Design and planning of vaccine supply chains

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Abstract — The manufacture and distribution of vaccines is undermined by bottlenecks and roadblocks occurring throughout its supply chain.

This study proposes a multi-objective and multi-period mixed integer linear programming (MILP) model for the simultaneous design and planning of vaccine supply chains. The model is applied to a representative European supply chain virtual case study (partly based in the European supply chain of Sanofi Pasteur). To address the pressing issue of sustainable supply chains, the developed model incorporates the three dimensions of the triple bottom line (TBL), as described in Elkington (2004). The results obtained with this study clearly show how strategic and tactical decision-making impacts on key performance indicators in a vaccine supply chain.

Key Words — Vaccine supply chains, Mixed-integer linear programming, Sustainable supply chains

1. Introduction

The global healthcare sector has undergone fundamental changes throughout the last years to cope with the new challenges of the modern economy (Papageorgiou et al., 2001). The major drivers that have been fuelling this shift are related to demographic factors such as unprecedented and enduring ageing of populations, healthcare factors such as growing demand for new innovative treatments and technology, and lastly, evolving financial and quality regulations (Deloitte, 2016).

Pharmaceutical companies are included in the group of healthcare companies facing the aforementioned obstacles. In particular, pharmaceutical companies have been dealing with reinforced regulations regarding economic, environmental and social issues, driving them towards sustainability. Moreover, these same companies are confronted with planning and designing their supply chain to reduce costs, waste and achieve highly effective supply networks. Supply chain optimisation is now a major research theme in process operations and management (Shah, 2004).

Within pharmaceutical companies, the ones dealing with vaccines face special challenges. To deepen the difficulties, vaccines are not like commodities since their primary objective is to eradicate harmful diseases and they have special storage conditions (refrigeration or freezing), thus leading to a much harder distribution planning. Bearing in mind this scenario for vaccine supply chains (VSC), the intent of this work is to study how to make better strategic and tactical decisions that will help to attain several key objectives, namely economic, environmental and social goals, and develop a model for the design and planning of VSC.

A multi-objective mathematical programming model for the design and planning of vaccine supply chains that simultaneously considers economic, environmental and social performances is proposed in this study.

For this objective, the associated background literature is presented in the next section. In section 3, the developed model is characterised. In section 4, the case study description is given, and subsequently, the results from the application of the model to the case study are presented in section 5. Lastly, in section 6, final conclusions are drawn and future work directions are discussed.

2. Vaccine supply chains

The complexity of a vaccine's manufacturing chain is, arguably, due to three main factors. The first factor is related with the complexity of vaccines, which result in large production lead times. Secondly, other factor of utmost importance concerns, what is called, globalised manufacturing chains. Thirdly, the regulatory requirements are becoming increasingly complex for manufacturers. To answer these complexities, vaccine supply chains need to be optimised in terms of structure, planning and operation taking into account the associated supply chain characteristics.

In this study, vaccine supply chains are characterised by two main parts, one being the manufacturing process and the other being the distribution process. Figure 1 demonstrates a generic representation of vaccine supply chains. The first two steps (suppliers and manufacture) may be included in the manufacturing process, whereas the three other steps may be included in the delivery process. For the sake of simplicity, and if one considers clustering customers, one can consider customers and consumers to be in the same step of the supply chain.

Vaccine manufacturing involves several steps and each one can be performed in different sites located in different countries. However, in this work, only one step is considered, and vaccines leave factories as final products. All of these steps can take up to 24 months to complete, approximately, which represents a huge lead time in the delivery of vaccines from factories to warehouses (IFPMA, 2014).

After manufacturing, vaccines are shipped for distribution. In the distribution process vaccines go through international shipping and finally arrive to warehouses where they are stored. To store vaccines, it is necessary to consider the available storage space and capacity, as well as the electricity supply. The last step encompasses delivering vaccines to final markets as countries.

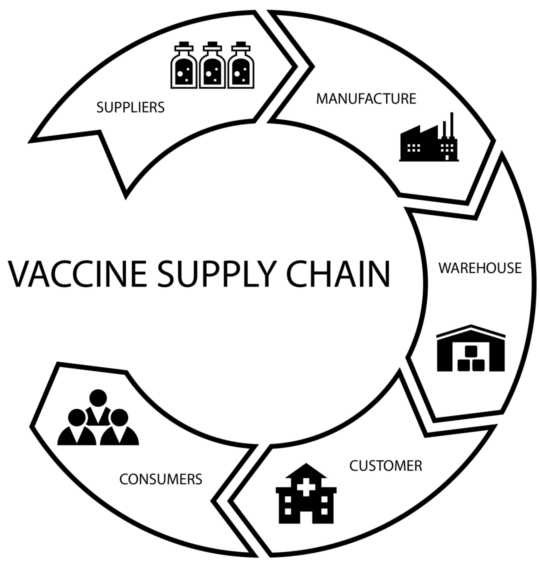

Figure 1. Vaccine supply chain structure

3. Literature Review

The pharmaceutical industry entails a complex set of processes, operations and organisations involved in the discovery, development and manufacture of drugs, medications and vaccines (Shah, 2004). The main goal of the pharmaceutical industry is to deliver drugs that help in the prevention of diseases, maintain health and cure or retard diseases, consequently reducing morbidity (Market Realist, 2015).

From its early days, the pharmaceutical industry has enjoyed a very satisfying economic status, with profits commonly growing steadily. Nevertheless, market pressures and harsh socio-political regulations are among the present causes changing the way in which the pharmaceutical business is operating (Gatica et al., 2003).

These companies invest large quantities of assets into their global supply chains so that they are able to deliver their products efficiently to markets, and ultimately to patients. Supply chain management (SCM) has been a pressing field in terms of research for pharmaceutical companies to further reduce costs, and thus maximise profits.

3.1. Supply chain management

Supply chains (SC) are normally considered as integrated systems that, traditionally, start at the supply of raw materials and end with the distribution and sales of goods to final consumers (Cardoso et al., 2013). In recent years, the literature on SC has been growing towards the integration of both forward and reverse logistics. In regard to forward logistics and strategic decision-making associated, various works have been published. One of the major reviews before the 20th century was Vidal et al. (1997), which only encompassed a strategic model. However, many authors further developed research (Goetschalckx et al., 2002). Addtionally, in Peidro et al. (2009), a review of the literature related to supply chain planning methods under uncertainty and quantitative approaches for modelling is given.

With the introduction of sustainability as an essential feature of supply chain structures, the preoccupation with social and environmental design and planning rose, representing now, along with economic concerns, crucial features of a supply network (Linton et al., 2007). The integration of environmental and social aspects with economic considerations is known as the triple-bottom-line (TBL) as stated by Elkington (2004). Being TBL a starting point for Corporate social responsibility (CSR) and Sustainable development (SD), activities of reverse logistics in the supply chain have been studied lately more often, mostly because they are now a reality.

3.2. Pharmaceutical supply chains

A supply network from a pharmaceutical company is similar to that of any other industry in the manufacturing sector. Among the substantial published research on Supply chain network design (SCND), only a small fraction of these studies directly deal with the pharmaceutical sector.

Despite all advances and improvements in the manufacturing, storage, and distribution methods, several pharmaceutical companies are still significantly far from effectively satisfying market demands in a consistent manner (Mousazadeh et al., 2015).

Inside the industry, the preferred mechanism to overcome the productivity crises has been to increase investment, primarily, in the two extreme ends of the supply chain, R&D and sales. However, supply chain optimisation is an excellent way to increase profit margins and is becoming current practice (Sousa et al., 2011).

Papageorgiou et al. (2001) developed a mathematical programming (MILP) model so as to facilitate the strategic supply chain decision-making process for pharmaceutical industries. In Shah et al. (2004), supply chain design difficulties are discussed. In this paper the low manufacturing velocities are highlighted and the quality assurance activities at several points are also mentioned.

3.3. Vaccine supply networks

The progression of the immunisation landscape throughout the years is described in Bloom et al. (2005). The paper provides a brief summary of the history of vaccination and its impacts on human health, at the beginning, and ends with the research-to-date and new researches on the economic benefits of immunisation.

Kaufmann et al. (2011) mention some regular problems in vaccine supply chains such as temperature controlled transport and storage and shelf life issues. They also state that if supply chain improvements do not occur, the money and time spent to develop and finance new vaccines will be put at risk.

In the same tone of describing supply network problems, yet also presenting solutions, Zaffran et al. (2013) argue that effective vaccine delivery should be achieved and environmental impact of energy, materials and processes used in immunisation should be minimised.

Recently, Lemmens et al. (2016), published a paper with the intention of providing a major literature review on supply chain network design (SCND) for vaccines.

The problem addressed in this research has the primary objective of proposing a model that not only designs a vaccine supply chain, but also provides a tactical plan for production, storage and distribution in a predefined time horizon.

4. Model characterisation

4.1. Problem definition

The problem discussed in this dissertation aims to determine the optimal supply chain structure for vaccines along with planning decisions that maximise the expected net present value (NPV), minimise environmental impact (e.g. energy consumption and CO_2 emission) and maximise social benefit (through the creation of jobs), in a solution of compromise.

The generic representation depicted in figure 2 is implemented in a MOMILP (multi-objective mixed-integer linear programming) model. The supply chain is formed by three echelons: factories with a given minimum and maximum capacity, warehouses, where final products are stored and delivered to markets and, finally, patients' markets.

Final products (vaccines) flow to warehouses or directly to markets. It is considered that inventory of final products is only allowed at warehouses. Final products entail both vaccines that rely on refrigeration and congelation to preserve their potency. At warehouses, technology selection is possible and both storage technologies (refrigerating and freezing technologies) can be allocated to each warehouse. Transhipment is allowed between warehouses and transportation between entities can be performed by unimodal or intermodal transportation. In this study, intermodal transportation includes road, train and sea freight modes.

The supply chain representation to use in the model was based on the work developed by Mota et al. (2015). A graph representation is utilised to characterise the supply chain structure that goes from the manufacturing sites to markets (countries). Nodes represent any supply chain entity (such as factories, warehouses and markets), whilst arcs between two nodes define an existing flow.

Nodes are characterised by the following set of properties:

- Input flows: arcs that represent products coming from the previous network level;
- Output flows: arc that represent products going to the next network level;
- Operation: nodes indicate the transformation that products undergo and that is responsible for turning input products into output products. This process can be a storage operation or simply a cross-docking operation. The operation varies according to the function that the entity has on the supply chain. Any operation has also some specific characteristic:
    - Time: any operation has a time of execution, which can take the value of zero if defined as instantaneous;
    - Capacity: the operation may be performed within maximum and minimum pre-established values.

On the other hand, arcs represent any kind of flows between two entities. They are characterised by:

- Origin: source entity;
- Destination: target entity;
- Material: one material is associated with each flow;
- Time: time needed to go from the origin to the destination;
- Capacity: maximum and minimum limits modelled for each flow. These limits are mostly related to transportation modes.

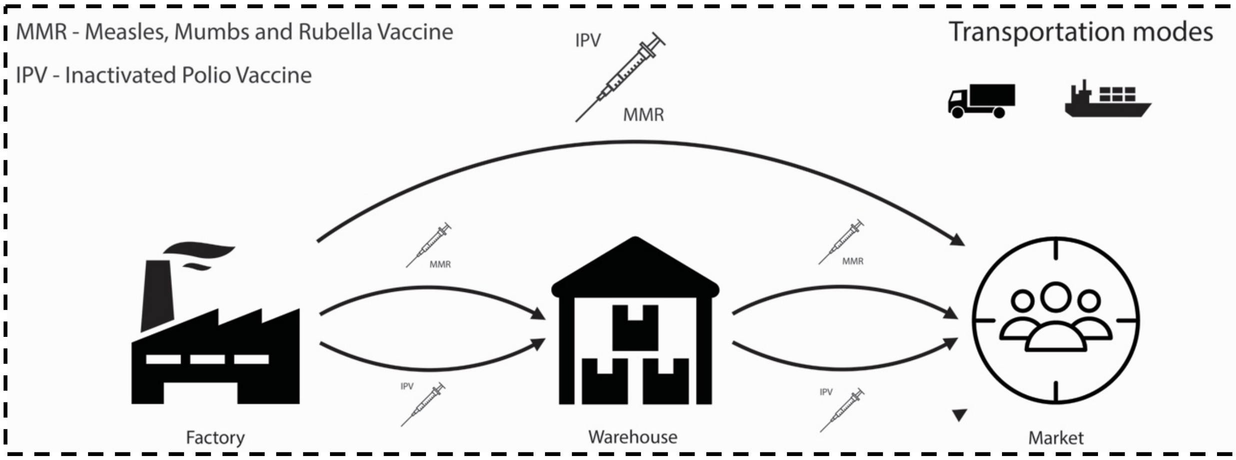

Figure 2. Supply chain representation

Overall, given:

A possible superstructure for the location of the supply chain entities, and for each location (when applicable):

- Investment costs;
- Maximum and minimum flow capacities;
- Maximum and minimum production capacities;
- Maximum storage capacities;
- Environmental factor of each facility for each impact category;
- Social factor based on GDP per capita;
- Maximum supply capacity;
- Initial stock levels;

Possible storage technologies and for each technology:

- Maximum storage capacities;
- Investment costs;
- Operating costs;
- Installation costs;
- Necessary number of workers;
- Environmental impact characterisation factor;

Possible transportation mode and for each transportation mode:

- Maximum and minimum transportation capacities;
- Investment/outsourcing costs;
- Variable transportation costs;
- Contracted fixed costs (for transport hub);
- Handling costs at transport hubs;
- Necessary number of workers;
- Environmental impact characterisation factor;

The products within the supply chain, and for each product:

- Product demand;
- Price per unit sold;
- Product weight;
- Product volume;

Distance between each pair of entities.

4.2. Mathematical formulation

4.2.1. Sets

Entities

Each level of the supply chain is defined by just one kind of entity (factory, warehouse, seaport, customer). Set I represents the set of entities.

Products

There are two types of products: refrigerated products and frozen products. Set M, which represents the set of products is divided into two subsets.

Technologies

There are two types of technologies: refrigerating technologies and freezing technologies. Set G represents the set of all technologies.

Transport modes

There are also two types of transport modes, truck and boat. Set A represents the set of all transport modes.

Extended entities

Extended entities are defined by the pair product-entity since entities and products.

$$V = \{(m, i) : m \in M \wedge i \in I\}$$

Flows

Flows are defined by the pair entity-entity, representing the edges of the graph.

$$U = \{(i, j) : i, j \in I\}$$

Extended flows

As for entities, flows and products are also related. Extended flows are defined by the pair extended entity-flow.

$$F = \{(m,i,j) : (m,i) \in V \wedge (i,j) \in U\}$$

Storage process

As each technology is related to a type of product, it is possible to define a set defined by the pair product-technology.

$$H = \{(m,g) : m \in M \wedge g \in G\}$$

Connected entities

This set represents the connections of two entities with a certain transportation mode.

$$Net = \{(a,i,j) : a \in A \wedge (i,j) \in U\}$$

Network superstructure

Finally, this set represents the allowed connections of the whole network, defined by the pair connected entities-extended flows.

$$NetP = \{(a,m,i,j) : (a,i,j) \in Net \wedge (m,i,j) \in F\}$$

4.2.2. Objective functions

Equation **(1)** represents the model economic objective function, which maximises the NPV for the time horizon modelled. Equations **(2)** to **(6)** are support equations used to calculate the NPV. This approach to quantify an economic objective is based on the work developed in Cardoso et al. (2013). The NPV is calculated, according to Brealey et al. (2014), as the sum of the discounted cash flows of each time period (denoted by CF_t), through the usage of the interest rate ir.

$$\max NPV = \sum_{t \in T} \frac{CF_t}{(1+ir)^t} \quad (1)$$

Equation **(2)** calculate the cash flow in each time period, obtained from the difference between the net earnings (NE_t) and the fraction of the total depreciable capital (FDC_t). Additionally, equation **(2)** also calculates the cash flow for the last time period, where it is taken into account part of the total fixed capital investment (FCI) that may be recovered at the end of the time horizon, using a salvage value sv.

$$CF_t = \begin{cases} NE_t - FDC_t, & t = 1, \dots, NT-1 \\ NE_t - FDC_t + sv \times FCI, & t = NT \end{cases} \quad (2)$$

Equation **(3)** represents the formula for the net earnings. Net earnings are given by the difference between the incomes and the total cost, as shown in equation **(3)**.

$$\begin{aligned} NE_t = (1-tr)\Bigg[& \sum_{\substack{(m,i,j) \in F_{INC} \\ (a,m,i,j) \in NetP}} pus_m X_{maijt} \\ & - \Bigg(\sum_{\substack{(m,g) \in H \\ i \in I_w}} opc_g S_{mgit} \\ & + \sum_{\substack{(a,m,i,j) \in NetP \\ a \in A_{truck}}} \left(\frac{avc_a}{100} \cdot fp + vmc \right) \cdot 2d_{ij} \cdot Q_{aijt} + \\ & + \sum_{\substack{(a,m,i,j) \in NetP \\ a \in A_{boat}}} tc_a \cdot pw_m \cdot d_{ij} \cdot X_{maijt} \\ & + \sum_{\substack{(a,m,i,j) \in NetP \\ j \in I_{port} \wedge i \notin I_{port}}} hhc_j \cdot X_{maijt} + \sum_{i \in I_{port}} cfp_i \cdot Y_i \\ & + \sum_{i \in I_w} w_i \cdot lc_i \cdot wwh \cdot wpt \cdot Y_i \\ & + \sum_{i \in I_w} wpsq \cdot lc_i \cdot wwh \cdot wpt \cdot YC_i \\ & + \sum_{\substack{(m,g) \in H \\ i \in I_w}} w_g \cdot lc_i \cdot wwh \cdot wpt \cdot Z_{gmi} \\ & + \sum_{\substack{(a,i,j) \in Net \\ a \in A_{truck}}} w_a \cdot lc_i \cdot wwh \cdot wpt \cdot K_{ai} \Bigg) \Bigg] + tr \cdot DP_t \end{aligned} \quad (3)$$

Firstly, the incomes are determined from sales through the multiplication of products' price per unit sold (psu_m) and the quantity that is delivered in markets in each time period t. The total cost terms include the following in the respective order:

- Storage operating costs;
- Transportation costs for road transportation;
- Transportation costs for sea transportation;
- Handling costs at the hub terminal;
- Contracted costs with the freighter;
- Labour costs at entities, which include labour costs for storage and labour costs for owned transportation modes (road transportation).

Finally, the last term defines the depreciation of the capital invested (DP_t) and tr represents the tax rate. For the capital invested it was considered a depreciation linear method as presented in equation **(4)**.

$$DP_t = \frac{(1-sv) \cdot FCI}{NT} \quad (4)$$

$$FDC_t = \frac{FCI}{NT} \quad (5)$$

$$FCI = \sum_{i \in I_w} sqmc_i \cdot YC_i + \sum_{\substack{(m,g) \in H \\ i \in I_w}} tec_g Z_{gmi} + \sum_{\substack{(a,i,j) \in Net \\ a \in A_{truck}}} ftc_a K_{ai} \quad (6)$$

$$\min EnvImpact = \sum_{c} \eta_c \left(\sum_{\substack{t \in T \\ (m,g) \in H}} ei_{mgc} pw_m S_{mgit} + \sum_{\substack{t \in T \\ (a,m,i,j) \in NetP}} ei_{ac} pw_m d_{ij} X_{maijt} + \sum_{i \in I_w} ei_{ic} YC_i \right) \quad \textbf{(7)}$$

In equation **(7)** the environmental impact of three different supply chain activities is calculated for each midpoint category c. The activities are the following, in respective order:

- The environmental impact of storage;
- The environmental impact of transportation;
- The environmental impact of entity installation.

The final calculation of the environmental impact is given by the normalised sum of the impact of each individual activity described just now with the normalisation factor η_c. The use of this normalisation factor is justifiable since the results of each impact category need to be in the same units.

The measurement of the social objective was performed through equation **(8)**. In this equation, preference is given to supply chain entities and activities that are going to be located in regions with lower GDP per capita. A map with the GDP per capita in the model applicable area is given in figure 8. Based on the GDP per capita, a regional factor characterises each region i. The contribution of each different activity to the creation of jobs in that location is given by the following terms of equation **(8)**, in respective order:

- Entity installation (warehouses);
- Technology installation;
- Transportation.

$$\max GDPInd = \sum_{i \in I_w} \mu_i^{GDP} w_i Y_i + \sum_{i \in I_w} \mu_i^{GDP} \cdot wpsq \cdot YC_i + \sum_{\substack{(m,g) \in H \\ i \in I_w}} \mu_i^{GDP} w_g Z_{gmi} + \sum_{\substack{(a,i,j) \in Net \\ a \in A_{truck}}} \mu_i^{GDP} w_a K_{ai} + \sum_{\substack{(a,m,i,j) \in NetP \\ a \in A_{boat} \\ t \in T}} \mu_i^{GDP} \frac{w_a}{yth} \cdot pw_m \cdot d_{ij} \cdot X_{maijt} \quad \textbf{(8)}$$

The model constraints are grouped into four categories, namely: (1) material balances at factories, warehouses and seaports; (2) entity capacity constraints; (3) transportations constraints; and (4) technology constraints.

5. Case study

The developed model was applied for the creation of an European vaccine supply chain. The virtual company, which will operate this supply chain, was created based on the information extracted from the corporate responsibility report of Sanofi, S.A. (Sanofi, S.A., 2015). The supply chain entities are all located in Europe.

Currently, the company owns two factories, which have sufficient capacity to meet the demand of their 21 clients, all in Europe. The superstructure representing this case study is depicted in figure 3.

Entities are characterised with a maximum and minimum capacity. Customers have additional characteristics to provide information for the social objective, thus they are characterised in terms of average labour cost, construction cost and GDP per capita.

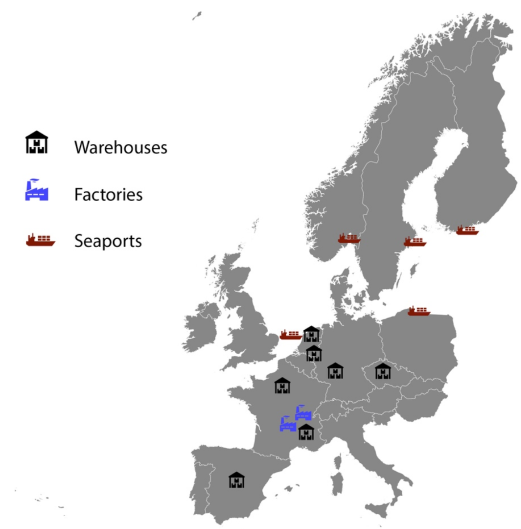

Figure 3. Case-study superstructure.

The company manufactures two types of products displayed in figure 4.

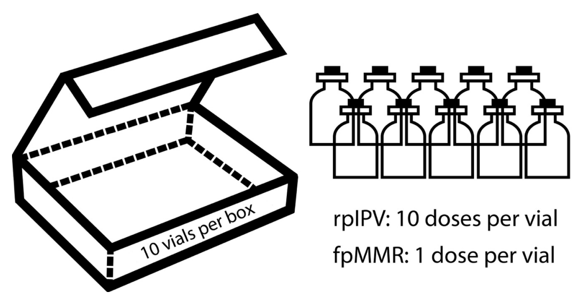

Figure 4. Products' presentation.

Both products are stored at warehouses with appropriate storage technologies. The technologies considered for this model are Walk-In Cold Rooms (WICR) and refrigerators for refrigerated vaccines, and Walk-In Freezer Rooms (WIFR) and freezers for frozen vaccines. They are also characterised in terms of maximum capacity.

Environmental impact of some supply chain activities was characterised using SimaPro Ecoinvent database version 8.01.

Extra economic parameters were defined such as an interest rate, a salvage value, and a tax rate.

The model was implemented in GAMS 24.7, and the case study solved using CPLEX 12.0.

The results obtained from the execution of the model were divided into three single objective scenarios:

- Scenario A: In this scenario, the optimum economic performance is prioritised, which means that Net Present Value is maximised;
- Scenario B: In this scenario, the optimum environmental performance is prioritised, which means that environmental impact is minimised;
- Scenario C: In this scenario, the optimum social performance is prioritised, which means that the creation of jobs in countries with lower socio-economic conditions is maximised.

In order to compare all cases, the NPV, the environmental impact and the social benefit are shown in table 1.

Table 1. Performance indicator's for scenarios A, B and C.

	Scenarios		
Performance Indicator	**A**	**B**	**C**
Economic	1,817,029,498	1,696,733,844	1,183,138,668
Environmental	1,172,908	280,488	4,136,377.37
Social	386.18	478.38	1,476.73

One can observe that the most profitable solution (Scenario A) does not have the worst environmental performance when compared with the other two scenarios (B and C). However, scenario A has the worst social performance in comparison with the other two cases. The environmentally sustainable solution (Scenario B) is obtained at the cost of a 7% reduction in the profit over the 5-year time horizon, and the social performance increases by 24%, which translates in 186 more job opportunities. In its turn, the socially beneficial solution (Scenario C) is obtained through the maximisation of job opportunities, at the expense of a 35% decline in the NPV. The environmental impact is also extremely affected (negatively), worsening around 1276% its performance, largely due to a massive usage of transportation. However, this solution increases the social performance by 283% when compared with Scenario A, which corresponds to the creation of 1,246 additional job opportunities. These scenarios are more detailed below.

In all scenarios both factories are operating but not at maximum capacity. However, in scenario A, warehouses are only installed in Madrid and Prague. In Madrid, the warehouse has the capacity of 266 m^2, and in Prague the warehouse has the capacity of 476 m^2. Storage is preferably done with WIFR and WICR, since their ratio of capacity to price is greater when comparing with refrigerators and freezers, respectively. Inventory of rpIPV is kept at warehouses. The warehouse of Prague is used almost exclusively to store product fpMMR, though inventory of this product is also kept at the warehouse in Madrid. In terms of transportation, trucks of bigger capacity were purchased in higher quantity in comparison with smaller trucks. In this case, 6 Trucks B were purchased, and only 2 Trucks A were acquired. Sea transportation is not used in this scenario. In terms of costs, this scenario has the lowest costs in total, when compared with scenario B and C.

In the environmental optimisation scenario, all possible warehouses were installed in order to decrease the number of trips travelled with trucks, therefore decreasing the overall number of travelled kilometres. As for their capacity, all warehouses have the capacity of 100 m^2 (minimum capacity), except for the warehouse in Lyon which was installed with the capacity of 142 m^2. As in the first scenario, refrigerators and freezers were preferred over WICR and WIFR. Inventory of product rpIPV is mostly kept at warehouses in Lyon, Paris, Rotterdam, Venlo and Prague, whilst inventory of product fpMMR is mostly kept at warehouses in Lyon, Paris, Venlo, Frankfurt and Prague. The number of small trucks purchased was zero, so that the environmental impact caused by trucks could also by diminished. On the other hand, 12 trucks B were acquired to guarantee that the number of trips among entities is minimised, thus reducing the environmental impact associated to transportation. For the same reason, sea transportation is used in this scenario because even though the environmental impact of boats is greater than that of trucks, boats may carry more products per trip. The environmental impact caused by storage, transportation and facility installation in scenario B is displayed in table 14. The environmental impact is greatly reduced in this scenario due to the decline of the number of transportation trips. Transportation is thus the most important pinpoint to consider when crafting strategies to reduce environmental impact.

In the social optimisation scenario, all warehouses were installed with maximum capacity, although their capacity was not being utilised. This occurred so as to maximise the number of jobs created. Similarly, small trucks were purchased in place of bigger ones. Since smaller trucks also have a smaller capacity, it means that more trucks are needed, thus creating more jobs for drivers. Hence, 45 trucks A were purchased, and 13 trucks B were also acquired. In terms of technology selection, refrigerators and freezers were chosen not because they were less costly, or even because their environmental impact was less than that of WICR and WIFR, but rather because the number of jobs they would create was bigger. Inventory is distributed among all warehouses. Sea transportation was also considered in this model to increase even further the creation of jobs. The results from this scenario clearly show that it is not feasible, that is, there are large quantities of resources not being used which are only making the company incurring in additional costs. It is possible to verify that scenario C is also environmentally unsustainable, besides being economically infeasible. The excessive impact to the environment from using such big fleet of trucks is unsustainable.

5.1. Environmental and social optimisation with profit constraint

As seen before, some of the solutions through single objective optimisation might not be viable to implement. Hence, it becomes necessary to analyse more than one objective simultaneously.

The goal of this section is to study how to better design and plan the supply chain in the face of multiple objectives. The multi-objective approach is applied to the economic and environmental objectives, and then to the economic and social objectives. In this case, the goal is to comprehend how to minimise environmental impact or maximise social benefit with an additional economic constraint, which offer an overview of the necessary trade-offs.

- Scenario D: In this scenario, the optimum environmental performance is prioritised with a maximum reduction of 5% in the NPV determined in scenario A. This results from the minimisation of the environmental impact function with an additional constraint stating that the NPV must be at least 95% of the profit obtained in scenario A;
- Scenario E: In this scenario, the optimum social performance is prioritised with a maximum reduction of 5% in the NPV determined in scenario A. This results from the maximisation of the social objective function with an additional constraint stating that the NPV must be at least 95% of the profit obtained in case A.
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Table 2. Performance indicator's for scenarios D and E.

Performance Indicator	Units	Scenarios D	Scenarios E
Economic	€	1,726,000,000	1,726,000,000
Environmental	-	284,593	1,038,437
Social	-	564.09	1,011.42

With the additional economic constraint, the profit has not declined as much as expected when the environmental impact is being minimised. In fact, profit has been increased by 2% when compared with scenario B. Yet, the environmental impact is significantly higher, approximately, 5% higher. Hence, it is possible to conclude that a trade-off exists between the economic and the environmental indicators. Similarly, when the social performance indicator is maximised under the additional economic constraint, the same effect is observable. The social performance suffered a substantial decline so that the profit could be maintained at 95% of the original profit in scenario A. Consequently, 531 fewer job opportunities were created, but with a profit growth of 46% in comparison to scenario C.

For the optimisation scenario D, all the decisions were taken envisioning the reduction of the negative environmental impact of transportation, storing products in electricity consuming technologies and the installation of warehouses, while maintaining the profit at 95% of that of scenario A. All warehouses were installed, except for the warehouse in Rotterdam. Their capacity was set to 100 m^2 (minimum capacity), except for the warehouse in Lyon which was built with a capacity of 242 m^2. The number of trucks A (small) purchased was null as in scenario B. As for the number of trucks B, 11 trucks were purchased, 1 less than in scenario B because the warehouse in Rotterdam was not installed. The picture for sea transportation remained the same as in scenario B.

The outcome from the execution of the model in scenario E showed that all warehouses were installed but not at full capacity. The warehouse in Madrid and Prague were installed with maximum capacity (500 m^2) while the remaining warehouses were installed with, approximately, half of the maximum capacity. In this scenario 50 trucks A and 10 trucks B were acquired, thus maximising the number of job opportunities created through transportation. Seaports were not used in this scenario, thus excluding intermodal transportation.

Lastly, scenario E demonstrates an example of how social benefit may be created while decreasing negative environmental impact and generating a higher profit.

The outcome from the execution of the model in this scenario shows clear improvements for the economic and environmental performance indicators while maintaining the social performance indicator close to the one obtained from the scenario where the social indicator is maximised.

Table 3. Decisions' results summary.

	Scenarios		
	A	B	C
Warehouses	Madrid Prague	All installed	All installed with maximum capacity
Storage	Refrigerators and freezers are the preferred storage technologies used		
Inventory	More inventory of rpIPV is kept	More inventory of fpMMR is kept	More inventory of fpMMR is kept
Transportation	Most trucks purchased are big trucks	Most trucks purchased are small trucks	Most trucks purchased are small trucks
	Sea transportation is not used	Sea transportation is used in all scenarios	

5.2. Sensitivity analysis

Since assumptions had to be made on some critical parameters a sensitivity analysis was performed in order to understand the impact of these parameters changes in the supply chain network structure and planning. Two different analysis were conducted where changes in the following parameters were considered: demand values and investment costs. For the case of demand values, variations of +5% and +10% were considered. Similarly, investments costs were also experimented with a +5% and +10% variation.

Demand uncertainty is a major problem that affects supply chains. In this study this uncertainty has been modelled through a variance of +5% and +10% in the demand value estimated initially. The values taken as base may be subject to some subjectivity and sensitivity analysis was therefore conducted.

The supply chain structure did not suffer any changes in terms of number and location of infrastructures in both runs, for +5% and +10%. However, some differences in terms of flows of products are noticeable.

Inflation may raise prices which will increase the investment capital needed for the construction of facilities, the installation of storing technologies and the purchase of trucks. Knowing that for a planning horizon of 5 years it is possible that prices rise, two increased values for investment costs were considered: +5% and 10%.

As expected when the investment costs increase the NPV decreases, since the profit is sensitive to and dependent of the investment costs. The difference between the NPV in scenario A and that from the +10% investment costs variance is only, approximately, 1%. Furthermore, the network structure remains stable. The activities and capacities of entities and transportation modes did not suffer any significant alterations

6. Conclusions

The developed model provides support for strategic and tactical decisions at several levels of the supply chain. Specifically, it allows to understand the effect of these decisions on each one of the performance indicators (economic, environmental and social), thus enabling derivation of potential trade-off strategies to balance them. Moreover, the model also facilitates the comprehension of connections among different supply chain activities, giving an opportunity to better understand the performance of the combined indicators across the supply chain. From the usage of environmental and indicators, it is possible to identify environmental sustainability foci and select actions to diminish environmental impact of supply chain activities. Similarly, from the usage of social indicators, it is possible to investigate socially responsible options while arranging compromises, either with the economic performance of the company, the environmental impact or both.

As future challenges, numerous features ought to be included in the model. Firstly, developing countries would be a much interesting case to explore with this methodology due to increased hurdles.

To further understand how to better plan inventory, other storing technologies such as solar refrigerators/freezers for zones with depleted electricity supply would also be useful. In the social dimension, health equity issues (in terms of the accessibility to vaccines) should also be addressed as to minimise the differences that exist among regions even inside the same country. However, to improve the social benefit in developing countries, the economic and environmental performance indicators would certainly be negatively impacted. Yet, ultimately, the objective of immunisation is to eradicate and prevent diseases in the world, which can arguably be classified as a social objective.

In terms of limitations one should note that a virtual case study was used to test the applicability of the model and collect the results. Thus, estimations were used for demands and data were collected to identify and select possible locations for entities. As for the rest of the parameters, most were search in statistics websites instead of values provided by a company.

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