interviewed in two years period (2009, 2010) about implementation of QMS principles in outsourcing process, to develop a conceptual model for pharmaceutical supply chain.

A case study about outsourcing of transport process is conducted in one Serbian pharmaceutical company.

An improvement of postgraduate course in Faculty of pharmacy using described case study will be evaluated in 3 years (2014).

RESULTS AND DISSCUSION

Analyzing the requirements for managing of outsource processes in most QMS principles, but keeping in mind the specificity in the pharmaceutical business, the authors propose a model that is based on the above mentioned principles, but gives emphasis to:

- Planning goals
- Compliance with regulatory requirements
- Follow up key performance indicators (KPI)
- Management review
- Continual improving with some respect to EU GMP guidelines[15]

Therefore, the authors propose the idea about the PDCA (plan, do, check, act) approach as a model of outsourcing management activities.

PDCA cycle stands for the following:

PLAN – decision about outsourcing (*business case*) which involves all Yes/No and Know how analyses;

DO – implementation of regulatory principles and establishing of Key Performances Indicators (KPI) related to outsource organization;

CHECK – monitoring of organizational Key Performance

Indicators (influence of outsourcing project on company profit and quality);

ACT – review decision about outsourcing, business KPIs connected to outsourcing.

In case that there are more than one outsourcing project (production, calibration, transport, quality control, ...), outsourcing management would suit an integrated management system, having continual improvement as an objective.

The key elements of outsourcing could be fit with PDCA cycle (Table No. 1).

Table 1: Conceptual PDCA model of outsourcing in pharmaceutical supply chain

PLAN phase	-	Project task
	-	Due diligence
	-	Risk assessment
	-	Pharmaceutical contract negotiation
DO phase	-	Regulatory requirements compliance (variations, audits)
	-	Pharmaceutical contract execution
	-	Defining of KPIs referred to outsourcing organisation
CHECK phase	-	Follow up of KPIs
	-	Audits of service supplier on regular basis
ACT phase	-	Objectives review
	-	Contract review
	-	Defining, implementation and tracking of preventive and corrective actions

"Plan" phase

Outsourcing means using a third party to perform certain operations on behalf of the parent company.[19] Outsourcing necessarily entails ceding control of formerly internal processes, a prospect that is frightening to managers on many levels. Each specific risk can be mitigated, but there is no way to remove all risk from outsourcing a project.[20]

Risks may include:

- Loss of strategic control;
- Hidden costs;
- Service quality problems;
- Regulatory compliance exposure.

Sweet noted that organisations involved in outsourcing are in danger of signing a blank check, as it is very difficult to detail what are provided by the vendor, and it is very easy for the vendor to persuade them to be given the trust.[21] These risks by Duening and Click can be placed in seven categories: human capital risks, project risks, intellectual property risks, legal risks, vendor organizational risks, value risks, and force majeure risks. It is vital that each of these risks is assessed—at both internal and external levels, as appropriate—and that effective strategies be put in place to anticipate, mitigate, and respond to them as circumstances require.[20] Although risk assessment for the intended outsourcing activity is not an explicit requirement of ISO 9001:2008 standards, the authors suggest that the process of planning outsourcing should be started that way- trough due diligence process.

In this phase, also, negotiation about Pharmaceutical agreements (Commercial, Technical/Quality, Supply) has to be initiated.

"Do" phase

Current GMP practice and ICH guidelines are very clear in defining roles of contract donor and contract acceptor. It is stated in Chapter 7:

"7.1. There should be a written contract covering the outsourced activities, the products or operations to which they are related, and any technical arrangements made in connection with it.

7.2. All arrangements for the outsourced activities including any proposed changes in technical or other arrangements should be in accordance with regulations in force and the Marketing Authorization for the product concerned".

In current practice, most companies outsourcing certain activities have only one document as evidence of control of outsourcing activities and that is a business contract. Such a contract is mainly a result of the negotiations regarding the transaction price, responsibilities and legal guidelines. Duening and Click concluded that finding the right Business Process Outsource vendor and developing an appropriate contract are essential to an organization's outsourcing initiative.[20]

However, in the outsource process, it is necessary to have another dimension of partnership - trust. Trust is a key element in the relational dimension of social capital: it stimulates the development of this dimension such as the idea of "give and take" and in turn is reinforced by such development.[18] Despite the crucial role of the contract and service level agreements in controlling the relationship, business process outsourcing governance should be built around a partnership to support the increasing dependency between the client and service provider.[1]

The existence of the procurement contract (commercial contract) and the Technical Agreement has so far been

sufficient to meet the requirements of GMP. Although the technical agreements, also known as Contracts for quality, attention to detail define the roles and responsibilities of both parties, in all segments, in most cases does not provide complete control of the contractual activities.

One of the most important issues in pharmaceutical legislation is the regulatory requirement compliance is certification of the contracted manufacturing site (audit, process validation, submission of variation). Before the contract execution, regulatory activities have to be considered.

This way of auditing the outsourcing company is a requirement of ISO 9001 standard and also, strongly recommended by many authors.[18-21]

Finally, any contract can not anticipate all the risks during the process can happen, especially not to have insight into the performance quality of all contract activity. Critical Key Performance Indicators (KPI) related to outsourced company has to be identified in this stage.

"Check" phase

Chapter 7.6 of cGMP states: The contract giver should monitor and review of the performance of the contract acceptor and the identification and implementation of any needed improvement. A service level agreement may be tied to anything that can be objectively quantified but is usually a measure of such indicators as quality, speed, availability, reliability, capacity, timeliness, or customer satisfaction.[20] The first important step is to make sure that agreed services are measured and monitored so both sides can compare outsourcing activities "in situ" and compare with contracted ones. One way of monitoring this is by having a checklist (scorecards, KPIs) of the expected results which are actually main indicators of the success of outsourcing. Ramu [22] found this method should define the frequency of monitoring indicators and information to be collected. The frequency of collection and analysis of these processes depends on: (i) their importance, (ii) the intensity change of information pertaining to them, and (iii) the difficulty in gathering this information.

It is inevitable to monitor financial KPIs, but the other KPIs have to considered and monitored.

Internal process KPIs could be:

- Time delivery (% delivery on time, % delay of 1 to 5 days, over 5 days, ...);
- Level eligibility (% of acceptance at different intervals, ...).

Quality KPI, as well as a customer satisfaction could be collected through a questionnaire (with graded answers: + agree, disagree - or neutral response - 0, also the degree of gradation can be defined with numerical responses). The report gives the results in histogram form with standard statistical parameters: average, standard deviation.

However, monitoring performance metrics serves no purpose if they are not reviewed by the involved parties at some intervals.[12]

"Act" phase

It is stated in Chapter 7.7 of cGMP: The Contract giver should be responsible for reviewing and assessing the records and the results related to the outsourced activities. Management review involves analysing the services / products obtained by outsourcing organizations, compared with expectations (in terms of quality, price, ...) of the vendor firm and make the corrective / preventive action if necessary.

Meisner and Lee highlighted seven factors leading to success outsource: reliability, tangibility, conformance, responsiveness, flexibility, assurance / empathy and security.[1] Based on these and other indicators, contracts are extended, ended or changed.

Based on the KPI results, top management decisions were made to review and may propose:

- Corrective and preventive measures;
- New ways of outsourcing or other outsourcing company.

Comparing our proposed model to previous,[1,17,18,19,20] the following similarities are recognised:

- Strategic point of view about outsourcing process;
- Risk based decision making
- Partnership with outsourced companies.

Besides that, this PDCA conceptual model gives added values for pharmaceutical supply chain:

- Integrate the key quality management system principles into outsourcing process;
- Implement the pharmaceutical regulatory requirements;
- Lead to continuous improvements.

CASE STUDY: OUTSOURCING OF TRANSPORT OF MEDICINES

Medicines are, in many cases, sensitive to light, heat, humidity and stability studies of medicines are given great attention. The consequences of inadequate environmental conditions during production, storage and transport can lead to degradation products in medicine which is sometimes toxic. Therefore, series of guidelines are issued in recent years for assessing the results in cases of temperature variations during production, storage and transportation.

International transport of medicines in most cases includes transport companies that use the common transport line (plane, ship, road transport).

The only way to monitor temperatures during transport is to use "data logger", which is placed in tertiary packaging and activated during drug delivery. At the time when drug arrives to a new location, special software is used to read the temperature during transport and assess compliance with specifications and drug stability studies, based on the mean kinetic temperature.

Having in mind this highly complex and critical process, it is necessary to anticipate all activities in place to manage contractual transport company.

At an organizational level, usually management monitors the impact of outsource activities on corporate goals and business key performance indicators:

- The aspect of the customer: whether the transport affects the quality of products (% of complaints, % of rejected series due to inadequate transport, % of non-compliant products during transport);
- Financial aspects: whether the transport affects company profits (% of realized profits, cost reduction %);
- The aspect of internal processes: for example, speed of delivery (% just in time delivery);
- Social aspects: respect the culture and corporate values of both companies, the possible transfer of knowledge (% of completed training in relation to the plan).

The proposed PDCA model applied to medicines transport as an outsourcing process is shown in Table No. 2.

Table 2: PDCA model for outsource of medicine transport

P	- Project task - Due diligence - Contract and technical agreement negotiation	- Risk/benefit analysis - Transport compliance evaluation in accordance with stability study (cold chain) - Transport company selection - Commercial and technical contract drafts preparation and defining responsibilities
D	- Regulatory requirements completeness (variation, audits) - KPI identification - Contract execution	- Defining of KPIs - example: - 100% of deliveries according to the plan, - 0 % delivery with more than 15 days late - 0 % delivery with temperature deviation - not more than 0.2% non compliant product during the transport
C	- KPI monitoring in regular periods - Outsource company audits in regular periods	- KPI trends analysis - Transport company audit
A	- Goals review - Contract review - Corrective and preventive action review- changes defining and execution	- Changes defining and execution

CONCLUSION

The constant development of management science has led to a new editions of the relevant standards, where more attention is paid to outsourcing management activities, as well as the critical phase of modern business.

Standardization reduces the complexity of operations, and thus, helps in reaching higher reliability responsiveness and conformance.

ISO 9001:2008, as a strict quality management standard requires managing of outsourcing processes, as follows: (i) establishing requirements for them, (ii) development of management models, (iii) evaluation and selection of suppliers, and (iv) development and application of models for monitoring scorecard and measure these processes.

The paper presents models for the management of outsourcing activities, where risk management is a starting point, but also the integration of all phases in the outsourcing process.

The developed model also integrates all other relevant standardized management systems (ISO 9001, ISO 13485, BS 25999), GMP principles and risk management trough PDCA steps, so the governance of outsourcing in pharmaceutical supply chain makes it viable for the modern pharmaceutical business.

Implementing of proposed conceptual model, the certification bodies and GMP inspectors will find the evidences through certification cycles about systemic approach to standard requirements.

Finally, this approach and the case study have been implemented in the curriculum of postgraduate study in Pharmaceutical management in Faculty of pharmacy, University of Belgrade, as a practical framework for understanding the outsourcing process.

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