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A NEW MATHEMATIC MODEL FOR HUMANITARIAN PHARMACEUTICAL SUPPLY CHAIN TO REDUCE OBSOLESENCE COST

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ABSTRACT

The unused drugs in Humanitarian supply chain (HSC) can lead to significant financial losses and environmental damages. It can also be the target of criminal organization for counterfeiting activities. This research aims to investigate a new model that's gives more responsibility to pharmaceutical companies to keep control on excess medications at recipient countries. It consists of motivating the humanitarian logistic provider to facilitate leftover returns. We have explored the game theory through studying the mathematical models of "non-cooperative" and "cooperative" decision-makers. A novel composition of "incentive/bonus allocation" and "Tax/penalties sharing agreement" is introduced to reach the expected level of synergy. The numerical analysis shows that using the "cooperative" model can enhance the whole HSC revenues, maintain sustainability commitment, and better serve vulnerable patients.

Keywords: *Humanitarian Supply Chain, Reverse Logistic (RL), Cooperative Decision-Making, Pharma Expired Drugs, Global Health Institution*

1. INTRODUCTION

Medicine's donation is considered as noble and generous acts from pharma companies and humanitarian organizations. It's performed for philanthropy or company social dimension aimed at supplying drugs for vulnerable countries[1]. The main focus of the humanitarian supply chain organizations is to insure equity to medication access[2]. It organizes lifesaving operations following pandemic, natural disasters, and regular medicines supply for underdeveloped countries. The humanitarian pharma inventory management is much more complicated comparing with managing the inventory of commercial product[3]. The main challenges are coming from:

- ✓ High forecast variance
- ✓ Nonrelevant inventory management policy
- ✓ Lack of trust and transparency
- ✓ Transportation and storage failures
- ✓ Product quality issue

The global humanitarian agencies (UNICEF, GAVI, USAID…) are concluding contracts and supply chain agreement with pharmaceutical companies to produce and deliver the medicines until arriving to the recipient countries[4]. The main weakness of the actual configuration is that the entire supply chain operations are build based on wrong demand signal[5], [6]. Figure 1 shows the forecast error consequences:

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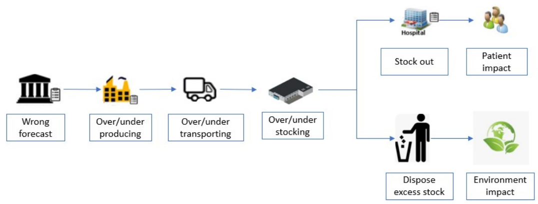

Figure 1: Forecast Error consequence on Humanitarian supply chain

Since the forecast is inaccurate, some Global health organizations prefer to overestimate the demand [7] and adopt an aggressive inventory policy to ensure the population is well covered by the medication program than look for the optimal forecast and take risk being in stock out situation. Furthermore, the high stock generated is not stored properly following the standards. Thus, the donated quantity is kept on hold until reaching the "end of live date". a Swiss pharmacist and disaster expert who codirected the audit, estimated that 50% of the donated drugs flowing into Albania by non-medical voluntary organizations were "inappropriate or useless and will have to be destroyed[8]. Also, a study published in the New England Journal of Medicine in 1997 found that about half the drugs donated to Bosnia were of little or no use[9]. To help prepare the new guidelines, WHO did a systematic review of drug donations during 1998 to 2008. It found that only 56% of donations were appropriate given the characteristics of the event and what the recipient needed, and only 12.5% of drugs requested by recipient countries were received[10].

The inventory management in humanitarian healthcare is very sensitive as the risk of counterfeiting drugs is significant. The expired medicines must be properly destructed to avoid human health & environment impact. Following the World Health Organization [10] Guidelines for the secure destruction of expired medicines, the pharma supply chain upstream actors are accountable of safely disposing the expired pharmaceutical stock and they are responsible to respect the strict regulations imposed by government to avoid paying high penalties for remaining expired drugs.

The reverse logistic applied to humanitarian pharmaceutical supply chain can be an excellent opportunity to reduce the impact of the over forecasting on inventory management and minimize the writ-off cost. It allows to save lives, profit and potentially the environment. The reverse logistic has been studied and analyzed by multiple authors in the context of commercial pharmaceutical business unit due to the growth objective. However, less attention has been given to its application in humanitarian supply chain. The recovery of the excess pharmaceutical product before reaching the minimum accepted shelf live in alternative countries can be an optimal concept for the humanitarian reverse logistic. In the vision to motivate and engage all HPSC stakeholders and create excitement around the RL process, a cooperative model structure is required to create synergy by sharing the risks and benefits between actors according to the contract agreement. Applying an appropriate cooperative condition can ensure HPSC actors' benefits and preserve the global health organization's objective which is serving the maximum of vulnerable patients.

In this paper, we investigate two-echelon stakeholders in HPSC including a pharmaceutical company and a humanitarian logistic provider (HLP) with a constant total shelf-life drug that follows stochastic forecast and requires a high % in stock. By applying the "incentive sharing" strategy as a common practice in the commercial area, we present a new approach in the proposed model to avoid potential destruction costs and high tax penalties from government. The main contribution of this paper "comparing with the existing literature" is introducing a reliable decision-making model to develop the reverse logistic process in HPSC. The purpose is to collect the high stock based on actuals before reaching the expiration date and redistribute it in an alternative country. Thus, avoiding significant legislated penalties, destruction costs and improving the global health. An optimal cooperative agreement mechanism is presented to motivate the HLP to participate to the proposed scheme. From the mathematical perspective, the model developed in this study involves decisions in multiple time for HPSC actors. Therefore, the research questions (RQ) of this study are as follows:

- ✓ RQ1 What's findings in view of previous literature
- ✓ RQ2 How to develop a cooperative supply chain model adapted to HSC.
- ✓ RQ2 What is the outcome expected behind applying the cooperative model.

This paper is organized as follow, section II presents the state of art overview of reverse logistic in commercial & HPSC. It's a deep dive into the potential benefits of its application for humanitarian operations. Section III describes the proposed HPSC model. It outlines a new interaction framework for managing the connections between the vendor and the customer. Section IV provides the mathematical formulation of the proposed model. Section V presents the proof of concept through a numerical analysis to illustrate the results. Section VI provides the conclusion, challenges, and future work.

2. LITERATURE REVIEW & PRACTICAL EXAMPLE FROM BIG PHARMA COMPANIES

The objective of this section is to build a full picture of the reverse logistic state of art applied to humanitarian supply chain. We have explored the academic literature for both "for profit" and "not for profit" pharmaceutical industry. We have also reviewed some literature around the strategic & operational annual reports communicated by the global humanitarian agencies. To add the practical aspect to our review, we have conducted a questionnaire shared within humanitarian agencies & pharma leaders to get their insight & testimony.

The research scope is limited to English-language articles published mainly between 2000-2021. The queries include the association of three keywords categories, (1) terms synonyms of Humanitarian supply chain and (2) terms associated with reverse logistic (RL) concept and (3) Cooperative decision-making. Multidiscipline databases were accessed (Scopus, Springer, research gate, IEEE) in addition to many web sites for global organizations and companies.

2.1 A. Deep dive of the RL in humanitarian supply chain in the academic state of art:

The reverse logistic concept provides multiples & various advantages and solutions to commercial pharma business unit, it might be profitable & beneficial to adapt it and apply it to humanitarian supply chain[11]. Meanwhile, the literature of reverse logistic incorporated in the context of the humanitarian supply chains looks isolated and its applications is scarce. The authors Kunz and Reiner conducted a literature review[12], [13] covering a total of 174 articles, of which 74% were published during the last three years. The main outcome of this research confirms that the reverse logistic has a limited attention on academic state of art in the humanitarian supply chain area[11]. Furthermore, there is a lack of framework for understanding challenges and solutions[14]. For example, the authors "Guide & Van Wassenhove" [15]proposed to incorporate the reverse logistic into the supply operations of the HSC. They have just explained the potential barriers that limit its development. Other authors "Sarkis, Kovacs, Eng Larson and Vega" [16] are proposing the RL to solve some environmental concerns and are suggesting using it to develop the green logistics. However, there is no discussion or recommendation on operational aspect. This is a gap that this paper aims to fill.

2.2 Academic Overview of the RL in the commercial context

The literature review for the RL in the commercial context is rich and well developed by many authors[17]. They have approached this concept from different perspectives[18], and they have surrounded both strategic and operational dimensions[19], [20]. They have focused on stock management[21], order processing policies[22], storage condition, and distribution model of drugs from the commercial point of view [23] and appropriate service levels [24][25][26] [27]. A recent interesting article of the authors "Roya Tat, Jafar Heydari and Masoud Rabbani" published in 2020 focused on redistributing medicines in an alternative market. They proposed a new mathematic model of coordination mechanism to support the reverse logistic in commercial area[28]. More attention has been given to environmental questions and collecting leftover and expired drugs due to negligible salvage value and complexity in pharmaceutical RL. The author "Ritchie, Burnes, and Whittle" [29] reviewed the elaboration and expansion of the pharmaceutical RL system in 28 hospital units in the UK. They advised that the improvement of RL in the collection of the not used and expired drugs would generate significant financial saving and operational benefits for the supply chain ecosystem and reduce pharma loss. Also, the author "Kumar & Craig" [30] shared a general framework for defining the RACI (responsibly, accountability, consulted, informed) matrix of each actor of the pharma RL and proposed the use of a secure information system to rationalize the process of collecting expired drugs in the SC. Xie and Breen [31] represented a green PSC model to decrease preventable pharmaceutical waste and properly dispose of unavoidable pharmaceutical waste. Their study revealed that the reverse SC practices in PSC are complex and costly to implement compared with other industries since end-of-life items cannot be reused or resold. Viegas [32] reviewed RL in PSC comprehensively and addressed restrictions and some recommendations for future research in this area.

2.3 Global Health Organization Report Review

Reviewing the global annual reports is very useful as it allows to understand what has been achieved so far and explain the future strategies that will be adopted in the future. It's a rich source of information highlighting the global directions and focus of the HSC. Tatham & Pettit [11] examined the available report for The TOP 14 Humanitarian agencies (UNICEF, WFP, UNHCR, WHO, UNDP, OCHA, VWI...). It has been noticed that the majority of global organizations didn't indicate the RL in their reports and only very limited documents discuss about the RL as a tool of sustainable supply chain. We understood that there is limited attention given to RL concept. To deep dive, (Peretti, Thatam, Wu and Sgarbossa)[11] reviewed all the post mission reports held on the IFRC field data base for a three-year period (2011-2013). They have examined 116 reports focusing on single operations conducted word wide by IFRC. Above authors advised that only 25% of operational reports include subjects linked to the RL. Which was expected as it's purely an operational concept. It's interesting to highlight that the main discussions were around donation activities and reconditioning.

2.4 Practical insight from interviews & questionnaires

We have conducted informal calls/interviews and shared questionnaires by email beside twenty-five humanitarian supply operations leaders working at global health alliance and big pharma companies. The objective is to get their insight from their experience and personal perspective. For confidentiality reason, the participants accepted to share their thoughts under the condition of remaining anonymous.

Below questions were used to conduct discussion:

1. What do you know about the Reverse logistic?
2. Does your agency/company use the RL practice? Or plan to do it in the future?
3. What are the challenges & constraints of applying the RL to the HSC?
4. What are the opportunities & benefits of applying the RL to the HSC?

The feedbacks collected from the twenty-five participants were similar and confirming the conclusion of few papers of the state of art. For the first question, 100% of participants are aware of the big potential that RL can bring to the HPSC. They have highlighted its green contribution to the environment. Also, they confirmed that it reinforces the HPSC resilience. Furthermore, it can be an excellent saving generator by reallocation the excess stock to other beneficiaries. Coming to the second question, 100% of participants confirmed that the RL was not planned in the previous humanitarian operations as per the current supply chain agreement. The responsibility of pharma companies & Humanitarian partners stopped once the donated order arrived at the recipient countries. Also, Certain beneficiaries consider the concept of RL against the donation notion. Hence, they haven't stipulated clear arrangement in the contracts to manage sensibilities between parties. The question 3 & 4, participants insights are summarized on Figures 2 & 3.

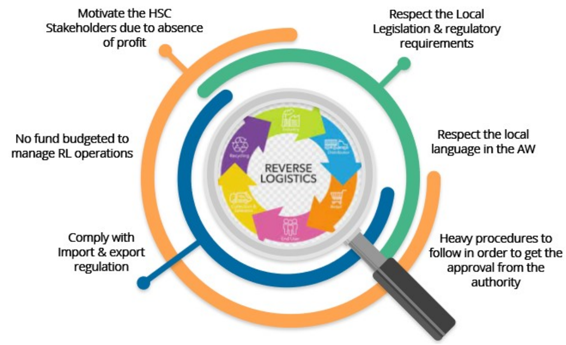

Figure 2: Challenges & Constraints

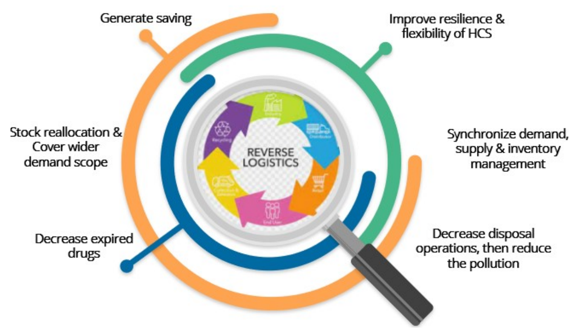

Figure 3: Opportunities & Benefits

This paper is one of the first research contributions in which a cooperative decision making has been developed & tested in Humanitarian supply chain context. Prior to this paper, a limited number of articles examined the win-win relationship between the HSC members. We noticed also that the humanitarian agencies need to share more experiences & lessons to develop operations in humanitarian supply chain. The investigated agreement is capable to establish climate of trust for HSC stakeholders, empower the reverse logistic and improve the profitability of the total chain.

5. HPSC NEW MODEL DESCRIPTION

We establish a two-echelon Humanitarian supply chain model constituted by pharmaceutical vendor and Humanitarian logistic provider. We consider

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the total shelf-life is constant and the forecast trend is dynamic. To avoid stock out situation, the demand planners of pharma suppliers build and maintain the most accurate demand using the statistical forecast system and the HLP give the green light to the pharmaceutical vendor to deliver the order quantity Q_i at the start of the monthly cycle process based on the replenishment schedule already defined inside the frozen horizon. We consider the pharmaceutical company follow closely the stock consumption at HLP warehouse based on the realized demand at defined time. Then, return Q_r and redistribute it to a secondary country to reduce waste items and avoid legislation penalties. Furthermore, to motivate the Humanitarian logistic provider to return excess products, the pharmaceutical company provide incentive and share tax risk with HLP.

Scientific Notations:
The scientific notations used are listed in Table 1. The exhibitors "nc" and "co" denote the game theory' model (non-cooperative and cooperative) respectively. The optimum value of the variable is indicated by (*).

Abbreviation:

PC	Pharma company
HLP	Humanitarian logistic provider
HPSC	Humanitarian pharmaceutical supply chain
GHP	Global Health partner
UP	Uniform probability
NP	Normal probability

Table 1: Mathematic Notations:
Financial Parameters:

$E(R_L)$ HLP expected revenue function
$E(R_p)$ PC expected revenue function
C_P Cost of good of PC
G_p GHP Gosse price purchased from PC
K_s HLP Keeping/storage cost for overstocking drugs
L_{AM} Logistic cost per unit for delivering drug to alt country
R_v Remuneration value obtained by the HLP from GHP
I_{AM} GHP Incentive given to PC by delivering drug to alternative country
T_E Environment Tax imposed by Government to HLP in case of product disposal
£ Rework expense
T_{WO} Tax write-offs by redistributing the inventories to alternative country.
D Destruction cost for each unit of expired medication
S Stock out penalty as the product is lifesaving. It's shared between PC following α ratio & HLP following α' ratio. It should respect the condition α'+ α =1

Forecast & Time Parameters:

P The random prevision forecast that follows probability density function f(x) and cumulative distribution function F(x)
P_r Realized prevision at time T = SL' ($0 \leq SL' < SL$) that follows probability density function $f(x_{SL})$ and cumulative distribution function $F(x_{SL})$
SL Pharma product total shelf-life
SL' Min accepted SL for redistribution within (0, SL) period

Variables to be optimized

Q_i Initial order quantity placed by HLP
Q_r Returned quantity decided at time t = SL'

The main idea of the proposed model is to give more responsibility to the pharmaceutical companies & the global health agencies to keep control on inventory management at recipient countries and put in place the necessary action plan to remediate.

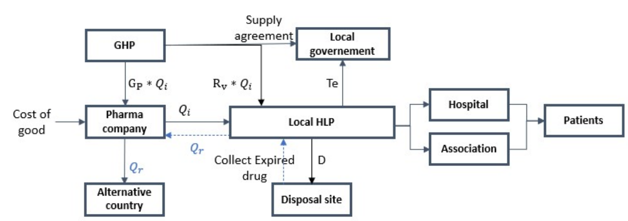

Figure 4: Proposed HPSC model

Figure 4 illustrates the architecture of the proposed model. We suggest below responsibility configuration:
The Global health institution:
- ✓ Build the humanitarian network and supply mechanism
- ✓ Collect & transfer the fund
- ✓ Develop contractual agreements based on the offers made by suppliers through their tendering processes Document manufacturer commitments to the mechanism
- ✓ Manage and coordinate requests for access to Medicines
- ✓ Act as the Verification Body for all procurement operations

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- ✓ Lead the annual monitoring of the mechanism implementation in collaboration with partners

Pharmaceutical company:
PC as vendor can play a key role by managing critical functions as Demand & supply planning, Production planning and logistic operation. This is to take the advantage of the large experience of pharma companies in commercial business on those functions. Also, because they are the owner of the medicine brands. They have a deep understanding of the ins and outs of regulatory processes for each country.

Demand planning: The main responsibilities of the vendor are:

- ✓ Perform the demand data analytics based on the data received from the GHP alliance
- ✓ Manage the statistical forecast for the drugs with low volatility demand and generate regular forecast on a monthly and rolling basis for dynamic products
- ✓ Define product requirements on a 24-36 monthly rolling forecast for production scheduling
- ✓ Define a 5-year long range volume forecast for additional strategic planning
- ✓ Monitor the Forecasting accuracy efficiency in monthly basis and measured through advanced statistical methods and incorporates market intelligence and other exogenous variables to predict future product demand trends

Supply Planning assurance: Pharma supplier to manage the replenishment inventory process.

- ✓ Production Plan: Vendor to develop the production plans to satisfy finished goods needs
- ✓ Logistic operations: Once production plans are completed, products are timely shipped to the appropriate country
- ✓ Master data management: Setup & Maintain material master data (Transportation Lanes & Product Master fields)
- ✓ Regulatory update: co-ordinate the new launch & product change management
- ✓ Reverse logistic: Lead the process to get back the excess stock, recondition it and redistribute it to alternative countries

Local Humanitarian logistic provider (recipient countries):

- ✓ Give the green light to the vendor to deliver the orders based on the agreed schedule
- ✓ Share the inventory update with pharma supplier following the calendar
- ✓ Manage all logistic functions (transport, custom clearance, product local release, warehousing, distribution…)
- ✓ Distribute the donated order within local hospitals & associations network
- ✓ Manage disposal process for expired medicines following
- ✓ Contribute to the reverse logistic process.

The temporal sequence of shelf-life evolution in the proposed model is represented in Figure 5:

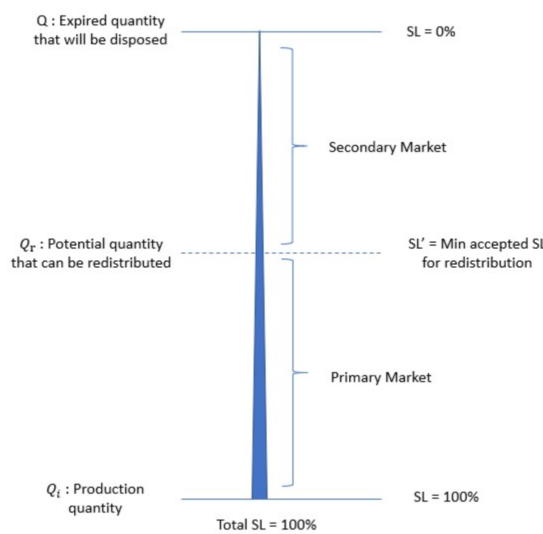

Figure 5: Medicines Shelf-life evolution

The flowchart for both "non-cooperative" & "cooperative" approaches is illustrated in Fig 7 to summarize the interaction between the HPSC members. Figure 6 represent the flowchart legend to provide information about the colors and symbols that have been used in the diagram.

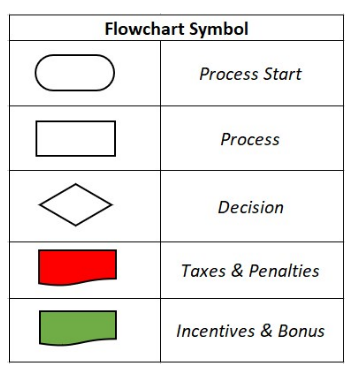

Figure 6: The flowchart legend

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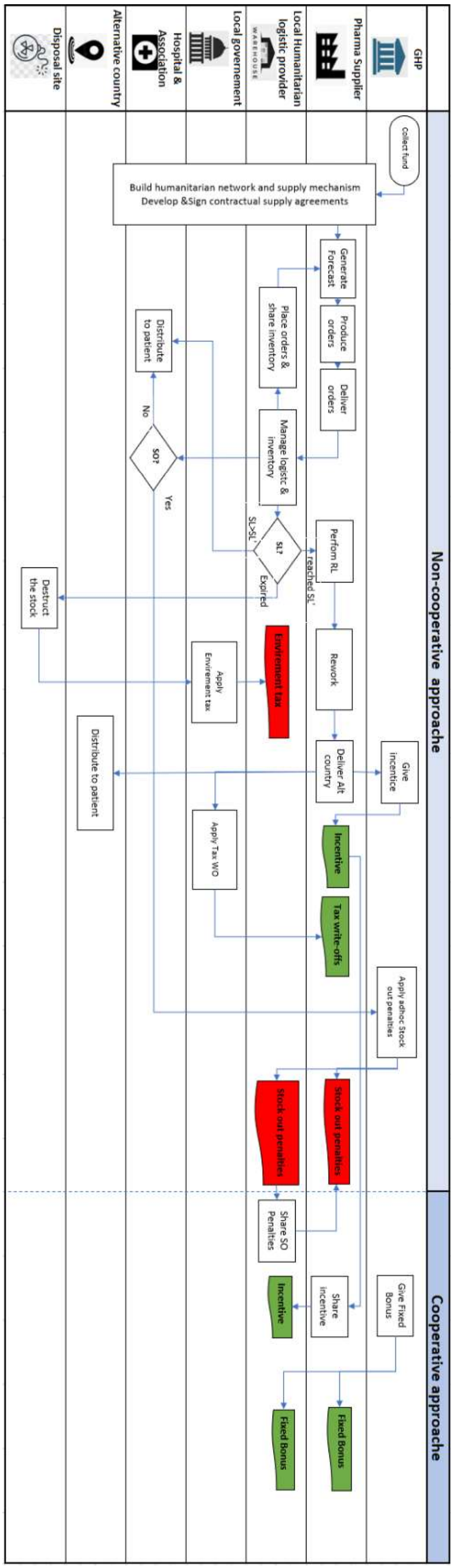

Figure 7: Flowchart of non-cooperative & cooperative

6. HPSC NEW MATHEMATIC MODEL DESCRIPTION

4.1 Non-cooperative Model:

In the context of non-cooperative model, each HPSC actor is the owner of the optimization decision to maximize his revenue. The HLP is considered as leader at (t = 0) as he determines the volume to be ordered Q_i^*. The vendor concludes on returned quantity Q_r^* at time t = SL' (0<SL'<SL) to lower the write-off costs. The expected revenue function of the HLP at time t = 0 is calculated as following:

$$E\left(R_L^{nc}(Q_i)\right) = \mathrm{R_v}\, E[min(Q_i, \mathrm{P})] - \mathrm{K_s} E[max(0, Q_i - \mathrm{P})]$$
$$- \alpha' SE[max(0, \mathrm{P} - Q_i))] - (D + \mathrm{T_E}) E[max(0, Q_i - \mathrm{P})]$$

Where the first term shows the total remuneration obtained by the GHP by distributing the medicines to the association & hospital that varies because of forecast volatility. The second term expresses the keeping cost for overstocking items. The third term states the stock out penalties per unit for the HLP. The last term states the destruction cost and the environment tax applied by governments for each expired unit.

Demonstration:

Let 's assume:

$\sigma \in [0,1]$ ➔ $Min(Q_i, P) = \sigma Q_i + (1 - \sigma) P$

$Max(0, Q_i - P) = (1 - \sigma)(Q_i - P)$

$Max(0, P - Q_i) = -\sigma(Q_i - P)$

$\delta = 1 - \sigma$ ➔ $Min(Q_i, P) = Q_i - \delta(Q_i - P)$

$Max(0, Q_i - P) = \delta\left(Q_i - P\right)$

$Max(0, P - Q_i) = (\delta - 1)(Q_i - P)$

We consider:

$U = Q_i - P$ ➔ $Min(Q_i, P) = Q_i - \delta U$

$Max(0, Q_i - P) = \delta U$

$Max(0, P - Q_i) = (\delta - 1) U$

We apply above result to the expectation equations:

$E(Min(Q_i, P) = E(Q_i) - \delta E(U) = Q_i - \delta E(U)$

$E\left(Max(0, Q_i - P)\right) = \delta E(U)$

$E\left(Max(0, P - Q_i)\right) = \delta E(U) - Q_i + E(P)$

The revenue function is calculated as follow:

$$E(R_L^{nc}(Q_i)) = R_v\left(Q_i - \delta E(U)\right) - K_s\,\delta E(U) - \alpha' S\left(\delta E(U) - Q_i + E(P)\right) - (D + T_E)\delta E(U)$$

$$E(R_L^{nc}(Q_i)) = Q_i(R_v + \alpha' S) - \delta E(U)(R_v + K_s + \alpha' S + D + T_E) - \alpha' S E(P)$$

As $\delta E(U) = \int_{-\infty}^{Q}\left(Q_i - P\right) f_P(Y)d(Y)$

Then the revenue function of HLP is:

$$E(R_L^{nc}(Q_i)) = Q_i(R_v + \alpha' S) - (R_v + K_s + \alpha' S + D + T_E)\int_{-\infty}^{Q}(Q_i - P) f_P(Y)d(Y) - \alpha' S E(P) \quad (1)$$

The second derivative of the HLP expected revenue function, with respect to Q_i, is:

$$\frac{\partial^2 E(R_L^{nc}(Q_i))}{\partial Q_i^{\,2}} = -(R_v + K_s + \alpha' S + D + T_E) f_P(Q_i) < 0$$

The expected revenue of the HLP is concave in Q_i as the second derivative is negative. The Q_i optimal is calculated after we zeroed the first derivative of HLP revenue function.

$$\frac{\partial E(R_L^{nc}(Q_i))}{\partial Q_i} = (R_v + \alpha' S) - (R_v + K_s + \alpha' S + D + T_E) F_P(Q_i^*) = 0$$

$$F_P(Q_i^*) = \frac{R_v + \alpha' S}{R_v + K_s + \alpha' S + D + T_E}$$

The optimal order quantity of Humanitarian logistics provider at t = 0

$$\mathbf{Q_i^*} = \mathbf{F_P^{-1}}\left(\frac{\mathbf{R_v + \alpha' S}}{\mathbf{R_v + K_s + \alpha' S + D + T_E}}\right)$$

The expected revenue function of the HLP at time t = SL' is calculated as following (Eq 2):

$$\begin{aligned} E(R_L^{nc}(Q_r)) &= R_v\, E[min(Q_i - Q_r, P_r)] \\ &- K_s E[max(0, (Q_i - Q_r) - P_r)] \\ &- \alpha' S E[max(0, P_r - (Q_i - Q_r))] \\ &- (D + T_E) E(max(0, (Q_i - Q_r) - P_r)) \end{aligned} \quad (2)$$

The first term shows the total remuneration obtained at a time of t = SL' by GHP by distributing the minimum quantity $(Q_i - Q_r)$ Vs P_r to the association & hospital that varies because of forecast volatility. The second term expresses the storage cost. The third term is the stock out penalties per unit and the last term states the destruction cost and the environment tax applied by governments for each unit of expired medications that varies because of forecast fluctuation.

The expected revenue of the pharmaceutical company at time t = SL' ($0 \leq SL' < SL$) is calculated as following (Eq 3):

$$E(R_P^{nc}(Q_r)) = (G_p - C_P)Q_i - L_{AM}Q_r - £Q_r + Q_r I_{AM} + T_{WO}Q_r - \alpha S E[max(0, (Q_i - Q_r) - P_r)]$$

The first term shows the margin obtained by selling the products to the GHP following the contract condition. The second term indicates the logistic cost for delivering the overstocking items before expiration to repack them and redistribute them in the secondary country. The third term states the rework expense. The fourth term represents the incentive obtained from GHP by redistributing the medicines to the secondary country. The fifth term corresponds to the tax write-offs by redistributing Q_r to alternative country. The last term indicates the stock out cost per unit for Pharma company.

$$E(R_P^{nc}(Q_r)) = (G_p - C_P)Q_i + Q_r(I_{AM} + T_{WO} - L_{AM} - £) - \alpha S E[max(0, (Q_i - Q_r) - P_r)] \quad (3)$$

The second derivative of the pharmaceutical company expected revenue function, with respect to Q_r, is:

$$\frac{\partial^2 E(R_P^{nc}(Q_r))}{\partial Q_r^{\,2}} = -\alpha S\, f_{Pr}(Q_i - Q_r) < 0$$

It shows the concavity of the pharmaceutical company expected revenue with respect to Q_r.

$$\frac{\partial E(R_P^{nc}(Q_r))}{\partial Q_r} = (I_{AM} + T_{WO} - L_{AM} - £) - \alpha S\left(\frac{\partial\left(\int_{-\infty}^{Q_i - Q_r}(Q_i - Q_r) f_P(Y)d(Y) - \int_{-\infty}^{Q_i - Q_r} P_r\, f_P(Y)d(Y)\right)}{\partial Q_r}\right)$$

Let's assume: $A = Q_i - Q_r$

$$\frac{\partial E(R_P^{nc}(Q_r))}{\partial Q_r} = (I_{AM} + T_{WO} - L_{AM} - £) + \alpha S \frac{\partial(\int_{-\infty}^{A} F_{Pr}\, d(Y))}{\partial Q_r}$$

$$\frac{\partial E(R_P^{nc}(Q_r))}{\partial Q_r} = (I_{AM} + T_{WO} - L_{AM} - £) + \alpha S F_{Pr}((A)$$

$$F_{Pr}^{-1}\left(\frac{L_{AM} + £ - I_{AM} - T_{WO}}{\alpha S}\right) = A^*$$

As: $A^* = Q_i^* - Q_r^*$

$$Q_r^* = Q_i^* - F_{Pr}^{-1}\left(\frac{L_{AM} + £ - I_{AM} - T_{WO}}{\alpha S}\right)$$

4.2 Non-cooperative Model:

To ensure the strategic goal of humanitarian operations and to follow the performance of it supply chain, we propose in this model a new combination of variable incentive, fixed bonus, and shortage/tax risk-sharing to ensure all stakeholder profitability.

The contract including three parameters:

- ✓ **B** Contractual Fixed bonus given by GHP. It's allocated by unit distributed and It's shared between Pharma company following **μ** ratio & HLP following **μ'** ratio. It should respect the condition **μ'**+ **μ** =1. The objective is to create synergy between both parties.
- ✓ **β** Adhoc Incentive sharing. The objective of this parameter is to motivate the HLP to collect the excess stock before expiration to redistribute in alternative country and avoid drug destruction and then avoid environment tax. In this model, we propose that the HLP will support 100% of environment tax as it's a direct consequence of not adhering to the process.
- ✓ **Ω** Tax sharing rate for Stock out. By redistributing the excess stock, the HLP may face stock out situation in case of demand increase which will lead to pay stock out penalties. Therefore, the pharma-supplier contributes to the HLP shortage risk and undertakes Ω percent of its shortage costs.

The expected benefit function of HLP at t = 0 is calculated as following (Eq 4):

$$E(R_L^{co}(Q_i)) = (R_v + B\mu')\,E[min(Q_i, P)] - K_s E[max(0, Q_i - P)] - (1-\Omega)\alpha' S E[max(0, P - Q_i))] - (D + T_E)E(\max(0, (Q_i - P)) + \beta\, I_{AM} Q_r \quad (4)$$

Where the first term shows the total remuneration and monthly bonus obtained by the GHP. The second term expresses the keeping cost for overstocking items. The third term states the stock out penalties and PC contribution. The fourth term states the destruction cost and the environment tax applied by governments for each expired unit. The last term is the adhoc incentive sharing.

After similar above demonstration, we obtain:

$$Q_i^* = F_P^{-1}\left(\frac{R_v + B\mu' + (1-\Omega)\alpha' S}{R_v + B\mu' + K_s + (1-\Omega)\alpha' S + D + T_E}\right)$$

The expected revenue of the pharma-supplier at time t = SL' is calculated as following (Eq 5):

$$E(R_P^{co}(Q_r)) = (G_p - C_P)Q_i - L_{AM}Q_r - £Q_r + Q_r I_{AM}(1-\beta) + T_{WO}Q_r + B\mu Q_r - (\alpha + \Omega\alpha')SE[max(0, (Q_i - Q_r) - P_r)] \quad (5)$$

Where the first term defines pharmaceutical-supplier margin, the second term corresponds to the logistic cost for collection. The third term represents the rework cost. The fourth term is the adhoc incentive and how is shared with HLP. The fifth term is the tax WO. The sixth term is the bonus given by GHP. The last term represents the stock out tax and shared stock out tax ratio with HLP.

After similar above demonstration, we obtain:

$$Q_r^* = Q_i^* - F_{Pr}^{-1}\left(\frac{L_{AM} + £ - I_{AM}(1-\beta) - T_{WO} - B\mu}{(\alpha + \Omega\alpha')S}\right)$$

7. PROOF OF CONCEPT: NUMERICAL ANALYSIS

The objective of this section is to assess the relevance of the proposed mathematic model by exploring & analyzing a set of numerical scenarios. Taking into consideration that the humanitarian pharmaceutical forecast is stochastic, we will consider a high forecast error demand at t = 0. For this reason, we are evaluating both uniform & normal probability distribution model through three forecast configuration cases. The experimental set of data has been defined & estimated based on real examples taken from global donation report published by some global health institutions [11] and from the WHO recommendation:

- ✓ Pharmaceutical companies are usually selling the medicines to the GHP with low margin. In some cases, the declared value of a medicine donation should be based on the wholesale price of its generic equivalent in the recipient country[10].
- ✓ All costs of international and local transport, warehousing, port clearance, quality testing and appropriate storage and handling should be paid by the donor. We are applying the same prices as commercial area[10].
- ✓ Certain pharmaceutical companies might be able to enjoy improved cash flow through an enhanced tax deduction for the charitable donation of inventory[33].
- ✓ All drug donations should be based on an expressed need and be relevant to the disease pattern in the recipient country. Drugs should not be sent without Prior consent by the recipient[10].
- ✓ After arrival in the recipient country all donated drugs should have a remaining shelf-life of at least one year. An exception may be made for direct donations to specific health facilities[10].

Comparison analysis between "non-cooperative" & "cooperative" model: Uniform distribution model

Two levels of analysis have been conducted under UP. The first part is basically a comparison of "non-cooperative" & "cooperative" decision making approaches by keeping the same forecast and same data. In the second part, the forecast has been considered as constant value and cooperative parameters B, β and Ω have been increased through three instances to follow their influence on variables $Q_r^*, E(R_L)$ *and* $E(R_p)$. Table 2 illustrates the parameters used in the simulation to analyze the difference between both structures. Table 3 shows the output of the mathematic model calculation for the three scenarios.

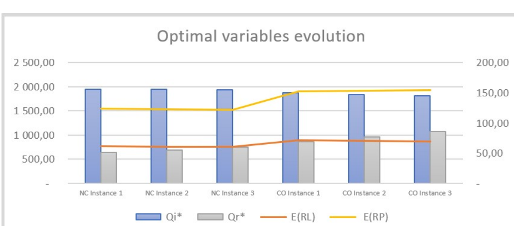

Figure 8: Optimal variable development

By adopting the cooperative mechanism, we noticed that a good synergy has been created between PC & HLP. The numerical analysis revealed that the proposed model can coordinate the whole humanitarian pharmaceutical supply chain and increase both HLP and PC expected income. The cooperative model suggests decreasing the initial order quantity Q_i^* by 5%. However, with the incentive & risk sharing approach, the expected HLP revenue increased by 16%. This is what motivate the HLP to commit to the reverse logistic process and increase the returned quantity by 39%. Consequently, the expected revenue of PC increased by 34%. The quantity returned Q_r^* is different in all instances and depends on forecast behavior.

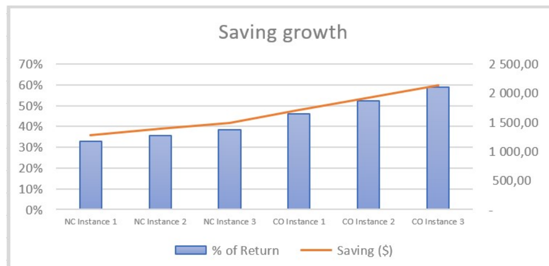

Figure 9: Saving increase

Saving rate increased by 39% behind redistributing Q_r^* to alternative countries. This concept created WIN-WIN relationship between both parties. The quantity kept at country level reduced by 30%. Thus, the HLP will reduce the disposal activities and will minimize paying environment penalties which constitute a good cost avoidance opportunity for them.

Figure 10: Cost avoidance increase

Moreover, we investigate in table 5 the effect of (B, β and Ω) changes on both optimal quantities (Q_i^*& Q_r^*) and expected revenue for HLP & PC. Fig 11 shows that once the GHP & PC increase their incentives and their contributions on taxes/penalties of HLP, the expected income for both partners grow significantly. It confirms that the cooperative approach creates trust between HLP & PC. The HLP will adopt a more rational behavior as he will be in safer financial situation. The cooperative approach will cover the HLP from the risks and taxes. Fig 12 shows that there is a net correlation

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respectively between α', Q_i^* and $E(R_L)$. More the HLP participate to the SO penalty, more the initial quantity ordered is high. It's an expected practice as to avoid the SO, HLP order more quantity. Also, we compare and analyze the effect of changes in governmental environment tax on Q_i^* and $E(R_L)$. Fig 13 shows that the HLP adopt a conservative approach to decide on order quantity Q_i^* when the environment tax T_e is significant.

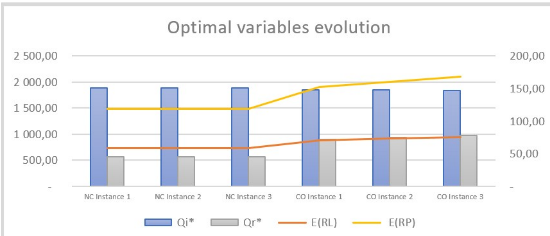

Figure 11: Optimal variable development

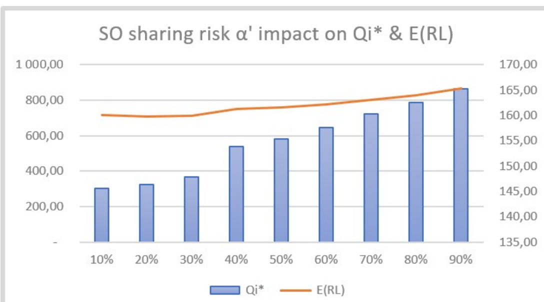

Figure 12: Evolution of Q_i^* & $E(R_L)$ following α' variation

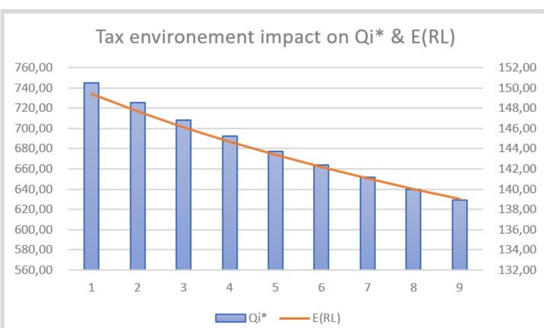

Figure 13: Evolution of Q_i^* & $E(R_L)$ following Te variation

Comparison analysis between cooperative & non-cooperative model: Normal distribution model

The objective is to test the cooperative model under NP and different dataset. we select other realistic parameters that satisfy the assumptions of enhancing HPSC actors expected revenue compared to the non-cooperative structure for the three instances.

The overall outcome of the analysis is similar to UP in the previous section. The cooperative mechanism implementation improved the synergy inside the HPSC ecosystem. The numerical analysis highlighted that the proposed model allows to reach the optimum quantity and increase both HLP and PC expected revenue. The cooperative structure in NP suggests decreasing the initial order quantity Q_i^*. However, the expected HLP revenue increased by 16% as the returned quantity increased from 12 unit to 47 unit. In the non-cooperative decision model, the expected revenue $E(R_L)$ is higher than $E(R_P)$. While by adopting the cooperative decision model, the trend is reversing and the $E(R_P)$ exceed $E(R_L)$. This is confirming that by investing a small amount on tax sharing & incentives, PC doubled its revenue.

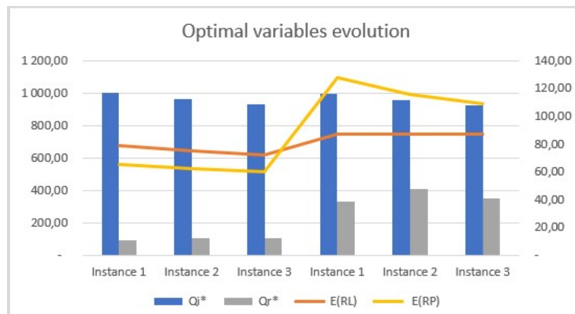

Figure 14: Optimal variable development

Figure 15: Saving increase

Fig 15 shows that saving rate quadrupled following Q_r^* increase. Furthermore, as shown in Fig 16, the quantity kept at country level reduced by 36%. Thus, the HLP will generate cost avoidance by reducing disposal activities and will minimize paying environment penalties.

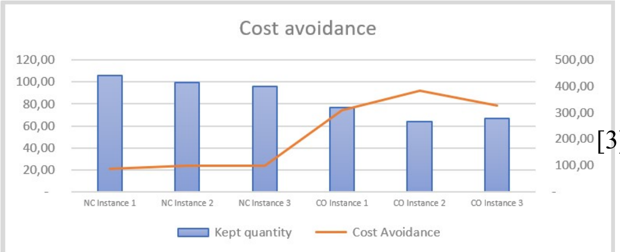

Fig 16: Cost avoidance increase

8. CONCLUSION

We have developed in this paper a cooperative decision-making approach to support the reverse logistic process implementation in the humanitarian PSC. The objective is to reduce the pharmaceutical waste through an efficient inventory management at recipient country and reduce it impact on environment. The contribution of this paper is to define a mechanism to convince & motivate the stakeholders to actively participate to the reverse logistic process. Numerical investigations reveal that the proposed approach can coordinate the whole HPSC and increase both PC & HLP expected profit. Our proposed model can help humanitarian agencies to decrease leftover & expired medicines related cost. Due to the uncertainty of demand, forecasting errors that lead to high financial losses in such chains are not avoidable. The proposed model can be attractive from a managerial point of view by considering the reducing pharmaceutical waste scheme to redistribute excess medications in the secondary market. Moreover, deciding on the correct returned quantity is one of the sensitive decisions in this scheme, and any wrong decision can lead to stock out situation in the principal country. Our proposed model helps humanitarian logistic provider to decide about quantity to be collected. Furthermore, the proposed coordinated model incentivizes the HLP to participate in the scheme. In this paper, the proposed model is limited to a basic ecosystem configuration (one PC collaborating with one HLP). In the future research we will extend the scoop by considering "multiple players". Also, we will explore other probabilistic distribution model.

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