

**A Supply Chain Generalized Network Oligopoly Model
for
Pharmaceuticals Under Brand Differentiation
and
Perishability**

Amir H. Masoumi, Min Yu, and Anna Nagurney*
Department of Finance and Operations Management
Isenberg School of Management
University of Massachusetts
Amherst, Massachusetts 01003

September 2011; revised January 2012

Transportation Research E **48**: (2012), pp 762-780.

Abstract: In this paper, we construct a generalized network oligopoly model with arc multipliers for supply chains of pharmaceutical products using variational inequality theory. The model captures the Cournot competition among the manufacturers who seek to determine their profit-maximizing product flows, which can be perishable, with the consumers differentiating among the products of the firms, whether branded or generic, and the firms taking into consideration the discarding costs. The numerical examples demonstrate that a brand pharmaceutical product may lose its dominant market share as a consequence of patent rights expiration and because of generic competition.

Keywords: Perishable products, pharmaceutical companies, healthcare, supply chains, brand differentiation, generalized network

* Corresponding Author; e-mail: nagurney@isenberg.umass.edu; phone: 413-545-5635; fax: 413-545-3858

1. Introduction

Pharmaceutical, that is, medicinal drug, manufacturing is an immense global industry. In 2003, worldwide pharmaceutical industry sales were at \$491.8 billion, an increase in sales volume of 9% over the preceding year with the US being the largest national market, accounting for 44% of global industry sales (cf. The Health Strategies Consultancy LLC (2005)). In 2011, the global pharmaceutical industry is expected to record growth of 5-7% on sales of approximately \$880 billion (Zacks Equity Research (2011)).

Although pharmaceutical supply chains have begun to be coupled with sophisticated technologies in order to improve both the quantity and the quality of their associated products (Yost (2005) and Breen and Crawford (2005)), despite all the advances in manufacturing, storage, and distribution methods, certain pharmaceutical drug companies are far from effectively satisfying market demands on a consistent basis. In fact, it has been argued that pharmaceutical drug supply chains are in urgent need of efficient optimization techniques in order to reduce costs and to increase productivity and responsiveness (Shah (2004) and Papageorgiou (2009)).

Product perishability is another critical issue in pharmaceutical / drug supply chains. In a 2003 survey, the estimated incurred cost due to the expiration of branded products in supermarkets and drug stores was over 500 million dollars (Grocery Manufacturers of America (2004) and Karaesmen, Scheller-Wolf, and Deniz (2011)). In 2007, in a warehouse belonging to the Health Department of Chicago, over one million dollars in drugs, vaccines, and other medical supplies were found spoiled, stolen, or unaccounted for (Mihalopoulos (2009)). In 2009, CVS pharmacies in California, as a result of a settlement of a lawsuit filed against the company, had to offer promotional coupons to customers who had identified expired drugs, including expired baby formula and children's medicines, in more than 42 percent of the stores surveyed the year before (WPRI (2009) and Business Wire (2009)). Other instances of medications sold more than a year past their expiration dates have occurred in other pharmacies across the US (WABC (2008)). According to the Harvard Medical School (2003), since a law was passed in the US in 1979, drug manufacturers are required to stamp an expiration date on their products. This is the date at which the manufacturer can still guarantee the full, that is, 100%, potency and safety of the drug, assuming, of course, that proper storage procedures have been followed. For example, certain medications, including insulin, must be stored under appropriate environmental conditions, and exposure to water, heat, humidity or other factors can adversely affect how certain drugs perform in the human body.

Ironically, whereas some drugs may be unsold and unused and / or past their expiration dates, the number of drugs that were reported in short supply in the US in the first half of 2011 has risen to 211 – close to an all-time record – with only 58 in short supply in 2004 (Emanuel (2011)). According to the Food and Drug Administration (FDA), hospitals have reported shortages of drugs used in a wide range of applications, ranging from cancer treatment to surgery, anesthesia, and intravenous feedings. The consequences of such shortages include the postponement of surgeries and treatments, and may also result in the use of less effective or costlier substitutes. According to the American Hospital Association, all US hospitals have experienced drug shortages, and 82% have reported delayed care for their patients as a consequence (Szabo (2011)).

While the real causes of such shortages are complex, most cases appear to be related to manufacturers' decisions to cease production in the presence of financial challenges. It is interesting to note that, among curative cancer drugs, only the older generic, yet, less expensive, ones, have experienced shortages. As noted by Shah (2004), pharmaceutical companies secure notable returns solely in the early lifetime of a successful drug, before competition takes place. This competition-free time-span, however, has been observed to be shortening, from 5 years to only 1-2 years. Hence, the low profit margins associated with such drugs may be forcing pharmaceutical companies to make a difficult decision: whether to lose money by continuing to produce a lifesaving product or to switch to a more profitable drug. Unfortunately, the FDA cannot force companies to continue to produce low-profit medicines even if millions of lives rely on them (Emanuel (2011) and Szabo (2011)). On the other hand, where competition has been lacking, shortages of some other lifesaving drugs have resulted in huge spikes in prices, ranging from a 100% to a 4,500% increase with an average of 650% (Schneider (2011)).

In addition to increasing generic competition, the lower reimbursements by government health programs have worsened the situation. For example, Merck & Co., Inc., the multinational pharmaceutical giant, in 2011, announced more than 13,000 layoffs, to be completed by 2015, so as to offset costs by lowering operational costs. With 35 to 40 percent of the layoffs being in the US, the pharmaceutical industry sector ranked first nationally in the number of job cuts in July 2011 (Wolf (2011) and Wall Street Journal (2011)). Adding to the economic pressures, pharmaceutical companies are expected to suffer a significant decrease in their revenues as a result of losing patent protection for ten of the best-selling drugs by the end of 2012 (De la Garza (2011)). For example, according to Zacks Equity Research (2011), several pharmaceutical products, including Lipitor and Plavix, that, presently, generate more than \$142 billion in sales, are expected, over the next five years, to be faced with

generic competition. In 2011, pharmaceutical products valued at more than \$30 billion are losing patent protection, with such products generating more than \$15 billion in sales in 2010.

Apart from the cost management pressures and challenges, the safety of imported / outsourced products is another major issue for pharmaceutical companies. In fact, the emergence of counterfeit products has resulted in major reforms in the relationships among various tiers in pharmaceutical supply chains (Dunehew (2005)). Maruchek et al (2011) noted that, while, in the past, product recalls were mainly related to local errors in design, manufacturing, or labeling, today, a single product safety issue may result in huge global consequences. Interestingly, more than 80% of the ingredients of drugs sold in the US are made overseas, mostly in remote facilities located in China and India that are rarely – if not ever – visited by government inspectors. Supply chains of generic drugs, which account for 75 percent of the prescription medicines sold in the US, are, typically, more susceptible to falsification with the supply chains of some of the over-the-counter products, such as vitamins or aspirins, also vulnerable to adulteration (Harris (2011)). Similarly, the amount of counterfeit drugs in the European pharmaceutical supply chains has considerably increased (Muller et al (2009)). Various aspects of outsourcing of vaccines and other products have been studied by Boulaksil (2009), Enyinda, Briggs, and Bachkar (2009), Nagurney, Yu, and Qiang (2011), and Liu and Nagurney (2011).

Another pressure faced by pharmaceutical firms is the environmental impact of their medical waste, which includes the perished excess medicine, and inappropriate disposal (cf. Mendoza (2008) and Nagurney and Masoumi (2012)). Jesson, Pocock, and Wilson (2005) discussed a method of reduction in prescribed medicine with the purpose of minimizing the medical wastage while achieving improved pharmaceutical care standards. See, also, Hernando et al (2006) and Schwab et al (2005) for health risk assessment methods associated with pharmaceutical products. For some of the trends and challenges associated with green supply chain management, in general, along with possible solutions, see Sheu and Talley (2011).

For industry reports on pharmaceutical supply chains, see IBM (2004) and The Health Strategies Consultancy LLC (2005) report for Kaiser.

In this paper, we develop a generalized network oligopoly model for pharmaceutical supply chain competition which takes into account product perishability, brand differentiation of the product, as well as discarding costs. Our generalized network-based framework captures competition among the firms in the various supply chain activities of manufacturing, storage,

and distribution. The firms are assumed to not only seek to maximize their own profits but also to minimize the discarding costs of waste throughout their respective supply chains.

We utilize a Cournot (1838) framework, in which the firms compete using their product flows as strategic variables, rather than a Bertrand framework, since recent empirical evidence (cf. Wiggins and Maness (2004)) concerning price competition supports Cournot competition in the pharmaceutical industry, where product differentiation in the form of brands and generic products is important. Deo and Corbett (2009) also used a Cournot formulation for the investigation of the influenza vaccine market in the US but did not consider the supply chain network aspects and focused on firms with identical manufacturing processes and with linear inverse demand functions.

The supply chain generalized network oligopoly model developed in this paper has the following novel features:

1. it handles the perishability of the pharmaceutical product through the introduction of arc multipliers;
2. it allows each firm to minimize the discarding cost of waste / perished medicine;
3. it captures product differentiation under oligopolistic competition, which can include both brands and generics.

We now provide a review of the relevant literature. Papageorgiou, Rotstein, and Shah (2001), Gatica, Papageorgiou, and Shah (2003), Amaro and Barbosa-Povoa (2008), Tsiakis and Papageorgiou (2008), and Sousa, Shah, and Papageorgiou (2008) applied mixed-integer linear programming techniques to solve various problems of planning, capacity allocation, and distribution of medication drugs. Papageorgiou (2009) and Yu et al (2010) surveyed the challenges and methodologies in the area of pharmaceutical supply chains. In addition, Goyal and Giri (2001) and Nahmias (2011) presented comprehensive surveys of perishable inventory management systems. Subramanian, Pekny, and Reklaitis (2001) developed an integrated optimization-simulation framework to resolve the uncertainties in the pipeline management problem. Niziolek (2008), in her thesis, applied simulation techniques to study various shipment strategies in medical drug supply networks. Recently, newly-applied technologies in the area of operations of pharmaceutical chains, including RFID-based frameworks, have been studied in the literature (see Yue, Wu, and Bai (2008) and Schapranow, Zeier, and Plattner (2011)). Rossetti, Handfield, and Dooley (2011) described the complexities of pharmaceutical supply chains based on interviews and text analysis, and provided insights into this industry and the challenges that it faces.

In particular, Blackburn and Scudder (2009), whose paper concentrated on food prod-

ucts, have emphasized that there is limited research on general supply chains for perishable products. With this paper, we hope to help to fill this void, but with a focus on pharmaceuticals, and we develop the most general competitive supply chain network model with relevant specific features to this industry. One can then parameterize the model to explore competition and pricing for specific pharmaceutical products.

We note that Nagurney (2010a) proposed a design approach for profit-maximizing firms under oligopolistic competition. Furthermore, Nagurney and Yu (2012) developed an oligopoly model for sustainable fashion supply chains. This paper, in contrast to the above two, takes into account the perishability of the product over various links of the supply chain network through the use of arc as well as path multipliers. Liu and Nagurney (2012) constructed a multiperiod supply chain network equilibrium model that captures both perishability of products as well as time delays associated with transportation through the appropriate changes in the underlying network topologies. However, that model did not incorporate arc multipliers and assumed that the product being produced was homogeneous (see also, e.g., Nagurney (1989)).

Nagurney and Aronson (1989), Nagurney, Masoumi, and Yu (2012), Nagurney and Masoumi (2012), and Nagurney and Nagurney (2011) have utilized arc multipliers to capture the perishability / waste of product flows in a network. However, in contrast to the latter three studies, in which a system-optimization approach with respect to a single firm / organization was developed, here, we introduce a network oligopoly model to capture the competition among supply chains of multiple pharmaceutical companies and also incorporate the branding aspect through product differentiation. In the pharmaceutical industry and, specifically, in the case of branded drugs, when choosing among similar products, consumers may be brand-sensitive, as a consequence of their perception of the product quality, the reputation of the firm, environmental issues, etc. Thus, in our model, the product of a given firm is assumed to be differentiated by brand from other similar drugs manufactured by competing firms. Moreover, in contrast to the separable operational cost functions utilized in the latter three studies, here we adopt non-separable total operational cost functions, which capture competition among the firms for resources used in their various supply chain network activities.

We emphasize that our proposed framework can also be applied – albeit after proper modifications – to other perishable products whenever competition exists among a finite number of firms providing differentiated brands. Examples of such applications include, but are not limited to, food products, cut flowers, and photographic films.

This paper is organized as follows. In Section 2, we develop the supply chain generalized network oligopoly model with perishability and brand differentiation and derive variational inequality formulations. We discuss special cases of the model and relate them to models that have appeared in the literature. Qualitative properties are also obtained. In Section 3, we present the computational algorithm, which we then apply to several numerical cases in Section 4. We summarize our results and present our conclusions in Section 5.

2. The Supply Chain Generalized Network Oligopoly Model for Pharmaceuticals

We consider I pharmaceutical firms, with a typical firm denoted by i . The firms compete noncooperatively, in an oligopolistic manner, and the consumers can differentiate among the products of the pharmaceutical firms through their individual product brands. The supply chain network activities include manufacturing, shipment, storage, and, ultimately, the distribution of the brand name drugs to the demand markets.

Our proposed supply chain network model can be applied to similar cases of oligopolistic competition in which a finite number of firms provide perishable products. However, proper minor modifications may have to be made in order to address differences in the supply chain network topologies in related industries.

Consider the supply chain network topology presented in Figure 1. Each pharmaceutical firm i ; $i = 1, \dots, I$, utilizes n_M^i manufacturing plants and n_D^i distribution / storage facilities, and the goal is to serve n_R demand markets consisting of pharmacies, retail stores, hospitals, and other medical centers.

L^i denotes the set of directed links corresponding to the sequence of activities associated with firm i . Also, $G = [N, L]$ denotes the graph composed of the set of nodes N , and the set of links L , where L contains all sets of L_i s: $L \equiv \cup_{i=1, \dots, I} L^i$.

In Figure 1, the first set of links connecting the top two tiers of nodes corresponds to the process of production of the drugs at each of the manufacturing units of firm i ; $i = 1, \dots, I$. Such facilities are denoted by $M_1^i, \dots, M_{n_M^i}^i$, respectively, for firm i . Note that we allow for multiple possible links connecting each top tier node i with its manufacturing facilities, $M_1^i, \dots, M_{n_M^i}^i$, in order to represent different possible manufacturing technologies that may be associated with a given facility. We emphasize that the manufacturing facilities may be located not only in different regions of the same country but also in different countries.

The next set of nodes represents the distribution centers, and, thus, the links connecting the manufacturing nodes to the distribution centers are shipment-type links. Such distribution nodes associated with firm i ; $i = 1, \dots, I$ are denoted by $D_{1,1}^i, \dots, D_{n_D^i,1}^i$ and represent the distribution centers that the produced drugs are shipped to, and stored at, before being delivered to the demand markets. There are alternative shipment links to denote different possible modes of transportation. In the shipment of pharmaceuticals that are perishable one may wish, for example, to ship by air, but at a higher cost.

The next set of links connecting nodes $D_{1,1}^i, \dots, D_{n_D^i,1}^i$ to $D_{1,2}^i, \dots, D_{n_D^i,2}^i$; $i = 1, \dots, I$ represents the process of storage. Since drugs may require different storage conditions /

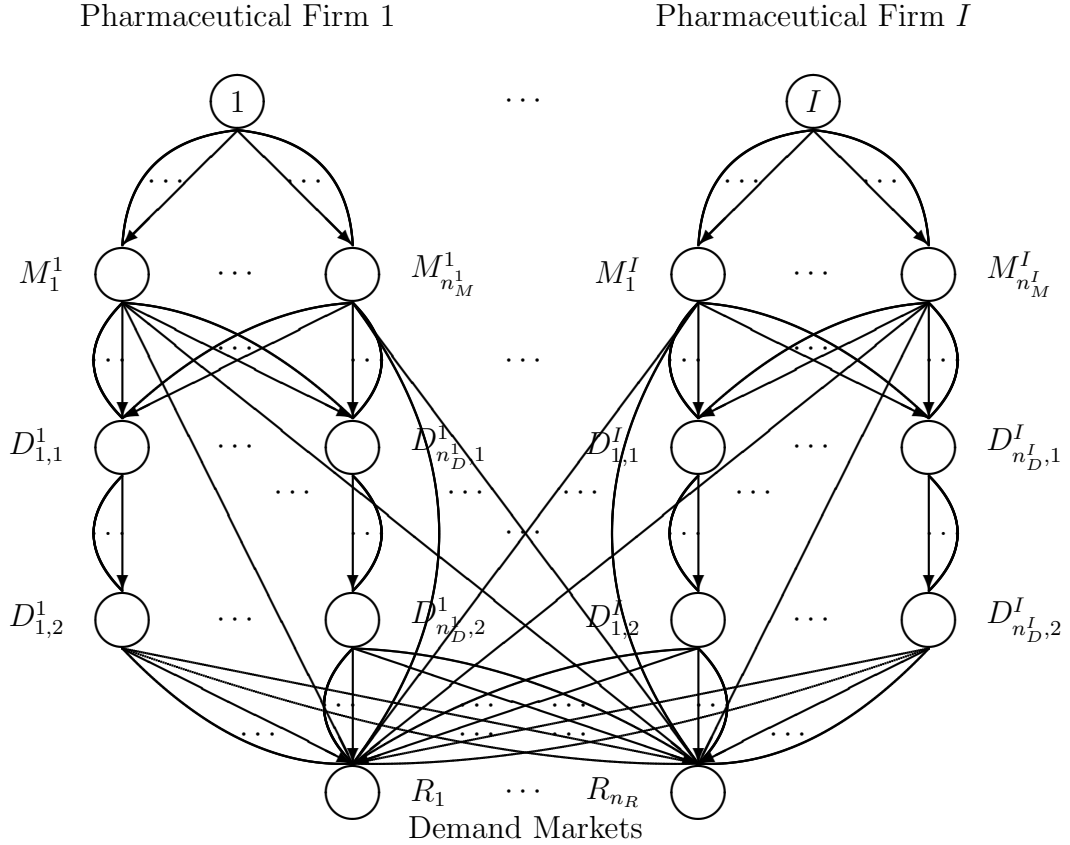


Figure 1: The Pharmaceutical Supply Chain Network Topology

technologies before being ultimately shipped to the demand markets, we represent these alternatives through multiple links at this tier.

The last set of links connecting the two bottom tiers of the supply chain network corresponds to distribution links over which the stored products are shipped from the distribution / storage facilities to the demand markets. Here we also allow for multiple modes of shipment / transportation.

In addition, in the supply chain network topology in Figure 1, there are direct links connecting manufacturing units with various demand markets in order to capture the possibility of direct mail shipments from manufacturers and the costs should be adjusted (see below) accordingly. While representing a small percentage of the total filled prescriptions (about 6.1 percent in 2004), mail-order pharmacy sales remained the fastest-growing sector of the US prescription drug retail market in 2004, increasing by 18 percent over the preceding year (The Health Strategies Consultancy LLC (2005)).

In our model, we take into account the perishability of the pharmaceuticals. Although

pharmaceutical products may have different life-times, we can assign a multiplier to each activity / link of the supply chain to represent the fraction of the product that may perish / be wasted / be lost over the course of that activity. The fraction of lost product depends on the type of the activity since various processes of manufacturing, shipment, storage, and distribution may result in dissimilar amounts of losses. In addition, this fraction need not be the same among various links of the same tier in the supply chain network since different firms and even different units of the same firm may experience non-identical amounts of waste, depending on the brand of drug, the efficiency of the utilized technology, and the experience of the staff, etc. Also, such multipliers can capture pilferage / theft, a significant issue in drug supply chains.

We, as in Nagurney, Masoumi, and Yu (2012), associate with every link a in the supply chain network, a multiplier α_a , which lies in the range of $(0,1]$. The parameter α_a may be interpreted as a throughput factor corresponding to link a meaning that $\alpha_a \times 100\%$ of the initial flow of product on link a reaches the successor node of that link.

Let f_a denote the (initial) flow of product on link a with f'_a denoting the final flow on link a ; i.e., the flow that reaches the successor node of the link after wastage has taken place. Therefore, we have:

$$f'_a = \alpha_a f_a, \quad \forall a \in L. \quad (1)$$

Consequently, the waste / loss on link a is the difference between the initial and the final flow, $f_a - f'_a$, where

$$f_a - f'_a = (1 - \alpha_a) f_a, \quad \forall a \in L. \quad (2)$$

Associated with this waste is a discarding total cost function, \hat{z}_a , which, in view of (2), is a function of flow on the link, f_a , that is

$$\hat{z}_a = \hat{z}_a(f_a), \quad \forall a \in L, \quad (3)$$

and which is assumed to be convex and continuously differentiable:

Let x_p represent the (initial) flow of product on path p joining an origin node, i , with a destination node, R_k . The path flows must be nonnegative, that is,

$$x_p \geq 0, \quad \forall p \in P_k^i; i = 1, \dots, I; k = 1, \dots, n_R, \quad (4)$$

where P_k^i is the set of all paths joining the origin node i ; $i = 1, \dots, I$ with destination node R_k .

Also, μ_p denotes the multiplier corresponding to the throughput on path p , defined as the product of all link multipliers on links comprising that path, that is,

$$\mu_p \equiv \prod_{a \in p} \alpha_a, \quad \forall p \in P_k^i; i = 1, \dots, I; k = 1, \dots, n_R. \quad (5)$$

Moreover, we define the multiplier, α_{ap} , which is the product of the multipliers of the links on path p that precede link a in that path, as follows:

$$\alpha_{ap} \equiv \begin{cases} \delta_{ap} \prod_{a' < a} \alpha_{a'}, & \text{if } \{a' < a\} \neq \emptyset, \\ \delta_{ap}, & \text{if } \{a' < a\} = \emptyset, \end{cases} \quad (6)$$

where $\{a' < a\}$ denotes the set of the links preceding link a in path p , and \emptyset denotes the null set. In addition, δ_{ap} is defined as equal to 1 if link a is contained in path p , and 0, otherwise. As a result, α_{ap} is equal to the product of all link multipliers preceding link a in path p . If link a is not contained in path p , then α_{ap} is set to zero. If a belongs to the first set of links; i.e., the manufacturing links, this multiplier is equal to 1. Hence, the relationship between the link flow, f_a , and the path flows can be expressed as:

$$f_a = \sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} x_p \alpha_{ap}, \quad \forall a \in L. \quad (7)$$

Note that the arc multipliers may be obtained from historical and statistical data. They may also, in the case of certain perishable products, be related to an exponential time decay function where the time, in our framework, is associated with each specific link activity (see, for instance, Blackburn and Scudder (2009) and Bai and Kendall (2009)). For example, Nagurney and Nagurney (2011) constructed explicit arc multipliers for molybdenum, which is used in nuclear medicine, which were based on the physics of time decay for this pharmaceutical product used in cancer and cardiac diagnostics, among other procedures.

Let d_{ik} denote the demand for pharmaceutical firm i 's brand drug; $i = 1, \dots, I$, at demand market R_k ; $k = 1, \dots, n_R$. The consumers differentiate the products by their brands.

The following equation reveals the relationship between the path flows and the demands in the supply chain network:

$$\sum_{p \in P_k^i} x_p \mu_p = d_{ik}, \quad i = 1, \dots, I; k = 1, \dots, n_R, \quad (8)$$

that is, the demand for a brand drug at the demand market R_k is equal to the sum of all the final flows – subject to perishability – on paths joining (i, R_k) . We group the demands d_{ik} ;

$i = 1, \dots, I; k = 1, \dots, n_R$ into the $n_R \times I$ -dimensional vector d . Note that, in this model the demands are variables – we, subsequently, show how the fixed demand case is a special case of this model.

A demand price function is associated with each firm's pharmaceutical at each demand market. We denote the demand price of firm i 's product at demand market R_k by ρ_{ik} and assume that

$$\rho_{ik} = \rho_{ik}(d), \quad i = 1, \dots, I; k = 1, \dots, n_R. \quad (9)$$

Note that the price of firm i 's product at a particular demand market may depend not only on the demands for its product at the other demand markets, but also on the demands for the other substitutable drugs at all the demand markets. These demand price functions are assumed to be continuous, continuously differentiable, and monotone decreasing.

The total operational cost on link a may, in general, depend upon the product flows on all the links, that is,

$$\hat{c}_a = \hat{c}_a(f), \quad \forall a \in L, \quad (10)$$

where f is the vector of all the link flows. Such total cost expressions address the competition among various firms for resources used in the manufacturing, storage, and distribution of the pharmaceutical products. The total cost on each link is assumed to be convex and continuously differentiable.

X_i denotes the vector of path flows associated with firm i ; $i = 1, \dots, I$, where $X_i \equiv \{\{x_p\} | p \in P^i\} \in R_+^{n_{P^i}}$, and $P^i \equiv \cup_{k=1, \dots, n_R} P_k^i$. In turn, n_{P^i} , denotes the number of paths from firm i to the demand markets. Thus, X is the vector of all the firm' strategies, that is, $X \equiv \{\{X_i\} | i = 1, \dots, I\}$.

The profit function of a pharmaceutical firm is defined as the difference between its revenue and its total costs, where the revenue is equal to the summation of the price times the terminal flows at each demand market. The total costs are composed of the total operational costs as well as the total discarding costs of waste over all the links in the supply chain network under control by each firm. Hence, the profit function of firm i , denoted by U_i , is expressed as:

$$U_i = \sum_{k=1}^{n_R} \rho_{ik}(d) d_{ik} - \sum_{a \in L^i} \hat{c}_a(f) - \sum_{a \in L^i} \hat{z}_a(f_a). \quad (11)$$

In lieu of the conservation of flow expressions (7) and (8), and the functional expressions (3), (9), and (10), we may define $\hat{U}_i(X) = U_i$ for all firms i ; $i = 1, \dots, I$, with the I -

dimensional vector \hat{U} being the vector of the profits of all the firms:

$$\hat{U} = \hat{U}(X). \quad (12)$$

In the Cournot-Nash oligopolistic market framework, each firm selects its product path flows in a noncooperative manner, seeking to maximize its own profit, until an equilibrium is achieved, according to the definition below.

Definition 1: Supply Chain Generalized Network Cournot-Nash Equilibrium

A path flow pattern $X^* \in K = \prod_{i=1}^I K_i$ constitutes a supply chain generalized network Cournot-Nash equilibrium if for each firm $i; i = 1, \dots, I$:

$$\hat{U}_i(X_i^*, \hat{X}_i^*) \geq \hat{U}_i(X_i, \hat{X}_i^*), \quad \forall X_i \in K_i, \quad (13)$$

where $\hat{X}_i^* \equiv (X_1^*, \dots, X_{i-1}^*, X_{i+1}^*, \dots, X_I^*)$ and $K_i \equiv \{X_i | X_i \in R_+^{n_{Pi}}\}$.

In other words, an equilibrium is established if no firm can unilaterally improve its profit by changing its production path flows, given the production path flow decisions of the other firms.

Next, we derive the variational inequality formulations of the Cournot-Nash equilibrium for the pharmaceutical supply chain network under oligopolistic competition satisfying Definition 1, in terms of both path flows and link flows (see Cournot (1838), Nash (1950, 1951), Gabay and Moulin (1980), and Nagurney (2006)).

Theorem 1

Assume that, for each pharmaceutical firm $i; i = 1, \dots, I$, the profit function $\hat{U}_i(X)$ is concave with respect to the variables in X_i , and is continuously differentiable. Then $X^* \in K$ is a supply chain generalized network Cournot-Nash equilibrium according to Definition 1 if and only if it satisfies the variational inequality:

$$-\sum_{i=1}^I \langle \nabla_{X_i} \hat{U}_i(X^*)^T, X_i - X_i^* \rangle \geq 0, \quad \forall X \in K, \quad (14)$$

where $\langle \cdot, \cdot \rangle$ denotes the inner product in the corresponding Euclidean space and $\nabla_{X_i} \hat{U}_i(X)$ denotes the gradient of $\hat{U}_i(X)$ with respect to X_i . Variational inequality (14), in turn, for our model, is equivalent to the variational inequality: determine the vector of equilibrium path flows and the vector of equilibrium demands $(x^*, d^*) \in K^1$ such that:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} \right] \times [x_p - x_p^*]$$

$$+ \sum_{i=1}^I \sum_{k=1}^{n_R} \left[-\rho_{ik}(d^*) - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d^*)}{\partial d_{ik}} d_{il}^* \right] \times [d_{ik} - d_{ik}^*] \geq 0, \quad \forall (x, d) \in K^1, \quad (15)$$

where $K^1 \equiv \{(x, d) | x \in R_+^{n_P} \text{ and (8) holds}\}$, and, for notational convenience, we denote:

$$\frac{\partial \hat{C}_p(x)}{\partial x_p} \equiv \sum_{b \in L^i} \sum_{a \in L^i} \frac{\partial \hat{c}_b(f)}{\partial f_a} \alpha_{ap} \text{ and } \frac{\partial \hat{Z}_p(x)}{\partial x_p} \equiv \sum_{a \in L^i} \frac{\partial \hat{z}_a(f_a)}{\partial f_a} \alpha_{ap}. \quad (16)$$

Variational inequality (15) can also be re-expressed in terms of link flows as: determine the vector of equilibrium link flows and the vector of equilibrium demands $(f^*, d^*) \in K^2$, such that:

$$\begin{aligned} & \sum_{i=1}^I \sum_{a \in L^i} \left[\sum_{b \in L^i} \frac{\partial \hat{c}_b(f^*)}{\partial f_a} + \frac{\partial \hat{z}_a(f_a^*)}{\partial f_a} \right] \times [f_a - f_a^*] \\ & + \sum_{i=1}^I \sum_{k=1}^{n_R} \left[-\rho_{ik}(d^*) - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d^*)}{\partial d_{ik}} d_{il}^* \right] \times [d_{ik} - d_{ik}^*] \geq 0, \quad \forall (f, d) \in K^2, \end{aligned} \quad (17)$$

where $K^2 \equiv \{(f, d) | x \geq 0, \text{ and (7) and (8) hold}\}$.

Proof: Variational inequality (14) follows directly from Gabay and Moulin (1980). See also Dafermos and Nagurney (1987). Note that:

$$\nabla_{X_i} \hat{U}_i(X) = \left[\frac{\partial \hat{U}_i}{\partial x_p}; p \in P_k^i; k = 1, \dots, n_R \right]. \quad (18)$$

For each path p ; $p \in P_k^i$, we have:

$$\begin{aligned} \frac{\partial \hat{U}_i}{\partial x_p} &= \frac{\partial [\sum_{l=1}^{n_R} \rho_{il}(d) d_{il} - \sum_{b \in L^i} \hat{c}_b(f) - \sum_{b \in L^i} \hat{z}_b(f_b)]}{\partial x_p} \\ &= \sum_{l=1}^{n_R} \frac{\partial [\rho_{il}(d) d_{il}]}{\partial x_p} - \frac{\partial [\sum_{b \in L^i} \hat{c}_b(f)]}{\partial x_p} - \frac{\partial [\sum_{b \in L^i} \hat{z}_b(f_b)]}{\partial x_p} \\ &= \rho_{ik}(d) \mu_p + \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d)}{\partial d_{ik}} \frac{\partial d_{il}}{\partial x_p} - \sum_{a \in L^i} \frac{\partial [\sum_{b \in L^i} \hat{c}_b(f)]}{\partial f_a} \frac{\partial f_a}{\partial x_p} - \sum_{a \in L^i} \frac{\partial [\sum_{b \in L^i} \hat{z}_b(f_b)]}{\partial f_a} \frac{\partial f_a}{\partial x_p} \\ &= \rho_{ik}(d) \mu_p + \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d)}{\partial d_{ik}} \mu_p d_{il} - \sum_{a \in L^i} \sum_{b \in L^i} \frac{\partial \hat{c}_b(f)}{\partial f_a} \alpha_{ap} - \sum_{a \in L^i} \frac{\partial \hat{z}_a(f_a)}{\partial f_a} \alpha_{ap}. \end{aligned} \quad (19)$$

Multiplying the expression in (19) by a minus sign and by the term $(x_p - x_p^*)$, and summing up over all paths p and making use of the definition of the feasible set K^1 , with notice to constraint (8), and recalling the definitions of $\frac{\partial \hat{C}_p(x)}{\partial x_p}$ and $\frac{\partial \hat{Z}_p(x)}{\partial x_p}$ in (16) – the equivalence of

which is established in Nagurney, Masoumi, and Yu (2012) – after algebraic simplification, yields variational inequality (15). By using then equation (7), variational inequality (17) follows from (15). \square

Variational inequalities (15) and (17) can be put into standard form (see Nagurney (1999)): determine $X^* \in \mathcal{K}$ such that:

$$\langle F(X^*)^T, X - X^* \rangle \geq 0, \quad \forall X \in \mathcal{K}, \quad (20)$$

where $\langle \cdot, \cdot \rangle$ denotes the inner product in n -dimensional Euclidean space. Let $X \equiv (x, d)$ and $F(X) \equiv (F_1(X), F_2(X))$, where

$$\begin{aligned} F_1(X) &= \left[\frac{\partial \hat{C}_p(x)}{\partial x_p} + \frac{\partial \hat{Z}_p(x)}{\partial x_p}; p \in P_k^i; i = 1, \dots, I; k = 1, \dots, n_R \right], \\ F_2(X) &= \left[-\rho_{ik}(d) - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d)}{\partial d_{ik}} d_{il}; i = 1, \dots, I; k = 1, \dots, n_R \right], \end{aligned} \quad (21)$$

and let $\mathcal{K} \equiv K^1$, then (15) can be re-expressed as (20). Similarly, for the variational inequality in terms of link flows, if we define the column vectors: $X \equiv (f, d)$ and $F(X) \equiv (F_3(X), F_2(X))$, where

$$F_3(X) = \left[\sum_{b \in L^i} \frac{\partial \hat{c}_b(f)}{\partial f_a} + \frac{\partial \hat{z}_a(f_a)}{\partial f_a}; a \in L^i; i = 1, \dots, I \right], \quad (22)$$

and let $\mathcal{K} \equiv K^2$, then (17) can be re-written as (20).

Since the feasible set K^1 is not compact, and the same holds for K^2 , we cannot obtain the existence of a solution simply based on the assumption of the continuity of F . However, the demand d_{ik} for each firm i 's pharmaceutical; $i = 1, \dots, I$ at every demand market R_k ; $k = 1, \dots, n_R$, may be assumed to be bounded, since the population requiring these products is finite (although it may be large). Therefore, we have that:

$$\mathcal{K}_b \equiv \{(x, d) | x \in R_+^{n_P}, 0 \leq d \leq b, \text{ and (8) holds}\}, \quad (23)$$

where $b > 0$ and $d \leq b$ means that $d_{ik} \leq b$; $i = 1, \dots, I$; $k = 1, \dots, n_R$. Then \mathcal{K}_b is a bounded, closed, and convex subset of K^1 . Thus, the following variational inequality

$$\langle F(X^b)^T, X - X^b \rangle \geq 0, \quad \forall X \in \mathcal{K}_b, \quad (24)$$

admits at least one solution $X^b \in \mathcal{K}_b$, since \mathcal{K}_b is compact and F is continuous. Therefore, following Kinderlehrer and Stampacchia (1980) (see also Theorem 1.5 in Nagurney (1999)), we have the following theorem:

Theorem 2: Existence

There exists at least one solution to variational inequality (15) (equivalently, to (17)), since there exists a $b > 0$, such that variational inequality (24) admits a solution in \mathcal{K}_b with

$$d^b \leq b, x^b \in R_+^{n_P}, \text{ and (8) holds.} \quad (25)$$

In addition, we now provide a uniqueness result.

Theorem 3: Uniqueness

With Theorem 2, variational inequality (24) and, hence, variational inequality (17) admits at least one solution. Moreover, if the function $F(X)$ of variational inequality (17), as defined in (22), is strictly monotone on $\mathcal{K} \equiv K^2$, that is,

$$\langle (F(X^1) - F(X^2))^T, X^1 - X^2 \rangle > 0, \quad \forall X^1, X^2 \in \mathcal{K}, X^1 \neq X^2, \quad (26)$$

then the solution to variational inequality (17) is unique, that is, the equilibrium link flow pattern and the equilibrium demand pattern are unique.

The above model is now related to several models in the literature. First, we note that, if the arc multipliers are all equal to 1, in which case the product is not perishable, then the model is related to the sustainable fashion supply chain network model of Nagurney and Yu (2012). In that model, however, the other criterion, in addition to the profit maximization one, was emission minimization, rather than waste cost minimization, as in the model in this paper.

If the product is homogeneous, and all the arc multipliers are, again, assumed to be equal to 1, and the total costs are assumed to be separable, then the above model collapses to the supply chain network oligopoly model of Nagurney (2010b) in which synergies associated with mergers and acquisitions were assessed.

In addition, if there is only a single organization / firm, in which case there is no product differentiation, and the demands are subject to uncertainty, with the inclusion of expected costs due to shortages or excess supplies, the total operational cost functions are separable, and a criterion of risk is added, then the model above is related to the blood supply chain network operations management model of Nagurney, Masoumi, and Yu (2012).

We now present a simple numerical example in order to illustrate the model.

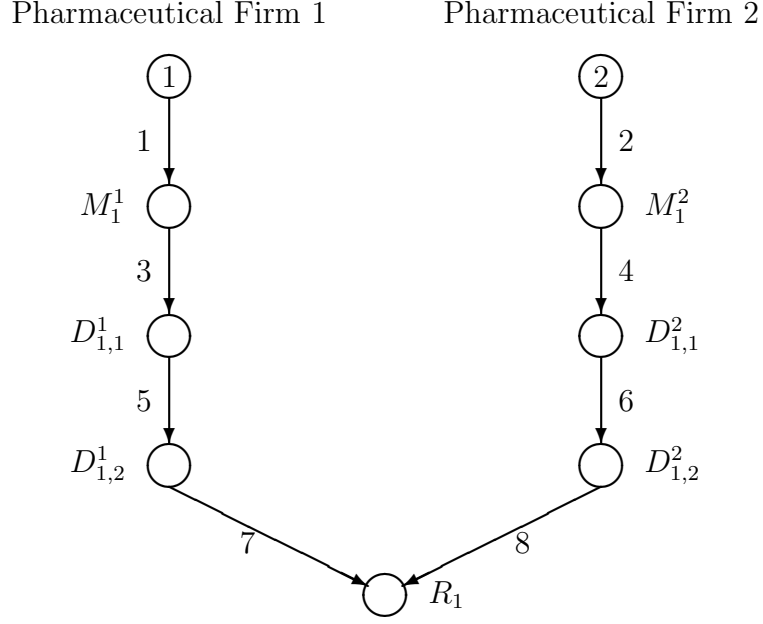


Figure 2: Supply Chain Network Topology for the Pharmaceutical Duopoly in the Illustrative Example

Illustrative Example

In this example, two pharmaceutical firms compete in a duopoly with a single demand market (See Figure 2). The two firms produce differentiated, but substitutable, brand drugs 1 and 2, corresponding to Firm 1 and Firm 2, respectively.

The total cost functions on the various links of manufacturing, shipment, storage, and distribution are:

$$\hat{c}_1(f_1) = 5f_1^2 + 8f_1, \quad \hat{c}_2(f_2) = 7f_2^2 + 3f_2, \quad \hat{c}_3(f_3) = 2f_3^2 + f_3, \quad \hat{c}_4(f_4) = 2f_4^2 + 2f_4,$$

$$\hat{c}_5(f_5) = 3f_5^2 + 4f_5, \quad \hat{c}_6(f_6) = 3.5f_6^2 + f_6, \quad \hat{c}_7(f_7) = 2f_7^2 + 5f_7, \quad \hat{c}_8(f_8) = 1.5f_8^2 + 4f_8.$$

The arc multipliers are given by:

$$\alpha_1 = .95, \quad \alpha_2 = .98, \quad \alpha_3 = .99, \quad \alpha_4 = 1.00, \quad \alpha_5 = .99, \quad \alpha_6 = .97, \quad \alpha_7 = 1.00, \quad \alpha_8 = 1.00.$$

The total discarding cost functions on the links are assumed identical, that is,

$$\hat{z}_a(f_a) = .5f_a^2, \quad \forall a.$$

The firms compete in the demand market R_1 , and the consumers reveal their preferences for the two products through the following nonseparable demand price functions:

$$\rho_{11}(d) = -3d_{11} - d_{21} + 200, \quad \rho_{21}(d) = -4d_{21} - 1.5d_{11} + 300.$$

In this supply chain network, there exists one path corresponding to each firm, denoted by p_1 and p_2 . Thus, variational inequality (15) can, in the case of this example, since $d_{11}^* = x_{p_1}^*$ and $d_{21}^* = x_{p_2}^*$, and $d_{11} = x_{p_1}$ and $d_{21} = x_{p_2}$, be re-expressed as:

$$\begin{aligned} & \left[\frac{\partial \hat{C}_{p_1}(x^*)}{\partial x_{p_1}} + \frac{\partial \hat{Z}_{p_1}(x^*)}{\partial x_{p_1}} - \rho_{11}(d^*)\mu_{p_1} - \frac{\partial \rho_{11}(d^*)}{\partial d_{11}}\mu_{p_1} \times d_{11}^* \right] \times [x_{p_1} - x_{p_1}^*] \\ & + \left[\frac{\partial \hat{C}_{p_2}(x^*)}{\partial x_{p_2}} + \frac{\partial \hat{Z}_{p_2}(x^*)}{\partial x_{p_2}} - \rho_{21}(d^*)\mu_{p_2} - \frac{\partial \rho_{21}(d^*)}{\partial d_{21}}\mu_{p_2} \times d_{21}^* \right] \times [x_{p_2} - x_{p_2}^*] \geq 0, \quad \forall x \in R_+^2. \end{aligned} \quad (27)$$

Under the assumption that $x_{p_1}^* > 0$ and $x_{p_2}^* > 0$, the two expressions on the left-hand side of inequality (27) must be equal to zero, that is:

$$\left[\frac{\partial \hat{C}_{p_1}(x^*)}{\partial x_{p_1}} + \frac{\partial \hat{Z}_{p_1}(x^*)}{\partial x_{p_1}} - \rho_{11}(d^*)\mu_{p_1} - \frac{\partial \rho_{11}(d^*)}{\partial d_{11}}\mu_{p_1} \times d_{11}^* \right] \times [x_{p_1} - x_{p_1}^*] = 0, \quad (28a)$$

and

$$\left[\frac{\partial \hat{C}_{p_2}(x^*)}{\partial x_{p_2}} + \frac{\partial \hat{Z}_{p_2}(x^*)}{\partial x_{p_2}} - \rho_{21}(d^*)\mu_{p_2} - \frac{\partial \rho_{21}(d^*)}{\partial d_{21}}\mu_{p_2} \times d_{21}^* \right] \times [x_{p_2} - x_{p_2}^*] = 0. \quad (28b)$$

Since each of the paths flows must be nonnegative, we know that the term preceding the multiplication sign in both (28a) and (28b) must be equal to zero.

Calculating the values of the multipliers from (6), and then, substituting those values, as well as, the given functions into (16), we can determine the partial derivatives of the total operational cost and the total discarding cost functions in (28a) and (28b). Furthermore, the partial derivatives of the given demand price functions can be calculated and substituted into the above. Applying (5), the path multipliers are equal to:

$$\mu_{p_1} = \alpha_1 \times \alpha_3 \times \alpha_5 \times \alpha_7 = .95 \times .99 \times .99 \times 1 = .93,$$

$$\mu_{p_2} = \alpha_2 \times \alpha_4 \times \alpha_6 \times \alpha_8 = .98 \times 1 \times .97 \times 1 = .95.$$

Simple arithmetic calculations, with the above substitutions, yield the below system of equations:

$$\begin{cases} 31.24x_{p_1}^* + 0.89x_{p_2}^* = 168.85, \\ 1.33x_{p_1}^* + 38.33x_{p_2}^* = 274.46. \end{cases} \quad (29)$$

Thus, the equilibrium solution corresponding to the path flow of brand drugs produced by firms 1 and 2 is:

$$x_{p_1}^* = 5.21, \quad x_{p_2}^* = 6.98.$$

Using (7), the equilibrium link flows can be calculated as:

$$\begin{aligned} f_1^* &= 5.21, & f_3^* &= 4.95, & f_5^* &= 4.90, & f_7^* &= 4.85, \\ f_2^* &= 6.98, & f_4^* &= 6.84, & f_6^* &= 6.84, & f_8^* &= 6.64. \end{aligned}$$

From (8), the equilibrium values of demand for products of the two pharmaceutical firms are equal to:

$$d_{11}^* = 4.85, \quad d_{21}^* = 6.64.$$

Finally, the equilibrium prices of the two branded drugs are:

$$\rho_{11} = 178.82, \quad \rho_{21} = 266.19.$$

Note that, even though the price of Firm 2's product is observed to be higher, the market has a slightly stronger tendency toward this product as opposed to the product of Firm 1. This is due to the willingness of the consumers to spend more on one product which can be a consequence of the reputation, or the perceived quality, of Firm 2's brand drug.

Next, we discuss a special case of our model in which the pharmaceutical firms produce a homogeneous drug.

Corollary 1

Assume that the pharmaceutical firms produce a homogeneous drug. We may then denote the demand for the homogeneous drug and its demand price at demand market R_k , respectively, by d_k and ρ_k , instead of by d_{ik} and ρ_{ik} . Consequently, the following equation, which replaces (8), must then hold:

$$\sum_{i=1}^I \sum_{p \in P_k^i} x_p \mu_p = d_k, \quad k = 1, \dots, n_R. \quad (30)$$

Then, the profit function (11) can be rewritten as:

$$U_i = \sum_{k=1}^{n_R} \rho_k(d) \sum_{p \in P_k^i} \mu_p x_p - \sum_{a \in L^i} \hat{c}_a(f) - \sum_{a \in L^i} \hat{z}_a(f_a). \quad (31)$$

The corresponding variational inequality (15) in terms of path flows can be rewritten as: determine $(x^, d^*) \in K^3$ such that:*

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} - \sum_{l=1}^{n_R} \frac{\partial \rho_l(d^*)}{\partial d_k} \mu_p \sum_{p \in P_l^i} \mu_p x_p^* \right] \times [x_p - x_p^*]$$

$$+ \sum_{k=1}^{n_R} [-\rho_k(d^*)] \times [d_k - d_k^*] \geq 0, \quad \forall (x, d) \in K^3, \quad (32)$$

where $K^3 \equiv \{(x, d) | x \in R_+^{n_P} \text{ and (30) holds}\}$.

Proof: According to the proof of Theorem 1, variational inequality (32) can be proved by replacing d_{ik} and ρ_{ik} in (19), respectively, by d_k and ρ_k . \square

It is interesting to note that our supply chain generalized network oligopoly model can also capture the competition in the pharmaceutical industry even when the demands d_{ik} are fixed, for all brands i ; $i = 1, \dots, I$, and all demand markets R_k ; $k = 1, \dots, n_R$, since we consider total cost functions of the form in (10). Fixed demands for pharmaceutical products arise, for example, in the case of certain hospital and medical procedures, which need to be scheduled in advance. For example, the supply chain for medical nuclear products, as discussed in Nagurney and Nagurney (2011), is characterized by fixed demands since medical procedures that use such radioisotopes, such as, for example, molybdenum, need to be scheduled a priori; moreover, radioisotopes, since they are subject to radioactive decay are not only perishable but also time-sensitive.

Corollary 2

Assume that the demand d_{ik} for firm i 's pharmaceutical; $i = 1, \dots, I$, at demand market R_k ; $k = 1, \dots, n_R$, is fixed. According to the demand price function (9), the demand price of firm i 's product at demand market R_k will then also be fixed; we denote this price by $\bar{\rho}_{ik}$. The profit function (11) can then be rewritten as:

$$U_i = \sum_{k=1}^{n_R} \bar{\rho}_{ik} d_{ik} - \sum_{a \in L^i} \hat{c}_a(f) - \sum_{a \in L^i} \hat{z}_a(f_a), \quad (33)$$

where the revenue of firm i , $\sum_{k=1}^{n_R} \bar{\rho}_{ik} d_{ik}$, is fixed. Therefore, the corresponding variational inequality (15) in terms of path flows simplifies, in this case, to: determine $x^* \in K^4$ such that:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} \right] \times [x_p - x_p^*] \geq 0, \quad \forall x \in K^4, \quad (34)$$

where $K^4 \equiv \{x | x \geq 0, \text{ and (8) is satisfied with the } d_{ik} \text{ known and fixed, } \forall i, k.\}$

Similarly, variational inequality (34) can be re-expressed in terms of link flows as: determine $f^* \in K^5$, such that:

$$\sum_{i=1}^I \sum_{a \in L^i} \left[\sum_{b \in L^i} \frac{\partial \hat{c}_b(f^*)}{\partial f_a} + \frac{\partial \hat{z}_a(f_a^*)}{\partial f_a} \right] \times [f_a - f_a^*] \geq 0, \quad \forall f \in K^5, \quad (35)$$

where $K^5 \equiv \{f | \exists x \geq 0, \text{ and (7) and (8) are satisfied with the } d_{ik} \text{ s known and fixed, } \forall i, k.\}$.

Proof: Based on the proof of Theorem 1, variational inequality (34) can be proved by eliminating the corresponding term of firm i 's revenue in (19), since the revenue of firm i , $\sum_{k=1}^{n_R} \bar{\rho}_{ik} d_{ik}$, is fixed. Also, using equation (7), variational inequality (35) follows from (34). \square

We further discuss the specific case in which the pharmaceutical companies produce a homogeneous drug and the demand at each demand market is fixed.

Corollary 3

Assume that the pharmaceutical firms produce a homogeneous drug. We may then denote the demand for the homogeneous drug and its demand price at demand market R_k , respectively, by d_k and $\bar{\rho}_k$, instead of by d_{ik} and ρ_{ik} . Consequently, the following equation, which replaces (8), must then hold:

$$\sum_{i=1}^I \sum_{p \in P_k^i} x_p \mu_p = d_k, \quad k = 1, \dots, n_R. \quad (36)$$

Assume also that the demand d_k at demand market R_k ; $k = 1, \dots, n_R$ is fixed, as well as the demand price $\bar{\rho}_k$. Then, the profit function (11) can be rewritten as:

$$U_i = \sum_{k=1}^{n_R} \bar{\rho}_k \sum_{p \in P_k^i} \mu_p x_p - \sum_{a \in L^i} \hat{c}_a(f) - \sum_{a \in L^i} \hat{z}_a(f_a). \quad (37)$$

The corresponding variational inequality in terms of path flows, akin to (34), is: determine $x^* \in K^6$ such that:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} \right] \times [x_p - x_p^*] \geq 0, \quad \forall x \in K^6, \quad (38)$$

where $K^6 \equiv \{x | x \geq 0, \text{ and (36) is satisfied with the } d_k \text{ s known and fixed, } \forall k.\}$.

Similarly, the corresponding variational inequality in terms of link flows, akin to (35), is: determine $f^* \in K^7$, such that:

$$\sum_{i=1}^I \sum_{a \in L^i} \left[\sum_{b \in L^i} \frac{\partial \hat{c}_b(f^*)}{\partial f_a} + \frac{\partial \hat{z}_a(f_a^*)}{\partial f_a} \right] \times [f_a - f_a^*] \geq 0, \quad \forall f \in K^7, \quad (39)$$

where $K^7 \equiv \{f | \exists x \geq 0, \text{ and (7) and (36) are satisfied with the } d_k \text{ s known and fixed, } \forall k.\}$.

Proof: Following the proof of Theorem 1, we have:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} - \bar{\rho}_k \mu_p \right] \times [x_p - x_p^*] \geq 0, \forall x \in K^6, \quad (40)$$

which is equivalent to:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} \right] \times [x_p - x_p^*] - \sum_{k=1}^{n_R} \bar{\rho}_k \left[\sum_{i=1}^I \sum_{p \in P_k^i} \mu_p x_p - \sum_{i=1}^I \sum_{p \in P_k^i} \mu_p x_p^* \right] \geq 0, \quad (41)$$

$$\forall x \in K^6.$$

Applying now equation (36) to (41), yields variational inequality (38). Also, using equation (7), variational inequality (39) then follows from (38). \square

3. The Algorithm

We now recall the Euler method, which is induced by the general iterative scheme of Dupuis and Nagurney (1993). Specifically, iteration τ of the Euler method (see also Nagurney and Zhang (1996)) is given by:

$$X^{\tau+1} = P_{\mathcal{K}}(X^{\tau} - a_{\tau} F(X^{\tau})), \quad (42)$$

where $P_{\mathcal{K}}$ is the projection on the feasible set \mathcal{K} and F is the function that enters the variational inequality problem (20).

As shown in Dupuis and Nagurney (1993) and Nagurney and Zhang (1996), for convergence of the general iterative scheme, which induces the Euler method, the sequence $\{a_{\tau}\}$ must satisfy: $\sum_{\tau=0}^{\infty} a_{\tau} = \infty$, $a_{\tau} > 0$, $a_{\tau} \rightarrow 0$, as $\tau \rightarrow \infty$. Specific conditions for convergence of this scheme as well as various applications to the solutions of network oligopolies can be found in Nagurney and Zhang (1996), Nagurney, Dupuis, and Zhang (1994), Nagurney (2010a), and Nagurney and Yu (2012).

In order to obtain explicit formulae at each iteration of the Euler method for the solution of variational inequality (15), we first note that variational inequality (15) can, through the use of (8), be re-expressed in terms of path flows, that is: determine $x^* \in K^8$ such that:

$$\sum_{i=1}^I \sum_{k=1}^{n_R} \sum_{p \in P_k^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} - \rho_{ik}(d^*) \mu_p - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d^*)}{\partial d_{ik}} \mu_p \sum_{p \in P_l^i} \mu_p x_p^* \right] \times [x_p - x_p^*] \geq 0, \quad (43)$$

$$\forall x \in K^8,$$

where $K^8 \equiv \{x | x \in R_+^{n_P}\}$.

Explicit Formulae for the Euler Method Applied to the Supply Chain Generalized Network Oligopoly

The elegance of this procedure for the computation of solutions to our supply chain generalized network oligopoly model with product differentiation can be seen in the following explicit formulae. In particular, we have the following closed form expressions for all the path flows $p \in P_k^i, \forall i, k$:

$$x_p^{\tau+1} = \max\{0, x_p^\tau + a_\tau(\rho_{ik}(d^\tau)\mu_p + \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d^\tau)}{\partial d_{ik}} \mu_p d_{il}^\tau - \frac{\partial \hat{C}_p(x^\tau)}{\partial x_p} - \frac{\partial \hat{Z}_p(x^\tau)}{\partial x_p})\}, \quad (44a)$$

with the demands being updated according to:

$$d_{ik}^{\tau+1} = \sum_{p \in P_k^i} \mu_p x_p^{\tau+1}. \quad (44b)$$

In the next Section, we solve several cases of pharmaceutical supply chain network problems using the above algorithmic scheme.

Furthermore, we emphasize that one can also utilize the Euler method to solve the supply chain generalized network models as in Corollaries 1, 2, and 3, with appropriate adaptations.

4. Case Study

In this section, we apply the Euler method to compute solutions to a set of pharmaceutical supply chain network oligopoly problems, based on real world scenarios. The examples focus on cholesterol regulating drug competition in the US. Although the examples are stylized, they illustrate the modeling and algorithmic framework developed in this paper. For purposes of transparency and reproducibility, we provide both the input and the output data.

Case I

Firm 1 represents a multinational pharmaceutical giant, hypothetically, Pfizer, Inc., which currently possesses the patent for Lipitor, the most popular brand of cholesterol-lowering drug. With more than \$5 billion of sales in the US alone in 2011, this drug was once the top-selling pharmaceutical brand in the world (Rossi (2011)).

Firm 2, on the other hand, which might represent, for example, Merck & Co., Inc., also is one of the largest global pharmaceutical companies, and has been producing Zocor, another cholesterol regulating brand, whose patent expired in 2006.

In this numerical example, we consider the case of these two competing brands in three

demand markets located across the US. Each of these two firms is assumed to have two manufacturing units and three storage / distribution centers, as illustrated in Figure 3.

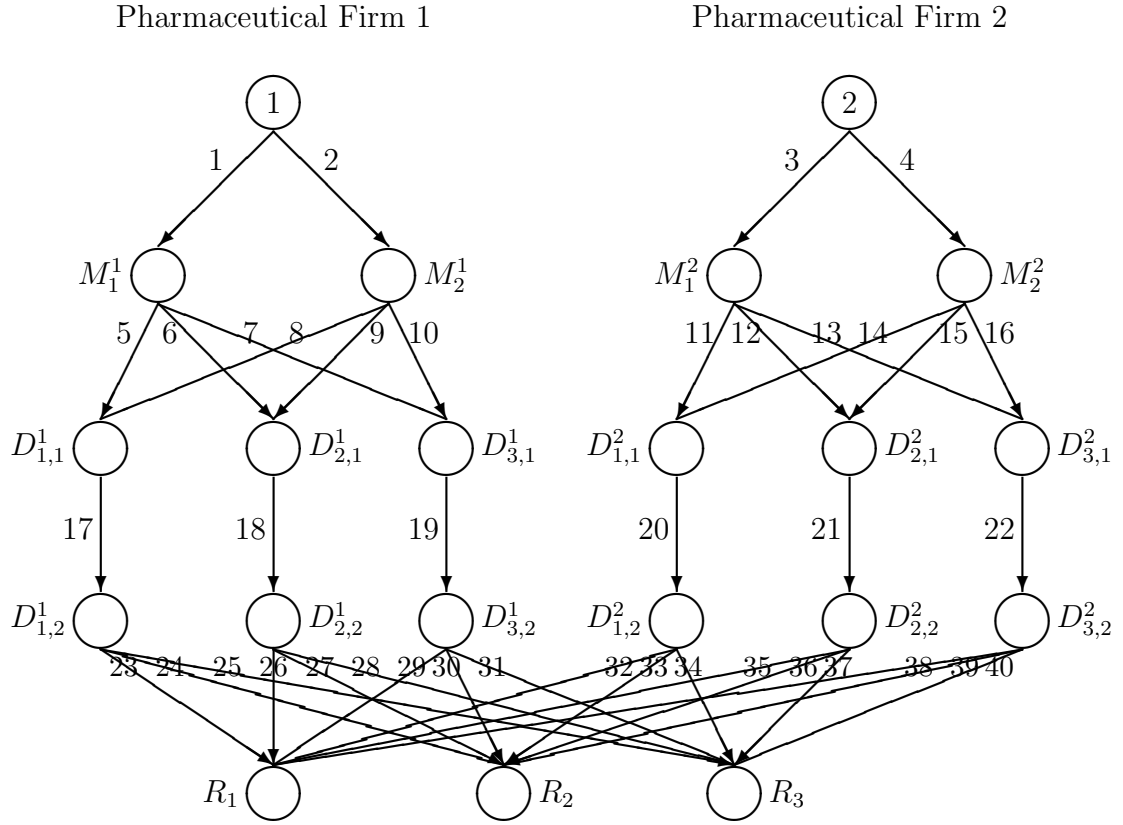


Figure 3: The Pharmaceutical Supply Chain Network Topology for Case I

The demand price functions corresponding to the three demand markets for each of the two brands 1 and 2 were as follows:

$$\rho_{11}(d) = -1.1d_{11} - 0.9d_{21} + 275; \quad \rho_{21}(d) = -1.2d_{21} - 0.7d_{11} + 210;$$

$$\rho_{12}(d) = -0.9d_{12} - 0.8d_{22} + 255; \quad \rho_{22}(d) = -1.0d_{22} - 0.5d_{12} + 200;$$

$$\rho_{13}(d) = -1.4d_{13} - 1.0d_{23} + 265; \quad \rho_{23}(d) = -1.5d_{23} - 0.4d_{13} + 186.$$

The arc multipliers, the total operational cost functions, and the total discarding cost functions were as reported in Table 1. These cost functions have been selected based on the average values of the data corresponding to the prices, the shipping costs, etc., available on the web. The values of arc multipliers, in turn, although hypothetical, are constructed in order to reflect the percentage of perishability / waste / loss associated with the various supply chain network activities in medical drug supply chains.

The Euler method (cf. (44a) and (44b)) for the solution of variational inequality (15) was implemented in Matlab on a Microsoft Windows 7 System with a Dell PC at the University of Massachusetts Amherst. We set the sequence $a_\tau = .1(1, \frac{1}{2}, \frac{1}{2}, \dots)$, and the convergence tolerance was 10^{-6} . In other words, the absolute value of the difference between each path flow in two consecutive iterations was less than or equal to this tolerance. We initialized the algorithm by setting the path flows equal to 10. Table 1 provides the computed equilibrium link product flows of each of the two competing branded drugs on every single link in the supply chain oligopoly network. We report the equilibrium link flows, rather than the path flows, due to space limitation.

The values of the equilibrium link flows in Table 1 demonstrate the impact of perishability of the product throughout the supply chain network links of each pharmaceutical firm. Under the above demand price functions, the computed equilibrium demands for each of the two brands were:

$$d_{11}^* = 10.32, \quad d_{21}^* = 7.66, \quad d_{12}^* = 4.17, \quad d_{22}^* = 8.46, \quad d_{13}^* = 8.41, \quad \text{and} \quad d_{23}^* = 1.69.$$

Furthermore, the incurred equilibrium prices associated with the branded drugs at each demand market were as follows:

$$\rho_{11} = 256.75, \quad \rho_{21} = 193.58, \quad \rho_{12} = 244.48, \quad \rho_{22} = 189.46, \quad \rho_{13} = 251.52, \quad \rho_{23} = 180.09.$$

Note that Firm 1, which produces the top-selling product, captures the majority of the market share at demand markets 1 and 3, despite the higher price. While this firm has a slight advantage over its competitor in demand market 1, it has almost entirely seized demand market 3. Consequently, several links connecting Firm 2 to demand market 3 have insignificant flows including link 40 with a flow equal to zero. In contrast, Firm 2 dominates demand market 2, due to the consumers' willingness to lean towards this product there, perhaps as a consequence of the lower price, or the perception of quality, etc., as compared to the product of Firm 1.

The profits of the two firms are:

$$U_1 = 2,936.52 \quad \text{and} \quad U_2 = 1,675.89.$$

Recall that Firm 1 still holds the patent rights of its branded drug, and, thus, makes a higher profit from selling cholesterol regulators. In contrast, Firm 2 has completed the competition-free timespan for its brand of cholesterol medicine a few years ago as a consequence of losing the patent rights to the manufacturers of generic drugs. Hence, fewer

Table 1: Link Multipliers, Total Operational Cost, and Total Discarding Cost Functions and Equilibrium Link Flow Solution for Case I

Link a	α_a	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	13.73
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	10.77
3	.96	$6.5f_3^2 + 4f_3$	$.3f_3^2$	8.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	10.55
5	1.00	$.7f_5^2 + f_5$	$.5f_5^2$	5.21
6	.99	$.9f_6^2 + 2f_6$	$.5f_6^2$	3.36
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	4.47
8	.99	$f_8^2 + 2f_8$	$.6f_8^2$	3.02
9	1.00	$.7f_9^2 + 3f_9$	$.6f_9^2$	3.92
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^2$	3.50
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	3.10
12	.99	$.8f_{12}^2 + 5f_{12}$	$.4f_{12}^2$	2.36
13	.98	$.9f_{13}^2 + 4f_{13}$	$.4f_{13}^2$	2.63
14	1.00	$.8f_{14}^2 + 2f_{14}$	$.5f_{14}^2$	3.79
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	3.12
16	1.00	$1.1f_{16}^2 + 3f_{16}$	$.6f_{16}^2$	3.43
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	8.20
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	7.25
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^2$	7.97
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^2$	6.85
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	5.42
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	6.00
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	3.56
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.66
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	2.82
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	3.34
27	.99	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^2$	1.24
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	2.59
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	3.45
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.28
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	3.09
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.54
33	.99	$.4f_{33}^2 + 3f_{33}$	$.3f_{33}^2$	3.43
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^2$	0.75
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^2$	1.72
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	2.64
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^2$	0.95
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^2$	3.47
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^2$	2.47
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^2$	0.00

numbers of consumers choose this product as compared to the product of Firm 1 leading to a higher profit for the producer of the newer brand.

The next case explores the situation in which the patent right of Firm 1's product is about to expire as well, and a third firm steps up to produce a generic substitute of this product.

Case II

In this case, we consider the scenario in which Firm 1 has just lost the exclusive patent right of its highly popular cholesterol regulator. A manufacturer of generic drugs, say, Sanofi, here denoted by Firm 3, has recently introduced a generic substitute for Lipitor by reproducing its active ingredient Atorvastatin (Smith (2011)). Firm 3 is assumed to have two manufacturing plants, two distribution centers as well as two storage facilities in order to supply the same three demand markets as in Case I (See Figure 4).

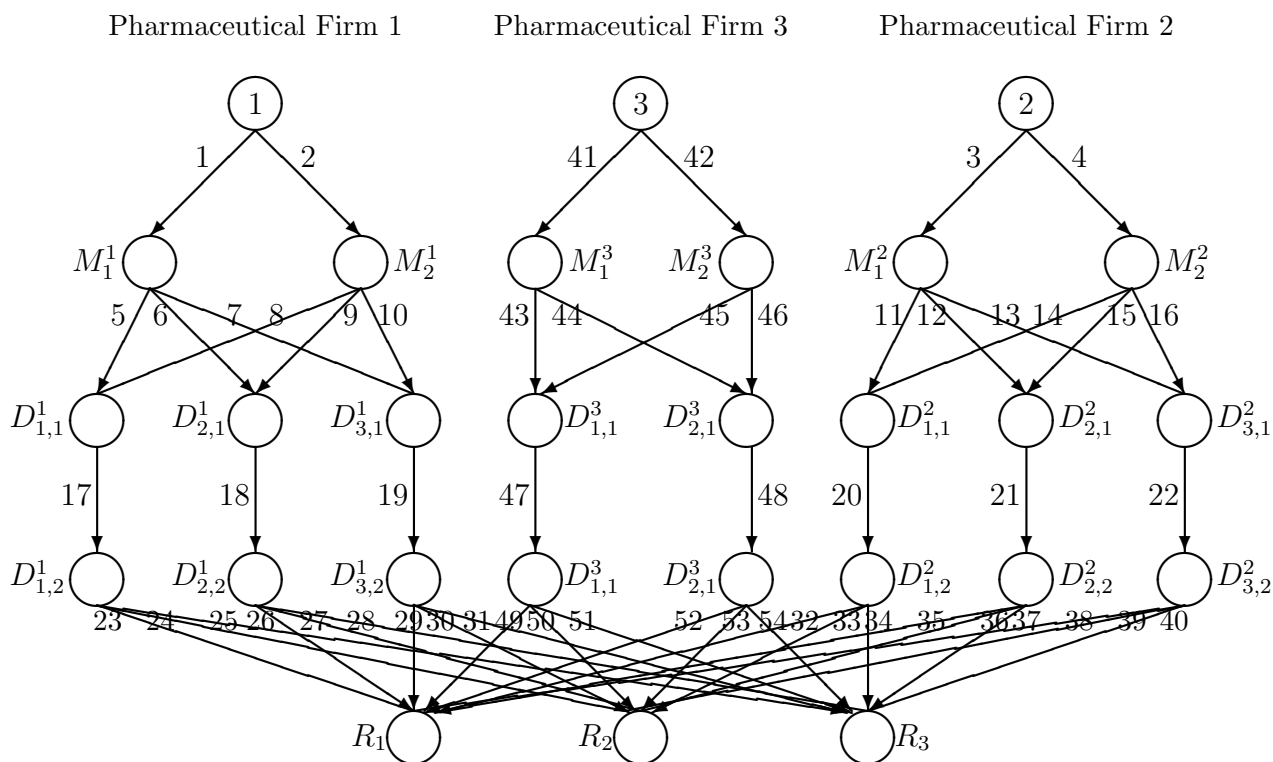


Figure 4: The Pharmaceutical Supply Chain Network Topology for Cases II and III

Since, in Case II, the new generic drug has just been released, we assume that the demand price functions for the products of Firm 1 and 2 will stay the same as in Case I. On the other hand, the demand price functions corresponding to the product of Firm 3 for demand

markets 1, 2, and 3 are as follows:

$$\begin{aligned}\rho_{31}(d) &= -0.9d_{31} - 0.6d_{11} - 0.8d_{21} + 150; & \rho_{32}(d) &= -0.8d_{32} - 0.5d_{12} - 0.6d_{22} + 130; \\ \rho_{33}(d) &= -0.9d_{33} - 0.7d_{13} - 0.5d_{23} + 133.\end{aligned}$$

Table 2 displays the arc multipliers, the total operational and the total discarding cost functions with regards to the existing links as well as the new links. The computed values of the equilibrium link flows are given in Table 2.

The equilibrium product flows of Firms 1 and 2 on links 1 through 40 are identical to the corresponding values in Case I. When the new product produced by Firm 3 is just introduced, the manufacturers of the two existing products will not experience an immediate impact on their respective demands of branded drugs. Consequently, the equilibrium computed demands for the products of Firms 1 and 2 at the demand markets will remain as in Case I. However, the equilibrium amounts of demand for the new product of Firm 3 at each demand market is equal to:

$$d_{31}^* = 5.17, \quad d_{32}^* = 3.18, \quad \text{and} \quad d_{33}^* = 3.01.$$

Furthermore, under the above assumptions, the equilibrium prices associated with the branded drugs 1 and 2 at the demand markets will not change, whereas the incurred equilibrium prices of generic drug 3 are as follows:

$$\rho_{31} = 133.02, \quad \rho_{32} = 120.30, \quad \text{and} \quad \rho_{33} = 123.55,$$

which is significantly lower than the respective prices of its competitors in all the demand markets. Thus, the profit that Firm 3 derived from manufacturing and delivering the new generic substitute to these 3 markets is:

$$U_3 = 637.38,$$

while the profits of Firms 1 and 2 remain unchanged. In the next case, we will investigate the situation in which the consumers are now more aware of the new generic substitute of cholesterol regulators.

Case III

In this case, we assumed that the generic product of Firm 3 has now been well established, and, thus, has affected the behavior of the consumers through the demand price functions of the relatively more recognized products of Firms 1 and 2. Hence, the demand price functions

Table 2: Link Multipliers, Total Operational Cost, and Total Discarding Cost Functions and Equilibrium Link Flow Solution for Case II

Link a	α_a	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	13.73
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	10.77
3	.96	$6.5f_3^2 + 4f_3$	$.3f_3^2$	8.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	10.55
5	1.00	$.7f_5^2 + f_5$	$.5f_5^2$	5.21
6	.99	$.9f_6^2 + 2f_6$	$.5f_6^2$	3.36
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	4.47
8	.99	$f_8^2 + 2f_8$	$.6f_8^2$	3.02
9	1.00	$.7f_9^2 + 3f_9$	$.6f_9^2$	3.92
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^2$	3.50
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	3.10
12	.99	$.8f_{12}^2 + 5f_{12}$	$.4f_{12}^2$	2.36
13	.98	$.9f_{13}^2 + 4f_{13}$	$.4f_{13}^2$	2.63
14	1.00	$.8f_{14}^2 + 2f_{14}$	$.5f_{14}^2$	3.79
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	3.12
16	1.00	$1.1f_{16}^2 + 3f_{16}$	$.6f_{16}^2$	3.43
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	8.20
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	7.25
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^2$	7.97
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^2$	6.85
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	5.42
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	6.00
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	3.56
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.66
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	2.82
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	3.34
27	.99	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^2$	1.24
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	2.59
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	3.45
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.28
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	3.09
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.54
33	.99	$.4f_{33}^2 + 3f_{33}$	$.3f_{33}^2$	3.43
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^2$	0.75
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^2$	1.72
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	2.64
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^2$	0.95
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^2$	3.47
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^2$	2.47
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^2$	0.00
41	.97	$3f_{41}^2 + 12f_{41}$	$.3f_{41}^2$	6.17
42	.96	$2.7f_{42}^2 + 10f_{42}$	$.4f_{42}^2$	6.23
43	.98	$1.1f_{43}^2 + 6f_{43}$	$.45f_{43}^2$	3.23
44	.98	$.9f_{44}^2 + 5f_{44}$	$.45f_{44}^2$	2.75
45	.97	$1.3f_{45}^2 + 6f_{45}$	$.5f_{45}^2$	3.60
46	.99	$1.5f_{46}^2 + 7f_{46}$	$.55f_{46}^2$	2.38
47	.98	$1.5f_{47}^2 + 4f_{47}$	$.4f_{47}^2$	6.66
48	.98	$2.1f_{48}^2 + 6f_{48}$	$.45f_{48}^2$	5.05
49	.99	$.6f_{49}^2 + 3f_{49}$	$.55f_{49}^2$	3.79
50	1.00	$.7f_{50}^2 + 2f_{50}$	$.7f_{50}^2$	1.94
51	.98	$.6f_{51}^2 + 7f_{51}$	$.45f_{51}^2$	0.79
52	.99	$.9f_{52}^2 + 9f_{52}$	$.5f_{52}^2$	1.43
53	1.00	$.55f_{53}^2 + 6f_{53}$	$.55f_{53}^2$	1.23
54	.98	$.8f_{54}^2 + 4f_{54}$	$.5f_{54}^2$	2.28

associated with the products of Firms 1 and 2 are no longer as in Cases I and II and are now given by:

$$\text{Firm 1: } \rho_{11}(d) = -1.1d_{11} - 0.9d_{21} - 1.0d_{31} + 192; \quad \rho_{21}(d) = -1.2d_{21} - 0.7d_{11} - 0.8d_{31} + 176;$$

$$\rho_{31} = -0.9d_{31} - 0.6d_{11} - 0.8d_{21} + 170;$$

$$\text{Firm 2: } \rho_{12}(d) = -0.9d_{12} - 0.8d_{22} - 0.7d_{32} + 166; \quad \rho_{22}(d) = -1.0d_{22} - 0.5d_{12} - 0.8d_{32} + 146;$$

$$\rho_{32}(d) = -0.8d_{32} - 0.5d_{12} - 0.6d_{22} + 153;$$

$$\text{Firm 3: } \rho_{13}(d) = -1.4d_{13} - 1.0d_{23} - 0.5d_{33} + 173; \quad \rho_{23}(d) = -1.5d_{23} - 0.4d_{13} - 0.7d_{33} + 164;$$

$$\rho_{33}(d) = -0.9d_{33} - 0.7d_{13} - 0.5d_{23} + 157.$$

The arc multipliers, the total operational and the total discarding cost functions are the same as in Case II, as reported in Table 3. The new computed equilibrium link flows are also reported in Table 3. The computed equilibrium demands for the products of Firms 1, 2, and 3 are as follows:

$$d_{11}^* = 7.18, \quad d_{12}^* = 4.06, \quad d_{13}^* = 2.93,$$

$$d_{21}^* = 7.96, \quad d_{22}^* = 0.00, \quad d_{23}^* = 5.60,$$

$$d_{31}^* = 4.70, \quad d_{32}^* = 6.25, \quad \text{and } d_{33}^* = 3.93.$$

As a result of the consumers' growing inclination towards the generic substitute of the previously popular Lipitor, the link flow and the demand pattern has now significantly changed. For example, Firm 2 has lost its entire share of market 2 to its competitors, resulting in zero flows on the corresponding distribution links: 33, 36, and 39. Similarly, Firm 1 now has declining sales of its brand in demand markets 1 and 3. As noted by Johnson (2011), a branded drug may decrease its market share by as much as 40% – 80% after the introduction of a generic rival. Hence, our model can capture what is happening in practice.

Furthermore, as expected, the introduction of the generic substitute of cholesterol regulators has also caused remarkable drops in the prices of the existing brands. Interestingly, the decrease in the price of Firm 1's product - Lipitor - in demand markets 2 and 3 exceeds 35%:

$$\rho_{11} = 172.24, \quad \rho_{12} = 157.97, \quad \rho_{13} = 161.33,$$

$$\rho_{21} = 157.66, \quad \rho_{22} = 138.97, \quad \rho_{23} = 151.67,$$

$$\rho_{31} = 155.09, \quad \rho_{32} = 145.97, \quad \text{and } \rho_{33} = 148.61.$$

Table 3: Link Multipliers, Total Operational Cost, and Total Discarding Cost Functions and Equilibrium Link Flow Solution for Case III

Link a	α_a	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	8.42
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	6.72
3	.96	$6.5f_3^2 + 4f_3$	$.3f_3^2$	6.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	8.01
5	1.00	$.7f_5^2 + f_5$	$.5f_5^2$	3.20
6	.99	$.9f_6^2 + 2f_6$	$.5f_6^2$	2.07
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	2.73
8	.99	$f_8^2 + 2f_8$	$.6f_8^2$	1.85
9	1.00	$.7f_9^2 + 3f_9$	$.6f_9^2$	2.44
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^2$	2.23
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	2.42
12	.99	$.8f_{12}^2 + 5f_{12}$	$.4f_{12}^2$	1.75
13	.98	$.9f_{13}^2 + 4f_{13}$	$.4f_{13}^2$	2.00
14	1.00	$.8f_{14}^2 + 2f_{14}$	$.5f_{14}^2$	2.84
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	2.40
16	1.00	$1.1f_{16}^2 + 3f_{16}$	$.6f_{16}^2$	2.60
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	5.02
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	4.49
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^2$	4.96
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^2$	5.23
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	4.11
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	4.56
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	2.44
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.47
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	1.02
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	2.48
27	.99	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^2$	1.31
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	0.66
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	2.29
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.29
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	1.28
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.74
33	.99	$.4f_{33}^2 + 3f_{33}$	$.3f_{33}^2$	0.00
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^2$	2.39
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^2$	1.82
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	0.00
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^2$	2.21
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^2$	3.46
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^2$	0.00
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^2$	1.05
41	.97	$3f_{41}^2 + 12f_{41}$	$.3f_{41}^2$	8.08
42	.96	$2.7f_{42}^2 + 10f_{42}$	$.4f_{42}^2$	8.13
43	.98	$1.1f_{43}^2 + 6f_{43}$	$.45f_{43}^2$	4.21
44	.98	$.9f_{44}^2 + 5f_{44}$	$.45f_{44}^2$	3.63
45	.97	$1.3f_{45}^2 + 6f_{45}$	$.5f_{45}^2$	4.62
46	.99	$1.5f_{46}^2 + 7f_{46}$	$.55f_{46}^2$	3.19
47	.98	$1.5f_{47}^2 + 4f_{47}$	$.4f_{47}^2$	8.60
48	.98	$2.1f_{48}^2 + 6f_{48}$	$.45f_{48}^2$	6.72
49	.99	$.6f_{49}^2 + 3f_{49}$	$.55f_{49}^2$	3.63
50	1.00	$.7f_{50}^2 + 2f_{50}$	$.7f_{50}^2$	3.39
51	.98	$.6f_{51}^2 + 7f_{51}$	$.45f_{51}^2$	1.41
52	.99	$.9f_{52}^2 + 9f_{52}$	$.5f_{52}^2$	1.12
53	1.00	$.55f_{53}^2 + 6f_{53}$	$.55f_{53}^2$	2.86
54	.98	$.8f_{54}^2 + 4f_{54}$	$.5f_{54}^2$	2.60

Finally, the computed amounts of profit for each of the three competitors through the production and delivery of their respective cholesterol-lowering medicines are as follows:

$$U_1 = 1,199.87, \quad U_2 = 1,062.73, \quad \text{and} \quad U_3 = 980.83.$$

Note that simultaneous declines in the amounts of demand and sales price has caused a severe reduction in the profits of Firms 1 and 2. This decline for Firm 1 is observed to be as high as 60%.

5. Summary and Conclusions

In this paper, we developed a new supply chain network model for the study of oligopolistic competition among the producers of a perishable product – that of pharmaceuticals. The supply chain of each pharmaceutical company consists of various activities of manufacturing, shipment, storage, and the ultimate distribution to the demand markets. The pharmaceutical firms have, as their strategies, their product flows on their supply chain networks and, hence, the competitive model is a Cournot one. The model has several novel features, which, in their totality, are a significant contribution to the literature. Specifically, the contributions to the literature in this paper are:

1. a new oligopolistic supply chain network model, based on variational inequality theory, that captures the perishability of pharmaceuticals through the use of arc multipliers, that assesses the discarding cost associated with the disposal of waste / perished products in the supply chain network activities, and that includes product differentiation by the consumers, capturing, for example, as to whether or not the products are branded or generic.
2. an adaptation of an algorithm and derivation of explicit formulae for computational purposes that yield the equilibrium product supply chain flows, the equilibrium product demands, and the incurred product prices; and
3. a case study focused on a real-world scenario of cholesterol-lowering drugs, with the investigation of the impacts of patent rights expiration and generic drug competition.

We also established special cases of our model in order to reflect situations and applications in which the drugs are homogeneous or the demands for the product remain differentiated but are known and fixed, rather than elastic.

Our proposed model of network competition for pharmaceutical supply chains can also be applied to other oligopolies of perishable products, albeit after appropriate modifications.

Future research may include the inclusion of the medical waste on the consumer side, as

well as the exploration of different competitive behaviors in this industry, such as Stackelberg behavior. In addition, it would be interesting to also capture R&D activities in this industry in a network framework.

Acknowledgments

The authors acknowledge the helpful comments and suggestions provided anonymously and by the Editor, which have improved the presentation of the results.

This research was supported, in part, by the John F. Smith Memorial Foundation at the Isenberg School of Management at the University of Massachusetts Amherst. This support is gratefully appreciated.

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