

Optimal Replenishment Policies for Two-Echelon Inventory Problems with Stationary Price and Stochastic Demand

Kizito Paul Mubiru

Kyambogo University, P.O. Box 1 Kyambogo, Uganda

Copyright © 2015 ISSR Journals. This is an open access article distributed under the *Creative Commons Attribution License*, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT: Planning and managing replenishment policies of items plays an important role in supply chain management. In this paper, a new mathematical model is developed to optimize replenishment policies of a two-echelon inventory system under demand uncertainty. The system consists of one factory warehouse at the upper echelon and three supermarkets at the lower echelon. A special case of this model is where sales price and scheduled inventory replenishment periods are uniformly fixed over all echelons. Demand at the supermarkets is stochastic and stationary. Adopting a Markov decision process approach, the states of a Markov chain represent possible states of demand for milk powder product. The objective is to determine in each echelon of the planning horizon an optimal replenishment policy so that the long run sales revenue is maximized for a given state of demand. Using weekly equal intervals, the decisions of when to replenish additional units are made using dynamic programming over a finite period planning horizon. A numerical example demonstrates the existence of an optimal state-dependent replenishment policy and sales revenue over the echelons.

KEYWORDS: Echelon, Inventory, Stationary price, Stochastic demand.

1 INTRODUCTION

In practice, inventory may be stored at the point of manufacture (one echelon of inventory system), then at national or regional warehouse (a second echelon), then at field distribution centers (a third echelon) etc. Some coordination is needed to effectively manage replenishment policies of the product at different echelons. Since the base stock level at each echelon (except the top one) is replenished from the next higher echelon, the base stock level needed at the higher echelon is affected by how soon replenishment will be needed at the various locations for the lower echelon. To cope with current turbulent market demands, there is still need to adopt coordinated inventory control across supply chain facilities by establishing optimal replenishment policies in a stochastic demand environment. Large industries continually strive to optimize replenishment policies of products in multi-echelon inventory systems. This is a considerable challenge when the demand for manufactured items follows a stochastic trend. One major challenge is usually encountered: determining the most desirable period during which to replenish additional units of the item in question given a periodic review production-inventory system when demand is uncertain. Derek and Iyogun (1988) examined the problem of managing inventories where there is a joint fixed cost for replenishing plus an item-by-item fixed cost for each item included in the replenishment order. Due to the complexity of the optimal solution, attention is focused on fixed heuristics, and in particular 'can-order' or (s,c,S) policies.

Fangruo C(2000) illustrated effective policies in a two-stage serial inventory system with stochastic demand. An inventory system is considered where Poisson demand occurs at stage 1.

A new lower bound in the cost of the optimal policy is produced and a simple periodic policy is proposed.

Stage 1 replenishes its inventory from stage 2; which in turn orders from an outside supplier with unlimited stock.

A fixed cost is incurred at stages 1 and 2 under the assumption that the supply lead time at stage 2 is zero. A simple heuristic policy is characterized where long-run average cost is guaranteed to be within 6% of optimality. Rodney and Roman (2004) extended the optimal policies study in the context of a capacitated two-echelon inventory system. This model includes installations with production capacity limits, and demonstrates that a modified base stock policy is optimal in a two-stage

system when there is a smaller capacity at the downstream facility. This is shown by decomposing the dynamic programming value function into value functions dependent upon individual echelon stock variables. The optimal structure holds for both stationary and non stationary customer demand.

Axsater S (2005) similarly examined a simple decision rule for decentralized two-echelon inventory control. A two-echelon distribution inventory system with a central warehouse and a number of retailers is considered. The retailers face stochastic demand and the system is controlled by continuous review installation stock policies with given batch quantities. A back order cost is provided to the warehouse and the warehouse chooses the reorder point so that the sum of the expected holding and backorder costs are minimized. Given the resulting warehouse policy, the retailers similarly optimize their costs with respect to the reorder points. The study provides a simple technique for determining the backorder cost to be used by the warehouse.

In related work by Haji R (2006), a two-echelon inventory system is considered consisting of one central warehouse and a number of non-identical retailers. The warehouse uses a one-for-one policy to replenish its inventory, but the retailers apply a new policy that is each retailer orders one unit to central warehouse in a predetermined time interval; thus retailer orders are deterministic not random. In a similar context, Abhijeet S and Saroj K (2011) considered vendor managed Two-Echelon inventory system for an integrated production procurement case. Joint economic lot size models are presented for the two supply situations, namely staggered supply and uniform supply. Cases are employed that describe the inventory situation of a single vendor supplying an item to a manufacturer that is further processed before it is supplied to the end user. Using illustrative examples, the comparative advantages of a uniform sub batch supply over a staggered alternative are investigated and uniform supply models are found to be comparatively more beneficial and robust than the staggered sub batch supply.

The literature cited provide profound insights by authors that are crucial in analyzing two-echelon inventory systems in a stochastic demand setting. However, a new dynamic approach is sought in order to relate state-transitions with customers, demand and price of item at the respective echelons so as to optimize replenishment policies and sales revenue in a multistage decision setting.

In this paper, a two-echelon production- inventory system is considered whose goal is to optimize replenishment policies and the sales revenue associated with item sales. At the beginning of each period, a major decision has to be made, namely whether to replenish additional units of the item or not to replenish and keep the item at prevailing inventory position in order to sustain demand at a given echelon. The paper is organized as follows. After describing the mathematical model in §2, consideration is given to the process of estimating the model parameters. The model is solved in §3 and applied to a special case study in §4. Some final remarks lastly follow in §5.

2 MODEL FORMULATION

2.1 NOTATION AND ASSUMPTIONS

i, j	=	States of demand
F	=	Favorable state
U	=	Unfavorable state
h	=	Inventory echelon
n, N	=	Stages
Z	=	Replenishment policy
$N^z(h)$	=	Customer matrix
$N_{ij}^z(h)$	=	Number of customers
$D^z(h)$	=	Demand matrix
$D_{ij}^z(h)$	=	Quantity demanded
$Q^z(h)$	=	Demand transition matrix
$R^z(h)$	=	Sales revenue matrix
$R_{ij}^z(h)$	=	Sales revenue
$e_i^z(h)$	=	Expected sales revenue
$a_i^z(h, n)$	=	Accumulated sales revenue
p	=	Unit sales price

$i, j \in \{F, U\}$ $h \in \{1, 2\}$ $Z \in \{0, 1\}$ $n = 1, 2, \dots, N$

We consider a two-echelon inventory system consisting of a manufacturing plant producing a single product in batches for a designated number of supermarkets at echelon 1. At echelon 2; customers demand the product at supermarkets. The demand during each time period over a fixed planning horizon for a given echelon (h) is classified as either *favorable* (denoted by state F) or *unfavorable* (denoted by state U) and the demand of any such period is assumed to depend on the demand of the preceding period. The transition probabilities over the planning horizon from one demand state to another may be described by means of a Markov chain. Suppose one is interested in determining an optimal course of action, namely to replenish additional units of the item (a decision denoted by $Z=1$) or not to replenish additional units of the item (a decision denoted by $Z=0$) during each time period over the planning horizon, where Z is a binary decision variable. Optimality is defined such that the maximum expected sales revenue is accumulated at the end of N consecutive time periods spanning the planning horizon under consideration. In this paper, a two-echelon ($h=2$) and two-period ($N=2$) planning horizon is considered.

2.2 FINITE - PERIOD DYNAMIC PROGRAMMING PROBLEM FORMULATION

Recalling that the demand can either be in state F or in state U, the problem of finding an optimal replenishment policy may be expressed as a finite period dynamic programming model.

Let $R_n(i, h)$ denote the optimal expected total sales revenue accumulated during the periods $n, n+1, \dots, N$ given that the state of the system at the beginning of period n is $i \in \{F, U\}$. The recursive equation relating R_n and R_{n+1} is

$$R_n(i, h) = \max_Z [Q_{iF}^Z(h)R_{iF}^Z(h) + R_{n+1}(F, h), Q_{iU}^Z(h)R_{iU}^Z(h) + R_{n+1}(U, h)] \tag{1}$$

$$i \in \{F, U\}, h = \{1, 2\}, n = 1, 2, \dots, N$$

together with the final conditions

$$R_{N+1}(F, h) = R_{N+1}(U, h) = 0$$

This recursive relationship may be justified by noting that the cumulative sales revenue $R_{ij}^Z(h) + R_{N+1}(j)$

resulting from reaching state $j \in \{F, U\}$ at the start of period $n+1$ from state $i \in \{F, U\}$ at the start of period n occurs with probability $Q_{ij}^Z(h)$.

$$\text{Clearly, } e^Z(h) = [Q_{ij}^Z(h)] [R^Z(h)]^T, Z \in \{0, 1\}, h \in \{1, 2\} \tag{2}$$

where 'T' denotes matrix transposition, and hence the dynamic programming recursive equations

$$R_n(i, h) = \max_Z [e_i^Z(h) + Q_{iF}^Z(h)R_{n+1}(F) + Q_{iU}^Z(h)R_{n+1}(U)] \tag{3}$$

$$R_N(i, h) = \max_Z \{e_i^Z(h)\} \tag{4}$$

result where (4) represents the Markov chain stable state.

2.2.1 COMPUTING $Q^Z(h)$ AND $R^Z(h)$

The demand transition probability from state $i \in \{F, U\}$ to state $j \in \{F, U\}$, given replenishment policy $Z \in \{0, 1\}$ may be taken as the number of customers observed over echelon h with demand initially in state i and later with demand changing to state j , divided by the sum of customers over all states. That is,

$$Q_{ij}^Z(h) = N_{ij}^Z(h) / ((N_{iF}^Z(h) + (N_{iU}^Z(h))) \quad i \in \{F, U\}, Z \in \{0, 1\}, h = \{1, 2\} \tag{4}$$

When demand outweighs on-hand inventory, the sales revenue matrix $R^Z(h)$ may be computed by means of the relation

$$R^Z(h) = p[D^Z(h) - I^Z(h)] + pI^Z(h) = pD^Z(h)$$

where p denotes the sales price of item.

Therefore,

$$R_{ij}^Z(h) = p[D_{ij}^Z(h) - I_{ij}^Z(h)] + pI_{ij}^Z(h) = pD_{ij}^Z(h) \quad (5)$$

for all $i, j \in \{F, U\}$, $h \in \{1, 2\}$ and $Z \in \{0, 1\}$.

3 OPTIMIZATION

The optimal replenishment policy and sales revenue are found in this section for each period over echelon h separately.

3.1 OPTIMIZATION DURING PERIOD 1

When demand is favorable (ie. in state F), the optimal replenishment policy during period 1 is

$$Z = \begin{cases} 1 & \text{if } e_F^Z(h) > e_U^Z(h) \\ 0 & \text{if } e_F^Z(h) \leq e_U^Z(h) \end{cases}$$

The associated total sales revenue is then

$$R_1(F, h) = \begin{cases} e_F^1(h) & \text{if } Z = 1 \\ e_F^0(h) & \text{if } Z = 0 \end{cases}$$

Similarly, when demand is unfavorable (ie. in state U), the optimal replenishment policy during period 1 is

$$Z = \begin{cases} 1 & \text{if } e_U^1(h) > e_U^0(h) \\ 0 & \text{if } e_U^1(h) \leq e_U^0(h) \end{cases}$$

In this case, the associated sales revenue is

$$R_1(U, h) = \begin{cases} e_U^1(h) & \text{if } Z = 1 \\ e_U^0(h) & \text{if } Z = 0 \end{cases}$$

3.2 OPTIMIZATION DURING PERIOD 2

Using (2),(3) and recalling that $a_i^Z(h)$ denotes the already accumulated sales revenue at the end of period 1 as a result of decisions made during that period, it follows that

$$\begin{aligned} a_i^Z(h) &= e_i^Z(h) + Q_{iF}^Z(h) \max[e_F^1(h), e_F^0(h)] + Q_{iU}^Z(h) \max[e_U^1(h), e_U^0(h)] \\ &= e_i^Z(h) + Q_{iF}^Z(h) R_2(F, h) + Q_{iU}^Z(h) R_2(U, h) \end{aligned}$$

Therefore when demand is Favorable (i.e. in state F), the optimal replenishment policy during period 2 is

$$Z = \begin{cases} 1 & \text{if } a_F^1(h) > a_F^0(h) \\ 0 & \text{if } a_F^1(h) \leq a_F^0(h) \end{cases}$$

while the associated sales revenue is

$$R_2(F, h) = \begin{cases} a_F^1(h) & \text{if } Z = 1 \\ a_F^0(h) & \text{if } Z = 0 \end{cases}$$

Similarly, when the demand is unfavorable (ie. in state U), the optimal replenishment policy during period 2 is

$$Z = \begin{cases} 1 & \text{if } a_U^1(h) > a_U^0(h) \\ 0 & \text{if } a_U^1(h) \leq a_U^0(h) \end{cases}$$

In this case the associated sales revenue is

$$R_2(U, h) = \begin{cases} a_U^1(h) & \text{if } Z = 1 \\ a_U^0(h) & \text{if } Z = 0 \end{cases}$$

4 CASE STUDY

In order to demonstrate use of the model in §2-3, real case applications from *Sameer Agriculture and Livestock Ltd*, a production plant for milk powder and three supermarkets: *Shoprite supermarket*, *Game supermarket* and *Uchumi supermarket* in Uganda are presented in this section. The production plant supplies milk powder at supermarkets (echelon 1), while end customers come to supermarkets for milk powder product (echelon 2). The demand for milk powder fluctuates every week at both echelons. The production plant and supermarkets want to avoid excess inventory when demand is Unfavorable (state U) or running out of stock when demand is Favorable (state F) and hence seek decision support in terms of an optimal replenishment policy and the associated sales revenue of milk powder product in a two-week planning period. The network topology of a two-echelon inventory system for milk powder product is illustrated in Figure 1 below:

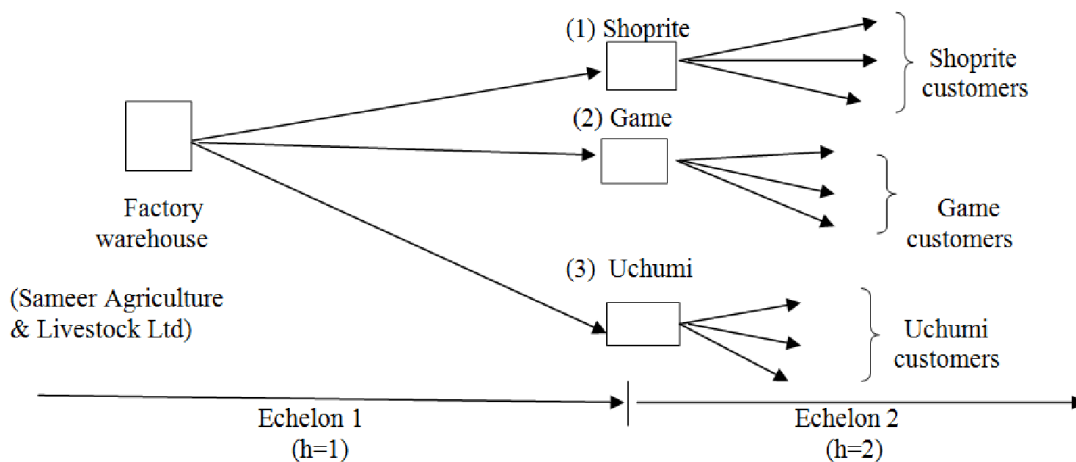


Figure 1: A two-echelon inventory system of milk powder product

4.1 DATA COLLECTION

Samples of customers, demand and inventory levels were taken for 400 gms packets of milk powder at echelons 1 and 2 over the state-transitions and the respective replenishment policies for twelve weeks.

Table 1: Customers, Demand and replenishment policies and sales price (in UGX) given state-transitions, and echelons over twelve weeks

State transition (i,j)	Echelon (h)	Replenishment Policy (Z)	Customers $N^z_{ij}(h)$	Demand $D^z_{ij}(h)$	Sales Price (p)
FF	1	1	91	156	6000
FU	1	1	71	15	6000
UF	1	1	64	107	6000
UU	1	1	13	11	6000
FF	1	0	82	123	6000
FU	1	0	30	78	6000
UF	1	0	55	78	6000
UU	1	0	25	15	6000
FF	2	1	45	93	6000
FU	2	1	59	60	6000
UF	2	1	59	59	6000
UU	2	1	13	11	6000
FF	2	0	54	72	6000
FU	2	0	40	77	6000
UF	2	0	45	75	6000
UU	2	0	11	11	6000

At echelon 1, when additional units were replenished (Z=1),

$$N^1(1) = \begin{bmatrix} N^1_{FF}(1) & N^1_{FU}(1) \\ N^1_{UF}(1) & N^1_{UU}(1) \end{bmatrix} \qquad N^1(1) = \begin{bmatrix} 91 & 71 \\ 64 & 13 \end{bmatrix}$$

$$D^1(1) = \begin{bmatrix} D^1_{FF}(1) & D^1_{FU}(1) \\ D^1_{UF}(1) & D^1_{UU}(1) \end{bmatrix} \qquad D^1(1) = \begin{bmatrix} 156 & 115 \\ 107 & 11 \end{bmatrix}$$

When additional units were not replenished (Z=0),

$$N^0(1) = \begin{bmatrix} N^0_{FF}(1) & N^0_{FU}(1) \\ N^0_{UF}(1) & N^0_{UU}(1) \end{bmatrix} \qquad N^0(1) = \begin{bmatrix} 82 & 50 \\ 56 & 25 \end{bmatrix}$$

$$D^0(1) = \begin{bmatrix} D^0_{FF}(1) & D^0_{FU}(1) \\ D^0_{UF}(1) & D^0_{UU}(1) \end{bmatrix} \qquad D^0(1) = \begin{bmatrix} 123 & 78 \\ 78 & 15 \end{bmatrix}$$

At echelon 2, when additional units were replenished (Z=1),

$$N^1(2) = \begin{bmatrix} N^1_{FF}(2) & N^1_{FU}(2) \\ N^1_{UF}(2) & N^1_{UU}(2) \end{bmatrix} \qquad N^1(2) = \begin{bmatrix} 48 & 55 \\ 59 & 13 \end{bmatrix}$$

$$D^1(2) = \begin{bmatrix} D_{FF}^1(2) & D_{FU}^1(2) \\ D_{UF}^1(2) & D_{UU}^1(2) \end{bmatrix} \quad D^1(2) = \begin{bmatrix} 93 & 60 \\ 59 & 11 \end{bmatrix}$$

When additional units were not replenished (Z=0),

$$N^0(2) = \begin{bmatrix} N_{FF}^0(2) & N_{FU}^0(2) \\ N_{UF}^0(2) & N_{UU}^0(2) \end{bmatrix} \quad N^0(2) = \begin{bmatrix} 54 & 46 \\ 45 & 11 \end{bmatrix}$$

$$D^0(2) = \begin{bmatrix} D_{FF}^0(2) & D_{FU}^0(2) \\ D_{UF}^0(2) & D_{UU}^0(2) \end{bmatrix} \quad D^0(2) = \begin{bmatrix} 72 & 77 \\ 75 & 11 \end{bmatrix}$$

4.2 SOLUTION PROCEDURE FOR THE TWO-ECHELON INVENTORY REPLENISHMENT PROBLEM

Using (4) and (5), the state transition matrices and sales revenue matrices (in million UGX) at each respective echelon for week1 are

$$Q^1(1) = \begin{bmatrix} 0.5697 & 0.4303 \\ 0.8312 & 0.1688 \end{bmatrix} \quad R^1(1) = \begin{bmatrix} 0.936 & 0.690 \\ 0.642 & 0.066 \end{bmatrix}$$

$$Q^1(2) = \begin{bmatrix} 0.4660 & 0.5340 \\ 0.8429 & 0.1571 \end{bmatrix} \quad R^1(2) = \begin{bmatrix} 0.588 & 0.360 \\ 0.354 & 0.066 \end{bmatrix}$$

Respectively, for the case when additional units were replenished (Z=1) during week 1,

While these matrices are given by

$$Q^0(1) = \begin{bmatrix} 0.6212 & 0.3722 \\ 0.6914 & 0.3086 \end{bmatrix} \quad R^0(1) = \begin{bmatrix} 0.738 & 0.468 \\ 0.468 & 0.090 \end{bmatrix}$$

$$Q^0(2) = \begin{bmatrix} 0.5400 & 0.4600 \\ 0.8036 & 0.1964 \end{bmatrix} \quad R^0(2) = \begin{bmatrix} 0.432 & 0.462 \\ 0.450 & 0.066 \end{bmatrix}$$

Respectively, When additional units were not replenished (Z=0) during week 1.

When additional units were replenished (Z = 1), the matrices $Q^1(1)$, $R^1(1)$, $Q^1(2)$ and $R^1(2)$ yield the sales revenue (in million UGX)

$$e^1_F(1) = (0.562)(0.936) + (0.438)(0.690) = 0.828$$

$$e^1_U(1) = (0.831)(0.642) + (0.169)(0.066) = 0.545$$

$$e^1_F(2) = (0.466)(0.642) + (0.5340)(0.066) = 0.334$$

$$e^1_U(2) = (0.8429)(0.558) + (0.1571)(0.066) = 0.527$$

However, When additional units were *not* replenished ($Z=0$), the matrices $Q^0(1)$, $R^0(1)$, $Q^0(2)$ and $R^0(2)$ yield the sales revenue (in million UGX)

$$e^0_F(1) = (0.6212)(0.738) + (0.3788)(0.468) = 0.636$$

$$e^0_U(1) = (0.6914)(0.468) + (0.3086)(0.090) = 0.351$$

$$e^0_F(2) = (0.5400)(0.432) + (0.4600)(0.462) = 0.446$$

$$e^0_U(2) = (0.8036)(0.450) + (0.1964)(0.066) = 0.375$$

When additional units were replenished ($Z = 1$), the accumulated sales revenue (in million UGX) at each respective echelon follows:

Echelon 1:

$$a^1_F(1) = 0.690 + (0.5697)(0.690) + (0.4303)(0.545) = 1.318$$

$$a^1_U(1) = 0.545 + (0.8312)(0.690) + (0.1688)(0.545) = 1.211$$

Echelon 2:

$$a^1_F(2) = 0.334 + (0.4660)(0.446) + (0.5340)(0.527) = 0.824$$

$$a^1_U(2) = 0.527 + (0.8429)(0.446) + (0.1571)(0.527) = 0.986$$

When additional units were *not* replenished ($Z = 0$), the accumulated sales revenue (in million UGX) follows:

Echelon 1:

$$a^0_F(1) = 0.636 + (0.6212)(0.690) + (0.37883)(0.545) = 1.265$$

$$a^0_U(1) = 0.351 + (0.6914)(0.690) + (0.3086)(0.545) = 0.996$$

Echelon 2:

$$a^0_F(2) = 0.446 + (0.5400)(0.446) + (0.4600)(0.527) = 0.929$$

$$a^0_U(2) = 0.375 + (0.8036)(0.446) + (0.1964)(0.527) = 0.836$$

4.3 THE OPTIMAL REPLENISHMENT POLICY

Week1: Echelon 1

Since $0.828 > 0.636$, it follows that $Z=1$ is an optimal replenishment policy for week 1 with associated sales revenue of 0.828 million UGX for the case of favorable demand. Since $0.545 > 0.351$, it follows that $Z=1$ is an optimal replenishment policy for week 1 with associated sales revenue of 0.545 million UGX for the case when demand is unfavorable.

Week1: Echelon 2

Since $0.446 > 0.334$, it follows that $Z=0$ is an optimal replenishment policy for week 1 with associated sales revenue of 0.446 million UGX when demand is favorable. Since $0.527 > 0.375$, it follows that $Z=1$ is an optimal replenishment policy for week 1 with associated sales revenue of 0.527 million UGX if demand is unfavorable.

Week 2: Echelon 1

Since $1.318 > 1.265$, it follows that $Z=1$ is an optimal replenishment policy for week 2 with associated accumulated sales revenue of 1.318 million UGX when demand is favorable. Since $1.211 > 0.996$, it follows that $Z=1$ is an optimal replenishment policy for week 2 with associated accumulated sales revenue of 1.211 million UGX if demand is unfavorable.

Week 2: Echelon 2

Since $0.929 > 0.824$, it follows that $Z=0$ is an optimal replenishment policy for week 2 with associated accumulated sales revenue of 0.929 million UGX when demand is favorable. Since $0.986 > 0.836$, it follows that $Z=1$ is an optimal replenishment policy for week 2 with associated sales revenue of 0.986 million UGX if demand is unfavorable.

5 CONCLUSION

A two-echelon inventory model with stochastic demand was presented in this paper. The model determines an optimal replenishment policy and sales revenue of a given item with stochastic demand. The decision of whether or not to replenish additional units is modeled as a multi-period decision problem using dynamic programming over a finite planning horizon. Results from the model indicate optimal sales revenue replenishment policies over the echelons for the given problem. As a sales revenue maximization strategy in echelon-based inventory systems, computational efforts of using Markov decision process approach provide promising results. It would however be worthwhile to extend the research and examine the behavior of replenishment policies under non stationary demand conditions over the echelons. In the same spirit, the model raises a number of salient issues to consider: Lead time of milk powder during replenishment and customer response to abrupt changes in price of the product. Finally, special interest is sought in further extending our model by considering replenishment policies in the context of Continuous Time Markov Chains (CTMC).

REFERENCES

- [1] Abhijeet S, Saroj K & Anil K, 2011, A vendor managed Two-Echelon inventory system for an integrated production procurement case, *Asia Pacific Journal of Operations Research*, **28**(2), 301-322.
- [2] Axsater S, 2005, A simple decision rule for decentralized two-echelon inventory control, *International Journal of Production Economics*, 94-93(1), 53-59.
- [3] Derek A & Iyogum P, 1988, Periodic versus 'can order' policies for coordinated multi item inventory systems, *Management Science*, **34**(6), 791-799.
- [4] Fangruo C, 2000, Optimal policies for multi-echelon Inventory problems with batch ordering, *Operations Research*, **48**(3), 376-388.
- [5] Neghab M, Baboli A, 2006, A new Replenishment policy in a Two-Echelon Inventory System with Stochastic Demand, *International Conference on Service Systems and Service Management*, Vol.1, 246-250.
- [6] Rodney P & Roman K, 2004, Optimal Policies for a capacitated Two-Echelon inventory system, *Operations Research*, **152**(5), 739-747.