Mitigation of Optimized Pharmaceutical Supply Chain Disruptions by Criminal Agents

Abhisekh Rana[1], Hamdi Kavak[1], Andrew Crooks[2], Sean Luke[1], Carlotta Domeniconi[1], and Jim Jones[1]

[1] George Mason University, Fairfax VA 22030 USA
{arana6,jjonesu,sean,cdomenic}@gmu.edu
[2] University at Buffalo, Buffalo NY 14261 USA
atcrooks@buffalo.edu

Abstract. Disruption to supply chains can significantly influence the operation of the world economy and this has been shown to permeate and affect a large majority of countries and their citizens. We present initial results from a model that explores the disruptions to supply chains by a criminal agent and possible mitigation strategies. We construct a model of a typical pharmaceutical manufacturing supply chain, which is implemented via discrete event simulation. The criminal agent optimizes its resource allocation to maximize disruption to the supply chain. Our findings show criminal agents can cause cascading damage and exploit vulnerabilities, which inherently exist within the supply chain itself. We also demonstrate how basic mitigation strategies can efficaciously alleviate this potential damage.

Keywords: Pharmaceutical Supply Chains · Criminal Agents · Evolutionary Computation · Mitigation

1 Introduction and Background

Supply chains are a critical part of modern society and the operation of the world economy. Recently, the COVID-19 pandemic has brought supply chains and disruptions to them front and center. These disruptions have not only led to massive shortages in critical goods such as semi-conductors, personal protective equipment and medical supplies, but also impacted the roll out of vaccinations [3, 12].Though the effects of disruptions to supply chains by natural disasters have been well studied (e.g., [6]), potential disruptions to their operations by nefarious criminal agents remains an area of limited research [9].

In this paper, we discuss our initial study of the effects of disruptions by a criminal agent to pharmaceutical supply chains and ways to mitigate their impact. We have developed a discrete event simulation model of a supply chain for drug production drawn from real systems in the pharmaceutical industry (e.g., [7, 14, 13]). Our ultimate goal is to build an agent-based model of a criminal organization and use it to disrupt the supply chain, then develop mitigation or protection strategies against this attack. As an initial step, we are using an optimizer to search for ways to maximize damage to the supply chain and analyze its recovery. This paper discusses results from this initial approach.

Given the importance of supply chains, it should not be surprising that efficient supply chain management has received a lot of attention, from mitigating the negative impacts of natural disasters, such as the current COVID-19 pandemic, and attacks by criminal or terrorist organisations (e.g., [6, 9, 3, 17]). In order to explore the effect of these different scenarios, supply chains have long been modelled and studied via simulation (e.g., [5]). Much of this work has focused on the supply chain itself, including the identification of potential bottlenecks, which represent the most vulnerable points in the chain [10]. Supply chain optimization is also another major research area. For example, in the pharmaceutical industry efforts have been made to balance capacity and future demand [14]. There is also a growing interest in disruptions to supply chains from external factors such as criminal organisations (e.g., [2, 9]). These disruptions include adulteration to key materials, physical attacks or theft of key ingredients and cyber-attacks on the software used in the logistics of the supply chain [7, 14, 17, 13].

To the reader it might seem obvious that there exists a significant risk stemming from supply chain disruptions to the operation of the global economy and individual companies. However, it has been argued that up to 75% of Fortune 500 companies, which include the major pharmaceutical companies, remain unprepared to handle disruptions to their supply chains [18]. Having basic mitigation strategies such as access to third party manufacturers and secondary materials suppliers, in case of disruptions to delivery from your main provider, have been shown to protect supply chains from disruptions [18, 15]. In the remainder of this paper we first present our supply chain simulation model in Section 2, we then discuss the results (Section 3), which include mitigation strategies. We then conclude with a summary and discussion of areas for further work (Section 4).

2 Methodology

This paper proposes to analyze supply chains and their bottlenecks using various computational modeling tools and technologies. We utilize discrete event simulation to model a simplified pharmaceutical supply chain [7, 14] as our case study (Section 2.1). We then simulate attacks (Section 2.2) on this supply chain by a criminal agent (Section 2.3) whose aim is to maximize damage to its operations. The supply chain is provided with mitigation strategies to protect itself from such attacks. Details of our methodology are outlined in the following subsections.

2.1 Supply Chain Model

Our example pharmaceutical supply chain is illustrated in Figure 1. This model represents a generic pharmaceutical company that purchases the materials required to produce drugs from a supplier pool (e.g., [7]). The resources available to the supplier pool to meet these purchase orders are assumed to be infinite. Thus,

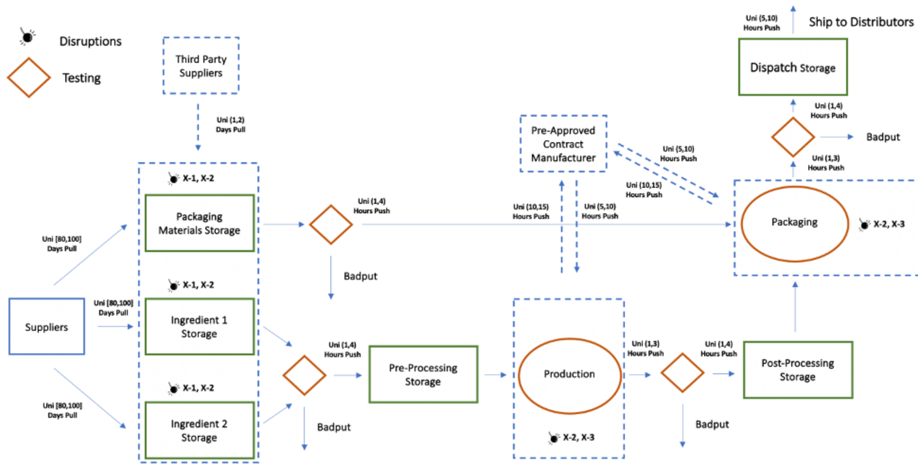

Fig. 1. A simplified version of a typical pharmaceutical supply chain.

a request for a purchase order for any material from the pharmaceutical company is always honored. There are three different types of materials the pharmaceutical company requires to produce its drugs and deliver them to its distributors: two separate ingredients that are combined to produce the actual drug and packaging materials used to package the drugs once production is completed. Once purchased, these materials are stored in separate storage facilities, all of which have a maximum capacity of 1000 units. If the number of units of the materials in any of the storage facilities falls below the critical threshold of 350 units, a restocking request is sent to the supplier pool for 800 additional units. The time to fulfill this restocking request is modeled using a uniform distribution between 80 and 100 hours. It should be noted these numbers and several of the values chosen below were arbitrarily chosen but mimic the basic principles and dynamics seen within supply chains. In future work, these values could be parameterized from real-world data.

Once the materials arrive at their respective storage facilities, they are separated into batches of 20 units and sent for testing, which is the norm in such supply chains [14]. The testing time for each batch is modeled using a uniform distribution between 1 to 4 hours. For each batch, a certain number of units fail at testing and are discarded as badput. The number of failed units in each batch is also modeled using a uniform distribution between 1 and 6 units. After testing, the two different ingredients are transferred to a pre-processing storage facility which has a capacity of 1000 units. Two batches, each containing 10 units of the two ingredients, are then combined during the production phase to produce 10 units of the actual drug. The time to produce these 10 units of the drug is modeled using a uniform distribution between 1 to 3 hours. Once a batch of drugs is produced, they are again sent for testing. The testing time for a batch follows the same uniform distribution as for the original materials. In each batch, the number of failed units is discarded as badput and is taken from

Table 1. Type of disruption and its effect on the supply chain.

X-Code	*Disruption Type*	*Effect on Supply Chain*
X-1	Adulteration of materials secured from the supplier pool	Failure rate increases during testing
X-2	Physical attack on storage facilities	Stored inventory destroyed at facility
X-3	Cyberattack in processing facilities	Processing halted at facility

a uniform distribution between 1 and 3 units. The tested drugs are then stored in the post-processing storage facility, which also has a capacity of 1000.

The next step in the supply chain is to package the drugs [7]. Batches, which include 10 units of packaging material and 10 units of the completed drugs, are packaged together and sent to the dispatch storage facility. The time for the packaging of each batch is modeled using a uniform distribution between 1 to 3 hours. Similar to the production phase, batches of 10 units of the packed drug are tested; units that fail testing are discarded from the batch as badput. The units that pass testing are moved to the dispatch storage facility for collection by the distributors. The dispatch storage facility has a capacity of 1000 units. Once the inventory of packaged drugs at the dispatch storage facility exceeds 50 units, a request is sent to the distributors to collect the drugs to be passed on to the end customer. The time for this pickup request to be fulfilled is modeled using a uniform distribution between 5 to 10 hours. For our simulation, once a drug has been picked up by the distributors, the drug is considered sold and leaves the system.

2.2 Disruptions

As noted before, supply chains can be disrupted in a number of ways. In this paper, we model the effects of three different types of disruptions, which can be executed by the criminal agent [7, 17]. There are five separate points in the supply chain, marked by a bomb symbol in Figure 1, where these disruptions can occur. These disruptions are represented using X-Codes (i.e., X1), and the type of disruption (X-Code) and its effect on the supply chain are detailed in Table 1. The effect and duration of each of these disruptions at different points in the supply chain are directly related to the resources allocated to the criminal agent, which is detailed in the next section.

2.3 The Criminal Agent

In this paper, we model a generic and lone criminal agent who can directly affect the supply chain via the disruptions outlined above. The design of the criminal agent is detailed in Figure 2. The criminal agent is allocated a fixed amount of resources, represented by a resource allocation vector (akin to money). The total amount of resources available to the agent is set to 1500. These resources can be allocated to disrupt the five points in the supply chain detailed in Figure 1. The allocation of these resources is represented by a vector of length

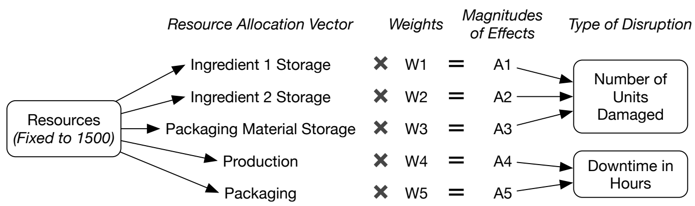

Fig. 2. Design of the criminal agent.

five (corresponding to the five potential disruption points). The first element in this vector represents the number of resources allocated to disrupt the ingredient one storage facility. Similarly, the other elements in the vector represent the resources allocated to disrupt the other four disruption points.

This resource allocation vector is then multiplied by a set of weights, represented by the weight vector, which equals one. These weights are used to quantify the effect on the supply chain from the resource allocation for each disruption at the corresponding five disruption points. Additionally, a lower weight results in a lower magnitude of disruption at each point. Thus, these weights can be changed to make certain points in the supply chain more difficult to disrupt (i.e., a point with heavy physical security). Once the resource allocation vector is multiplied by the weight vector, we obtain a vector that represents the magnitude of each disruption at the five different disruption points. The first three elements of this vector represent a disruption to the storage facilities. They measure the number of drugs destroyed or adulterated by a physical attack. The last two elements represent a cyber or physical attack on the production and packaging facilities. They disable the operation of the facilities and their effect is represented by the number of hours either facility is unable to produce or package any drugs. Using this design the criminal agent is able to directly interact and disrupt the operation of the supply chain. This is executed by optimizing the resource allocation vector while the elements of the weight vector remains fixed at 0.2.

2.4 Simulation and Optimization

The supply chain model was implemented using Python's SimPy [11] library and the optimization is carried out using the Optuna [1] library. Each simulation in this study is run for 6 months, representing a total of 3600 hours of simulation time. We measure the efficacy of the disruptions caused by the criminal agent using the total number of drugs sold by the supply chain during the simulation.

We use an optimization algorithm to find how the criminal agent might apply fixed resources, via the resource allocation vector, to attack the supply chain so as to minimize the number of drugs sold during the simulation period. Because the parameter space involved has no known derivative, we rely on the *CMA-ES* algorithm to accomplish this task [4]. CMA-ES is part of a family of sample-based optimization techniques collectively known as *evolutionary algorithms* [8]. Broadly speaking, CMA-ES starts with a sample of random candidate solutions to optimize. It then iteratively assesses the quality of each candidate solution, then performs resampling based on their quality to produce a new sample of candidates. In CMA-ES, the resampling is done by fitting a multidimensional Gaussian distribution over the samples warped according to their respective quality. The new samples are then randomly sampled under the distribution. By combining our supply chain model with our criminal agent, and by leveraging CMA-ES, in what follows we attempt to identify the main bottlenecks and the most vulnerable points in the pharmaceutical supply chain.

We also investigate the effects of adding mitigation strategies to the supply chain. There are two types of standard mitigation strategies made available to the supply chain, both based on using third-party suppliers or contractors [16]. For disruptions to the inventory storage facilities, when an attack destroys units stored, the supply chain has access to a third party supplier to quickly re-stock its goods. The restocking request is fulfilled at a faster rate than if secured from its regular supplier. This restocking request is triggered if the inventory at a point in the supply is depleted by amount 3X or greater than the average hourly depletion rate. A depletion in inventory of this size is used by the supply chain to determine an attack has occurred and a mitigation should be implemented. The second set of mitigations involve the production and packaging facilities. These mitigations are triggered when these facilities lie idle for more than 80 hours. This value is chosen since it is 4X greater than the max average idle time across 500 simulations. Thus, if the facility lies idle for longer than this time the supply chain assumes an attack has occurred. The mitigation involves outsourcing production or packaging to a third party. An additional, time delay is also added in order to model the extra time taken to transport the goods from the pharmaceutical companies facilities to the third-part facility and return the produced or packaged goods.

3 Results

In our first set of simulations, we explore the effect on the supply chain from a disruption by the criminal agent where all its resources are focused on a single disruption point. These simulations model a single disruption that occurs halfway through the 6-month simulation period. These simulations allows us to ascertain the weakest points in the supply chain. Figure 3 details representative sample simulations for the baseline model, which is a simulation without any disruption, and results for an attack at the five disruption points in the supply chain. It charts the total weekly drug sales during the entire simulation period. The dotted red line indicates the time the disruption took place. Correspondingly, Table 2 outlines the key statistics derived from running the simulations 500 times.

The first result of interest is the lag between the time the disruption occurs and its effect on the weekly drug sales between the packaging materials facility and the ingredient facilities. This lag is the due to the location of the facilities in the supply chain. The ingredient facilities are located at the beginning of the chain, thus the result of a disruption at these locations takes time to permeate through

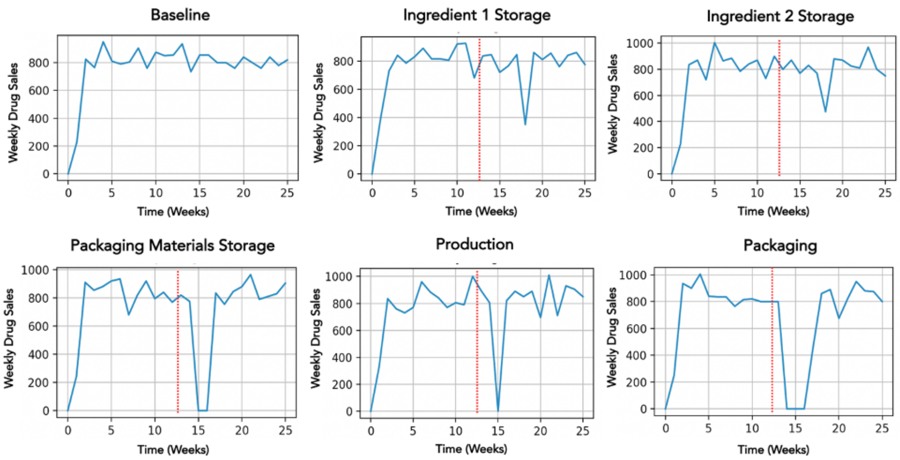

Fig. 3. Sample simulations for the baseline model, without any disruption, and attacks at the five main disruption points in the supply chain.

the network. In contrast, a disruption to the packaging materials facility, which is directly linked to the end of the supply chain, creates a more immediate and more damaging effect. The magnitude of this effect is larger since the packaging material facility also represents a bottleneck. Without access to packaging materials no drugs can be packaged and sold.

Table 2. Key statistics for the baseline model, without any disruption, and attacks at the five main disruption points in the supply chain.

Disruption Point	*Mean Drugs Sold*	*Std. Dev.*	*99% Confidence Interval*
Baseline	20947	211	[20971 - 20923]
Ingredient 1 Storage	20667	352	[20708 - 20626]
Ingredient 2 Storage	20635	392	[20680 - 20590]
Packaging Materials Storage	19358	276	[19390 - 19326]
Production Facility	19641	183	[19662 - 19620]
Packaging Facility	18283	158	[18301 - 18265]

It is also important to note that none of the 99% confidence intervals for the average drugs sold for the disruptions overlap with the baseline. Thus, all the disruptions implemented significantly affect the operation of the supply chain. Furthermore, the most vulnerable point in the supply chain was identified as the packaging facility. This is because it represents a bottleneck in the supply chain and is located at the end point.

Next, we utilize CMA-ES to optimize the resource allocation vector of the criminal agent (as discussed in Section 2.4). This allows us to not only analyze the best way for the criminal agent to attack the supply chain, but also determine whether causing multiple disruptions at the same time creates additional vulnera-

CMAES Single Attack *(Disruption Time Fixed)*

Disruption Time	1800 Hours
Optimal Resource Allocation	[60,18,61,37,1324]
Mean (Drugs Sold)	18647
STD	156
99% Mean Confidence Interval	[18634 – 18659]

CMAES Single Attack *(Disruption Time Optimized)*

Disruption Time	1800 Hours
Optimal Resource Allocation	[42,15,58,12,1373]
Mean (Drugs Sold)	18372
STD	176
99% Mean Confidence Interval	[18357 – 18386]

CMAES Two Attacks *(Disruption Time Optimized)*

Disruption Times	1202 & 2625
Optimal Resource Allocation	[22,15,242,59,32] [99,29,32,426,544]
Mean (Drugs Sold)	16390
STD	281
99% Mean Confidence Interval	[16357 – 16422]

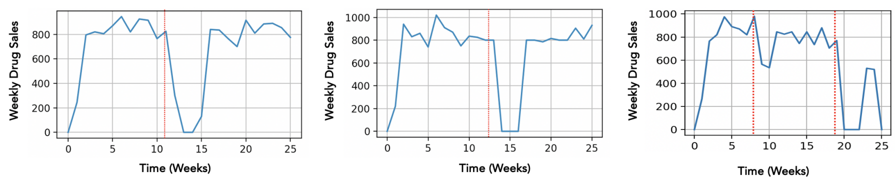

Fig. 4. Summary statistics and sample simulations for CMA-ES optimized disruptions.

bilities and therefore does more damage. For consistency with the previous results, we carry out this optimization at the same time as the attacks in the previous simulations and then pass the timing of the attack as a further parameter to the CMA-ES. This enables us to analyze whether there is an optimal time in the simulation to mount an attack.

We also study the effect of multiple attacks on the supply chain at different times using the same number of resources utilized for a single attack (i.e., 1500 as discussed in Section 2.3). Specifically, we focus on two attacks with the aim being to establish whether the first attack significantly weakens the supply chain so that a second attack creates a cascading effect and thus causes more damage. The results for 500 simulations is outlined in Figure 4. From the results (Figure 4) one can observe that the optimal resource allocation derived from using the CMA-ES optimizer allocates the majority of its resources to disrupting the packaging facility. This again illustrates the point that there exist bottlenecks in supply chains and bottlenecks further down the chain are the most vulnerable points. The mean 99% confidence intervals for the drugs sold during the simulation when the timing of the attack is fixed and optimized also do not overlap. Thus, we demonstrate that optimizing the timing of disruptions does greater damage. It is also clear from these results that distributing the resources of the criminal agent over two separate attacks does result in generating additional vulnerabilities to the supply chain and that there exists a cascading effect.

In our final set of experiments, we study the efficacy of mitigation strategies, outlined in Section 2.4, our rationale being that many companies are not geared towards supply chain disruptions [18]. However, our methodology could help alleviate this. Specifically, we use the single attack model optimized via CMA-ES with and without mitigation in place. The results for 500 simulations are detailed in Figure 5. From these results, one can observe that having adequate mitigation strategies in place protects the supply chain from disruptions. The mean 99% confidence intervals also do not overlap; thus, this result is significant.

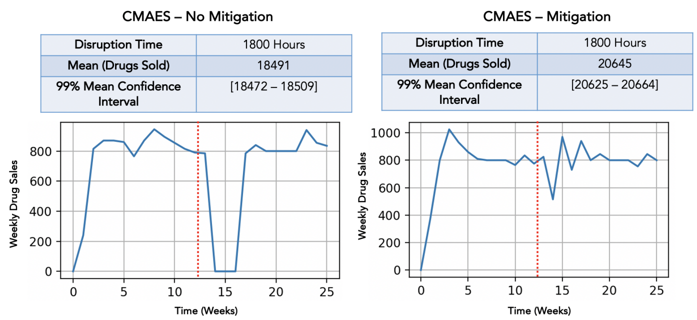

Fig. 5. Summary statistics and sample simulations for CMA-ES optimized disruptions with and without mitigation in place.

4 Summary and Outlook

In this paper we analyze the operations of a pharmaceutical supply chain and the effects on it from disruptions by a single criminal agent. We demonstrate how a supply chain can be effectively simulated via a discrete event simulation. We then construct a single simple criminal agent with fixed resources whose goal is to disrupt the supply chain. The design of the criminal agent allows it to interact with the supply chain and attack and damage key points within it. By studying the operation of the supply chain and using CMA-ES to optimize the criminal agents resource allocation, we are able probe and identity the main bottlenecks and weak points in the supply chain. This also allows us to discover the optimal approach for a criminal agent to disrupt the supply chain and to optimize the timing of its attacks. We also demonstrate how mounting multiple attacks on the supply chain creates additional vulnerabilities and creates a cascading effect of damage to its operations. Finally, we study the effects of utilizing basic mitigation strategies to protect the supply chain from attacks. We find that these basic strategies are effective in ameliorating the damage caused by attacks from the criminal agent.

The effects and possible damage to supply chains from disruptions caused by nefarious criminal agents remains an understudied area [15]. One of the limitations in our approach is that we utilize a simplified version of a typical pharmaceutical supply chain. Thus, implementing a more complex model would further improve the analysis of the key aspects of our results. The complexity and structure of the criminal agent can also be improved. Studying the typical disruptions these criminal agents cause and adding probabilistic distributions to these disruptions would be additionally informative. However, even using our current approach we are able to demonstrate how bottlenecks and their locations in the supply chain represent its most vulnerable points. We also show how optimization approaches such as CMA-ES can be used to find optimal attack strategies for a criminal agent and how these attacks can be timed to cause the most damage to the supply chains operations. We also demonstrate how different mitigation strategies can be studied and implemented to protect the supply chain from disruptions.

References

1. Akiba, T., Sano, S., Yanase, T., Ohta, T., Koyama, M.: Optuna: A next-generation hyperparameter optimization framework. In: ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. pp. 2623–2631 (2019)
2. Basu, G.: The role of transnational smuggling operations in illicit supply chains. Journal of Transportation Security **6**(4), 315–328 (2013)
3. Chowdhury, P., Paul, S.K., Kaisar, S., Moktadir, M.A.: COVID-19 pandemic related supply chain studies: A systematic review. Transportation Research Part E: Logistics and Transportation Review **148**, 102271 (2021)
4. Hansen, N., Ostermeier, A.: Adapting arbitrary normal mutation distributions in evolution strategies: The covariance matrix adaptation. In: IEEE International Conference on Evolutionary Computation (CEC). pp. 312–317. IEEE (1996)
5. Kleijnen, J.P.: Supply chain simulation tools and techniques: a survey. International Journal of Simulation and Process Modelling **1**(1-2), 82–89 (2005)
6. Kleindorfer, P.R., Saad, G.H.: Managing disruption risks in supply chains. Production and Operations Management **14**(1), 53–68 (2005)
7. Koh, R., Schuster, E.W., Chackrabarti, I., Bellman, A.: Securing the pharmaceutical supply chain. Tech. rep., Auto-ID Labs, Massachusetts Institute of Technology, 400 Technology Sq., Building NE46, 6th Floor, ambridge, MA 02139 (2003)
8. Luke, S.: Essentials of Metaheuristics. Lulu, second edn. (2013), available for free at http://cs.gmu.edu/∼sean/book/metaheuristics/
9. Männistö, T., Hintsa, J., Urciuoli, L.: Supply chain crime–taxonomy development and empirical validation. International Journal of Shipping and Transport Logistics **6**(3), 238–256 (2014)
10. Mizgier, K.J., Jüttner, M.P., Wagner, S.M.: Bottleneck identification in supply chain networks. International Journal of Production Research **51**(5), 1477–1490 (2013)
11. Muller, K., Vignaux, T.: SimPy. https://gitlab.com/team-simpy/simpy/
12. Rizou, M., Galanakis, I.M., Aldawoud, T.M., Galanakis, C.M.: Safety of foods, food supply chain and environment within the COVID-19 pandemic. Trends in Food Science & Technology **102**, 293–299 (2020)
13. Settanni, E., Harrington, T.S., Srai, J.S.: Pharmaceutical supply chain models: A synthesis from a systems view of operations research. Operations Research Perspectives **4**, 74–95 (2017)
14. Shah, N.: Pharmaceutical supply chains: Key issues and strategies for optimisation. Computers & Chemical Engineering **28**(6-7), 929–941 (2004)
15. Shekarian, M., Nooraie, S.V.R., Parast, M.M.: An examination of the impact of flexibility and agility on mitigating supply chain disruptions. International Journal of Production Economics **220**, 107438 (2020)
16. Tang, C.S.: Robust strategies for mitigating supply chain disruptions. International Journal of Logistics: Research and Applications **9**(1), 33–45 (2006)
17. Urciuoli, L., Männistö, T., Hintsa, J., Khan, T.: Supply chain cyber security—potential threats. Information & Security: An International Journal **29**(1) (2013)
18. Wu, T., Blackhurst, J., OGrady, P.: Methodology for supply chain disruption analysis. International Journal of Production Research **45**(7), 1665–1682 (2007)

Acknowledgement

This project has been funded in whole or in part with Federal funds from the Department of Homeland Security under BOA No. 70RSAT18G00000001, task order no. 70RSAT21FR0000127. The content of this publication does not necessarily reflect the views or policies of the Department of Homeland Security, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government