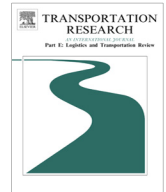




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Toward an integrated sustainable-resilient supply chain: A pharmaceutical case study

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ABSTRACT

In this paper, a novel multi-objective integrated sustainable-resilient mixed integer linear programming model for designing a pharmaceutical supply chain network under uncertainty is presented. To cope with the uncertainty aspect of the model, a new fuzzy possibilistic-stochastic programming approach is developed. Additionally, due to NP-hard nature of the problem, we propose a novel Pareto-based lower bound method as well as a new meta-heuristic algorithm. Several numerical examples, as well as a case study targeting Truvada[®] supply chain for the LGBTQ community, as they account for majority of the market for such product, in France is proposed.

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1. Introduction

The pharmaceutical, as an immense global industry, is responsible for the manufacturing, development and marketing of medications. Based on the 2015 CMR Pharmaceutical R&D Factbook, global sales reached a milestone of \$1 trillion in 2014, and will reach \$1.4 trillion in 2020, driven by increased healthcare access in emerging markets and high-priced new drugs for cancer and other diseases (<http://reuters.com>).

In general, a pharmaceutical supply chain (PSC) is a 5-tier supply chain which includes primary manufacturers, secondary manufacturers, main and local distribution centers (DCs), and destination zones/demand points (e.g., pharmacies, hospitals, clinics, etc.). The primary manufacturers are in charge of the production of required active ingredients (RAI), which normally include either several chemical synthesis and separation stages to build up the involved complex molecules, or purification and product recovery in case of biochemical processes (Shah, 2004). Secondary manufacturers are responsible for further production processes with different technology levels, packaging and finalizing the products that are usually in SKU form. Compared to a typical manufacturing supply chain, primary manufacturers can be referred to as *suppliers of raw materials*, and secondary manufacturers as *manufacturing centers*. Consequently, secondary manufacturers do not only play a major role in the production of final goods, but they can also store up a limited amount of products within the facility. Both main

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and local DCs are in charge of stocking goods to satisfy the market demand. Compared to main DCs, local ones are often more dispersed to cover more demand points, and more limited in terms of capacity levels.

Despite coupling with sophisticated technologies and improvements in quantity and quality of associated products in PSCs, many companies are far from effectively satisfying market demands with respect to arisen concerns (Masoumi et al., 2012).

With ever-increasing awareness of sustainability among government, industry, and the general public over the last two decades, policymakers worldwide have sought to incorporate sustainability considerations into urban and industrial development, and pharmaceutical industry has not been an exception (Fiksel, 2006, 2003). Sustainability is mainly referred to as a balance between social, economic, and environmental issues involved in human development. Social aspect, which has rarely been addressed in the literature, corresponds to forcing non-governmental organizations to take responsibilities for the social impacts of their actions.

One of the main aspects of social responsibility is community involvement and development since there is a consensus that the communities around the workplace should be enhanced both socially and economically. More precisely, increasing employment opportunities as well as providing a balanced economic development for local communities are the main goals of social responsibility (Zhalechian et al., 2016). Based on the World Summit of Sustainable Development, environmental impacts are considered an important pillar of sustainability.

There is an ever-increasing consensus that environmental impacts (EIs) left uncontrolled, may result in major changes to both the climate and the environmental systems. Governments are under immense pressure to enact legislation to curb these impacts. These restrictions, which include controlling greenhouse gas emissions, more specifically carbon dioxide (CO₂), is becoming a growing interest and companies are being urged to incorporate these issues into supply chain management schemes (Pagell and Wu, 2009; Benjaafar et al., 2013; Ding et al., 2016). Among these mechanisms and legislations, carbon emission trading or cap-and-trade system is generally accepted as one of the most effective market-based mechanisms, which has recently been broadly adopted by the EU, UN, etc. More precisely, the cap-and-trade approach provides economic incentives to decrease the emissions of pollutants, and is considered as market-based government-mandated mechanism. To respond to this issue, and in addition to cap-and-trade approach, companies tend to adopt more energy efficient technologies, equipment, or vehicles. On the other hand, these goals can be approached with optimizing production decisions, facility locations, transportation and inventory (Hua et al., 2011; Stavins, 2003). Upon doing so, an optimized supply chain network design (SCND) toward sustainability can not only correspond to economically beneficiary, but also lead to a significant change in social and environmental impacts.

However, with all increases in complexities in supply chains as in PSCs, vulnerabilities to disruptions have significantly been increased in such a way that any temporary stoppage out of disruption source either external (e.g., natural disasters, fire, theft, etc.) or internal (e.g., labor strike, technology malfunctions, etc.) leads to a significant loss. In order to improve the ability to respond rapidly and cost effectively to such unpredictable changes, SCs must adopt new strategies and incorporate the concept of resiliency in the designing process of the SC (Cardoso et al., 2015; Craighead et al., 2007). Supply chain resilience is defined as the capacity for a SC to survive and retain its basic function in the face of any turbulent change (Pettit et al., 2010).

Despite the increasing efforts on design and management of a sustainable SC, the quantitative impact of sustainability interventions on the supply chain resiliency has remained unexplored. Following sustainability in an environment characterized by frequent inevitable disruptions necessitates modeling and analysis that can accommodate this dynamism and complexity. Additionally, static sustainability analysis is simplistic, since both the economic and non-economic sustainability performance of a SC can be affected by disruptive events. Accordingly, this requires further optimization techniques and management tools to develop resilient and sustainable SCs, in such a way that the effect of any disruptions on sustainability performance is minimized (Fahimnia and Jabbarzadeh, 2016). Given these two mainstream topics that were discussed (i.e., sustainability and resiliency), we aim to investigate how PSC can be coupled with these two goals.

It should be mentioned that due to high volatility and dynamic nature of parameters, most especially supply and demand in such an industry, and knowing the fact that such change can greatly affect the structure of network designs, they are considered under uncertainty. In general, the techniques to cope with uncertainty can be divided into three main categories; Fuzzy programming, Robust optimization, and Stochastic programming. More details on how we coped with such uncertainty are provided in Section 4.

With respect to the abovementioned issues, this paper develops a new integrated sustainable-resilient pharmaceutical supply chain network design (ISRSPSCND) in a multi-period planning horizon under uncertainty. The considered objective functions try to minimize total network cost, maximize total sustainability in terms of minimizing environmental impact and maximizing social impacts, and minimize de-resiliency based on the developed measures. The main contributions of this paper that differentiate it from the existing literature are listed as follows:

- Proposing a new multi-period pharmaceutical network design including both strategic decisions (e.g., location decisions) and tactical ones (i.e., network allocation).
- Simultaneously considering both resiliency and sustainability as the objective functions and setting a trade-off between these two measures.
- Both introducing and developing resilience measures for the considered network and applying them as optimization tools.

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