Insights on pharmaceutical sustainable supply chains

Ana Margarida Santos Bravo*, José Crespo de Carvalho**

* Researcher in Pharmaceutical Supply Chains – ISCTE-IUL – Lisbon University Institute, Lisbon, Portugal; ** Full Professor, ISCTE-IUL – Lisbon University Institute, Lisbon, Portugal
Email: margarida.bravo@gmail.com, crespo.carvalho@gmail.com

Abstract
There is no industry where firms search for quality more closely to compliance than those in the pharmaceutical industry. Yet a major paradigm change is occurring in this industry and an increase of returns and recalls has been seen. Hence, in this paper we combine the findings of previous literature reviews conducted by the authors. In particular, explore the links between pharmaceutical drugs quality, reverse logistics, and sustainability. A case study on a global corporation manufacturing in the area of generic drug products has been selected for application. This approach leads to an understanding on the type of returns companies receive, in particular from hospital pharmacies. With this approach it is expected to link both parties in the application of a quality by design risk management approach as well as reduce variability and risk of noncompliance.

Keywords: Recall, Reverse, Sustainability, Pharmaceutical Industry

1 Introduction
This paper is motivated by the changes that the pharmaceutical industry is undergoing to cope with new challenges of the global economy. Intensive globalization processes, increased competitiveness, fast changing structure of competitors, complex strategic positioning, shrinking pipelines, expiring patents, counterfeit drugs, increased regulatory scrutiny on profits and a fight for global market share, are some of the factors giving the pharmaceutical companies new challenges (Papageorgiou et al. 2001, Reuters 2009, Almor 2009, Edwards 2010).

Complex requirements are forcing pharmaceutical manufacturers to adopt more formal business processes and stricter reporting methods (Souza et al. 2005); Pharmaceutical companies undergo strong regulations dictated by FDA (Food and Drugs Administration) and EMA (European Medicines Agency), for example. Even small irregularities in product or process can lead to the elimination of the whole production batches and in the worst case enormous civil penalties (Graunaeur et al. 2009). Furthermore, as John Avellanet (2009) suggests ‘as long as the industry fails to take a holistic cross-functional view of regulatory compliance, risk management and operational excellence, it will continue to see consent decrease, product recalls and tremendous waste’.

The pharmaceutical industry as a whole has traditionally been very profitable. On a global scale, the total size of the global pharmaceutical market has been forecasted to experience grow 4-6% exceeding $825 billion. The global pharmaceutical market sale is expected to grow at a 4-7% rate (CAGR) through 2013. Global pharmaceutical market value is expected to expand to $975+ billion by 2013 (IMS Health 2010). Besides, total pharmaceutical sales from the top 10 companies accounted for more than 4% of the total market. Additionally, the US pharmaceutical market grew by 3.0% in 2009 to $300.3 billion with highest growth in mail services and clinics; the major five Germany, France, Italy Spain and the UK, together accounted for over 60% of all European pharmaceutical sales in 2009 (Pharmaceutical Market Trends, 2010). Conversely, product recalls in the pharmaceutical industry are becoming extensive and increased radically, according to CNN (2010) in 2009 alone, the Food and Drug Administration reported more than 1,984 recalls comparing to 379 426 from 2008, from that more than 1,000 was from a contract
manufacturer; with an estimated $5 billion dollars and more than $700 million in fines since 2001 and billions more in lost revenues (Kumar et al. 2009, Souza et al. 2007). Industry sources have estimated the total of returns cost to be 3 to 6% of the annual pharmaceutical sales (Hunter et al. 2005). Product recalls has increased with ranges from 5 to 10% (Abboud and Hensley, 2003) with an estimated $5 billion dollars (Kumar et al. 2009).

Despite of the industry focus on quality, pharmaceutical manufacturing has failed to keep up with other industries in terms of efficacy and productivity. Therefore, all stages of the business value chain are affected, from development of new drugs to the management of the manufacturing and supply networks (Papageorgiu et al. 2001; Almor 2009; Edwards 2010). Organizations that cannot show a clear ethical conscience in supply risk significant tend to see their customers change their preferences to rival companies over time (Harwood and Humby 2008). These drivers show how organizations are facing increasing pressures from a wider range of stakeholders to engage with social and environmental corporate responsibility activities (Reuters 2009).

The purpose of this paper is to combine the findings of previous literature reviews conducted by the authors. In particular, explore the links between pharmaceutical drugs quality, reverse logistics, and sustainability. An introduction where to the global organization where the case-study will be applied is also exposed. The organization of this paper is as follows. After this introductory section, the relevant literature of Pharmaceutical applications these three main topics has been reviewed. In section 3, discussion has been presented with implications to management. Section 4 discusses limitation, conclusions and the next steps in this research.

2 Literature review

2.1 Pharmaceutical Recalls

We shall first start to comprehend the process behind drug products approval. No pharmaceutical product can be placed on the market without receiving prior authorization from the regulatory authorities, upon successful completion of a lengthy procedure for evaluating the quality, safety and efficacy of the product. Moreover, regulators around the world have become more sophisticated in ensuring that drugs are safe and effective (Levis and Papageorgiou 2004, Souza et al. 2007). The evaluation goes primarily against the drug manufacturing regulations which are based in the FDA Good Manufacturing Practices (GMP). These regulations have been improved through a management of system approach, in particular with the harmonization between risk analysis and quality systems. These changes have improved the approach to GMP compliance, marketing compliance more comprehensive, integrated, and focused on areas of the greatest impact (ICH 2011, Pluta and Poska 2010, Souza et al. 2007).

Changes made within an operation should be made for a reason with positive business outputs, or else quality improvements would not exist (Dale, 2003). Then again, in pharmaceuticals, any change that a company wants to make is always going to be subject to the pervasive requirements of safety, efficacy, quality and cost, making some companies to remain locked into an ancient mindset that says that providing outcome meet specifications, all is well (McConnel et al. 2009). However, this type of approach has been demonstrated fallacious, and to be likely to increase deviations and recalls (Mahboubian-Jones 2009), as demonstrated in the introduction section.

Table 1 highlights the parallels between the types of recall classification by the FDA (Food and Drug Administration) and EMA (European Medicines Agency), as can be seen high similarities cab be identified.
Table 1 – Recall classification comparison

<table>
<thead>
<tr>
<th>Class</th>
<th>FDA</th>
<th>EMA</th>
</tr>
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<tbody>
<tr>
<td>Class I recall</td>
<td>A situation in which there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse consequences or death</td>
<td>The defect presents a life threatening or serious risk to health</td>
</tr>
<tr>
<td>Class II recall</td>
<td>A situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse consequences is remote</td>
<td>The defect may cause mistreating or harm to the patient or animal, but is not life threatening or serious</td>
</tr>
<tr>
<td>Class II recall</td>
<td>A situation in which use of or exposure to a violative product is not likely to cause adverse health consequences</td>
<td>The defect is unlikely to cause harm to the patient, and the recall is carried out for other reasons, such as non-compliance with the market authorization or specification</td>
</tr>
</tbody>
</table>

Source: FDA and EMA (2011)

The decision to recall a product may be due to comprise issues related mix-ups, volume, potency, tampering, quality of dosage forms, questioned generic substitutions, labeling defects, lacking therapeutic effects, question formulations, dispenser malfunction and container defects, for example (Cheah et al. 2007, EMA 2011, FDA 2011). In the next table, a comparison of the most common incidents registered by both FDA and EMA for the 2007 period can be found.

Table 2 - Reported Drug Quality Defects

<table>
<thead>
<tr>
<th>Category</th>
<th>Incidence (%)</th>
<th>Category</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Defects</td>
<td>27%</td>
<td>Product defects</td>
<td>15%</td>
</tr>
<tr>
<td>Formulation/ Substitution</td>
<td>24%</td>
<td>Deviation Manufacturing Authorization</td>
<td>15%</td>
</tr>
<tr>
<td>Labeling</td>
<td>13%</td>
<td>Product literature information</td>
<td>23%</td>
</tr>
<tr>
<td>Packaging</td>
<td>6%</td>
<td>Packaging material</td>
<td>14%</td>
</tr>
<tr>
<td>Fill Problem</td>
<td>5%</td>
<td>Ancillary materials</td>
<td>14%</td>
</tr>
<tr>
<td>Delivery</td>
<td>13%</td>
<td>OOS</td>
<td>12%</td>
</tr>
<tr>
<td>Other</td>
<td>12%</td>
<td>GMP findings</td>
<td>7%</td>
</tr>
</tbody>
</table>

Source: CDER (FDA), 2007 & EMA, 2007
Although increasing, the recall or removal from the market of pharmaceutical products is not a regular event. When the product involved is a drug which is being dispensed to hospital patients, a product recall has to be carried out quickly and effectively (Autry 2005, Bowersox and Closs 1996, Ritchie et al. 2000), the replacement with a new one should also be done promptly. Ritchie et al. also state that due to the potential severity of using expired or ineffective drugs, it is critical that pharmaceutical companies get the reverse logistics right from the beginning. Companies must react quickly to problems, as well as clear the supply chain of non-conforming material, so that an appropriate supply chain can be reissued to those waiting for their medications (Kumar et al. 2009).

Summing up, no effective medicine is without risk and the benefits of a medicinal product always needs to be weighted up against its risks. The challenge to regulators is to find the right balance between timely availability of new medicines and the fact that knowledge on the safety profile is limited at the time of marketing authorization (EMA 2011). The next section will discuss the best approaches when dealing with returns of recalled pharmaceutical products.

2.2 Pharmaceutical Reverse Logistic

Nowadays, pharmaceutical companies are multi-product, multi-purpose and multi-site facilities operating in different countries and dealing with a global-wide international clientele. It is very often the case that multi-national companies operate in many geographically distributed manufacturing facilities while dealing with an international clientele located in different customer zones. Therefore, the issues related to the trading structure of the company have to be taken into account when deciding on the optimal multi-site investment strategy of the company (Levis and Papageorgiou 2004); therefore, the return of the drug products can be very complex. Returns from the pharmaceutical industry are mainly, end of shelf life drugs and recalls.

When dealing with a recalled product, the same system as a forward logistic cannot be applied, as the reverse supply chain is not a symmetrical image of the forward supply chain, due to the difference in the flows of materials and information demanded by either of them as stated by In de la Fuente (2008). Plus, forecasting and planning in reverse logistics also differ from that of the forward supply chain mainly because of the high level of uncertainty concerning returned products and waste materials. Therefore, companies who work in collaboration, become more effective and efficient with the integration within the supply chain.

It is possible to reduce the possible transportation costs of returned materials by taking possession when delivering newly manufactured products in the area or to the same client. In this case, it is convenient to design transport to facilitate the delivery of the new products with collection of used materials and products to recover; in this case the coexistence between forward and reverse materials is possible, moreover the incorporation of reverse logistics in the existing supply chain means benefits the manufacturing company, both with regards to quality, by improving customer assistance and product delivers and collection with regard to quantity (de la Fuente et al. 2008; Stock (1998).

To sum up, product recalls are generally viewed unfavorably by investors, and a failure to their systems quality (Cheah et al. 2007, Krumwiede et al. 2002). In the same line, product returns can present a significant challenge for manufacturing firms whose primary objective is usually geared towards producing and selling products to customers. The impact of returns is sometimes disregarded, or at least, not well-understood in most firms. In others, returns are often considered just a necessary cost-of-doing business (Mollenkopf et al. 2011), like the pharmaceutical. During a drug product recall the company must rely on the distributors or wholesalers distribution information (Kumar et al. 2009), in particular customer service, depot repair, end-of-life manufacturing, IT management, recycling, refurbishing/screening, replacement management, returns authorization, spare parts management, transportation, warehousing and warranty management (Kumar and Putman 2008). In addition, reverse logistics leads to an increase
of customer satisfaction and recovery of value; as well as reduces pharmacy costs, maximizing manufacturer credit benefits and/or reduce cycle times (Fassoula 2005; Biederman 2010).

2.3 Pharmaceutical Sustainability

Pharmaceutical companies are being accounted as more responsible towards sustainability. As the industry experiences an increasing pressure from regulation markets in the demand for more sustainable products, the need to become more sustainable increases, and the responsibility of its activities should be expanded from the production site to the whole product chain (Jorgensen 2008, Linton et al. 2007).

Pharmaceutical companies are using the Global Reporting Initiative (GRI) as a way to implement and measure their level of sustainability. The GRI guidelines have been developed and revised through a process involving various stakeholders (GRI 2011). As part of the standard sustainability report, the GRI guidelines suggest the use of indicators to measure an organizations performance in environmental, social and economic areas. They list over 100 possible indicators for companies to use, both generally applicable and organization-specific, such as total water used and recycle material for example. The GRI guidelines act as an educational vehicle and promote corporate social responsibility reporting for integrating environmental, social and economic aspects, and promote transparency and improved dialogue between business and stakeholders (Veleva and Ellenbecker 2001). In addition, due to the fact that financial and social criteria are crucial parts, these truly differentiate 'sustainability' reporting from straight environmental reporting (Morhardt and Freedman 2002).

The sustainability Report from 2009 for the pharmaceutical industry revealed the PSI scores (Pacific Sustainability Index (PSI) which uses two systemic questionnaires: one base questionnaire for reports across sectors and a sector specific questionnaire for companies within the same sector) for 26 largest pharmaceutical companied in the world. The findings of the reports include: 1) companies in the pharmaceuticals sector place varying importance on sustainability reporting transparency; 2) As in many sectors, environmental performance was the most underreported section. Fewer than half of the sector’s companies reported using environmental accounting, green purchasing and chemistry, or concern for biodiversity, and fewer than 60% of the companies mentioned climate change; 3) Across the sector, social reporting scores were generally better than scores for environmental reporting; 4) the pharmaceutical sector certainly should continue to address social issues on which it has a direct effect, such as health disparities, as well as the important environmental challenges all corporations face; 5) Many pharmaceutical companies have room for extensive improvements in their sustainability reporting, although there are some leaders in the sector setting a ‘stellar’ example. Ten of the 26 companies in the sample were GRI reporters, all of which finished in the top half of the reports ‘Overall Grade’ list (Sustainability Report 2009).

Summing up, expectations on safety and health are increasingly, more and more due to globalization. Firms in the pharmaceutical industry are now expected to be responsible to economic, societal and environmental needs. Moreover, environmental protection and sustainability cannot only be used to improve the public perception of the manufacturing efficiency as costs for input and output resources (Stegemann 2010). The adoption of sustainable practices helps business to distinguish them from competition through the reduction of unnecessary risks, generation of waste, increasing efficiency of materials and energy, innovating by new and environmental friendly products and services as well as gaining operating licenses from local communities (Székely and Knirsch 2005), and as soon as any harm is discovered and brought to the stakeholders attention, its root causes are identified and properly rectified (Campbell 2007). This type of approach leads to the increase business performance and profitability, sustaining their activities longer (Linton et al. 2007).
3 Discussion

Even though is well known what type of returns the pharmaceutical industry receives, like end of shelf life drugs, and recalls, pharmaceutical companies need to identify the product attributes that most affect quality so that operation managers can tap internal sources, including sales, marketing, product development and technical staff. Integration of QA processes is also a critical success factor. The other option could be the type of policy companies are making business, in particular the use of more risk management approaches through the application of techniques such as pharmaceutical Quality by Design (QbD), for example, which is a “systematic, scientific, risk-based, holistic and proactive approach to pharmaceutical development that begins with predefined objective and emphases product and processes understanding and process control” (Yu 2008). Part of this should involve the joint development and maintaining of performance metrics between the service provider and their business partners. Building performance metrics into the service agreement should also be given consideration, with on-going measurement of results taking place (Sartori 2011), as global, green and social capital, can have in a firm’s overall economic security. In addition, direct interaction with supply chain partners can enable a company to reduce total inquiry levels, decrease product obsolescence, lower transaction costs, react more quickly to changes in the market, and respond more promptly to customer requests. Managers can improve their materials management performance by fist understanding how their decisions affect the purchasing, storage, handling, and asset recovery activities throughout their organization (Markey and Davis 2007). From the exposed analysis, one could see that, the major paradigm change the industry is facing, i.e. the increase of recalls, is making companies to understand their process better, from the research and development phase by designing the products beyond compliance regulations until the end user, in this particular case the hospital patient. With this approach it is expected that drug product recalls and returns will decrease. It is also expected the reduction of wasted revenues in reverse logistic operations and an improvement of more sustainable pharmaceutical supply chains.

4 Conclusion

The goal of this paper was to merge finding from previous work developed by the authors in areas like pharmaceutical recalls, retains and sustainable practices, challenges that the industry is facing not only to be accounted as responsible, but also to keep up with other industries.

The limitations of this study open the door for extended research in pharmaceutical supply chains. The next step to our research is to understand the type of returns companies receive, not taking into consideration end-of-shelf life products, but the ones coming from complaints mainly from hospital pharmacies. This approach is consistent with the application of a case study to a global corporation manufacturing in the area of generics injectable drug products.

Phama Co. develops manufacturers and market generic and in-licensed pharmaceutical products within three core business. The operations span 49 countries and focus on key therapeutic areas such as anti-infectives, cardiovascular, alimentary tract and central nervous system. The injectable business markets 120 branded and non-branded injectable products in 215 dosage, strengths and forms, including 7 in-licensed products. Why Pharma Co. was selected? The 2010 revenue was $731m; by region: 61% MENA, 28% from the US and for Europe and the rest of the world accounts for 10.9%. Selecting it by segment, 23.9% are generics; 21.5% injectable drug products and 54% are branded. It has more than 400 products marketed in 2010. And an operating cash flows over $140.0m. It is the second largest generic injectable supplier by volume in the US with combined market share of more than 15%. Comparing to the introductory section one can expect that it is a good fit of the current pharmaceutical industry scenario. Towards the understanding of their major complains, semi-structure interviews will be applied not only to the company in question, but also to several hospital pharmacies in different countries of action. With this approach it is expected to link both parties in the application of a quality by design (QbD) risk
management approach as well as reduce variability and risk of noncompliance. With this approach a more sustainable pharmaceutical supply chain is expected to flourish, reducing waste, and increase of corporate social responsibility.

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