



The Axia Institute:  
Delivering Value Chain Solutions®  
MICHIGAN STATE UNIVERSITY



## **End-to-End Traceability:** The Needed Solution to Secure the Medical Supply Chain

The Axia Institute, May 2020 | By Bahar Aliakbarian and Katherine A. Franz

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## Summary - Background

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The COVID-19 pandemic has paralyzed the world's current supply chains highlighting their severe shortcomings. The pharmaceutical ecosystem is a dynamic, complex, and highly segmented chain comprised of upstream (manufacturers and re-packagers) and downstream (third-party logistics providers and dispensers). Medical supply chains operate in a highly regulated environment. For example, the Drug Supply Chain Security Act (DSCSA) is the latest in a series of regulations to outline steps to identify and trace prescription drugs as they are distributed in the United States.

The need for a responsive, secure medical supply chain is more evident in scenarios such as wars, natural disasters, disease epidemics, or the current COVID-19 pandemic. Authorities in different countries need to manufacture and distribute essential supplies (e.g., medications, medical devices, personal protective equipment (PPE)) to end-users, as needed, in a secure manner.

Improved data sharing and more accurate supply chain information will facilitate timely supply chain monitoring, improve the ability to recognize impending shortages, and provide a secure safe distribution of a COVID-19 vaccine throughout the world, reducing the risk of tampering and counterfeiting. The Axia Institute and eAgile are working together to address the current crisis and ongoing medical supply chain shortcomings through an enhanced digital solution.

## Summary - Goal

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The goal of this whitepaper is to identify the main challenges facing the pharmaceutical supply chain and to identify strategies to address the major issues. The current pharmaceutical supply chain is broken. It is imperative that we take the necessary steps to prevent recurrence of such catastrophic failures.

## Summary – Overview

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### *Section One:*

- Pharmaceutical Supply Chain Main Challenges
- Potential Solutions to Overcome Main Pharmaceutical Supply Chain Challenges

### *Section Two:*

2

- Case study – Develop a Smart Value Chain Platform to Secure the Drug Supply Chain During Emergency Situations: Case of Antibiotic
- Conclusion and Impact

## Section 1: Pharmaceutical Supply Chain Main Challenges

The medical supply chain in its current form is particularly vulnerable. Disruptions happen at all levels of the system from raw materials to the final point of use. Threats such as product tampering, counterfeit, or fraud are frequent occurrences in a vulnerable supply chain. The medical supply chain in particular is highly susceptible when the demand surges for medications during emergencies like COVID-19. The demand for surgical anesthesia drugs, high blood pressure treatment drugs, antibiotics, medical devices, and personal protective equipment can push an unsecured supply chain to the breaking point.

For example, the following are in high demand across the globe:

- antimalarials and antivirals which may be effective in treating COVID-19,
- antibiotics used to cure infections,
- bronchodilators for keeping airways open,
- basic over-the-counter drugs like Tylenol, and
- sedatives and neuromuscular blockers used to intubate patients.

This sharp increase in demand for these medications and devices and the restrictions on movement of goods and people imposed by international governments due to isolation restriction policies elevate the risk of pharma supply chain disruption (Figure 1). A smart end-to-end (E2E), traceable value chain approach offering full visibility, leveraging the power of Artificial Intelligence (AI) and machine learning, will predict and mitigate the risk. DSCSA mandates that the medical health industry adopts a solution. The E2E supply chain that we envision goes far beyond the minimal requirements of the DSCSA.

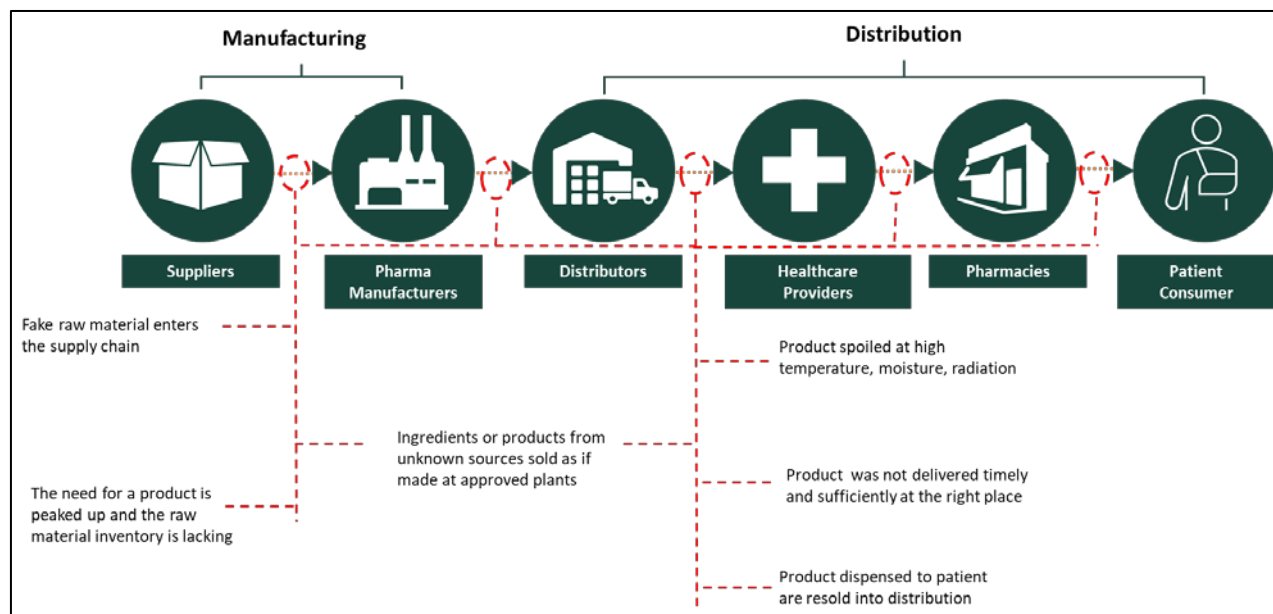


Figure 1. Pharmaceutical Supply Chain and Potential Disruptions

## Product Quality

The first major challenge for pharmaceutical manufacturers is the lack of visibility and traceability once medication leaves their facilities. The conditions of the drug (temperature, moisture, sunlight, etc.) during its journey within the E2E supply chain can have a detrimental effect on the safety and quality of these medications. Many must be stored within a predefined temperature range. Lack of positive control will ultimately result in product damage. Given the lack of traceability and sensing, it is difficult to identify if and when the product's environment exceeded a safe range. Therefore, it is not possible to identify and intercept the product before being delivered to the patient. Spoiled products can be damaged, destroyed, weaker in dosage, stronger in dosage, less effective, harmful or, in some cases, deadly.

Environmental temperature during transport is not the only factor causing product quality and safety issues. For instance, a medication may have a sensitivity light and air, being shaken, and exposed to vibrations and mishandling. Tampering can result in product dilutions, ingredient additions and even product substitutions with fakes.

## Product Authenticity – Diversion & Counterfeiting

The second major challenge is counterfeit medication and diversion. Their definitions are presented as follows:

- A counterfeit drug is a medication or pharmaceutical product which is produced and sold with the intent to deceptively represent its origin, authenticity, or effectiveness.
- Product diversion is a means for counterfeiters to access the product, to insert fraudulent goods into the system, which ultimately results in revenue loss.

Diversion and counterfeiting are nefarious, illegal practices which result in tainted or fake medications entering the medical supply chain. These practices can be harmful or deadly when counterfeit medications are dispensed and administered to patients.

A product can be considered a counterfeit for many reasons. Counterfeit products are not of the same quality, formula or ingredients. Typically, counterfeiters disguise their non-authentic product by reusing authentic packaging, labels, vials, bottles, and syringes. Increased visibility and traceability throughout the entire product life cycle are crucial to significantly reduce diversion and leaks within the supply chain. In order to fight the scourge of counterfeiting, the E2E supply chain must have the ability to verify the authenticity of the products at any point within the supply chain.

The key point is this: E2E visibility and direct end-user feedback are essential for traceability. The ability to deliver high-quality, authentic, adequately dispensed medications when and where needed is critical to patient health.

## Profitability

The third major challenge is profitability. In order to stay competitive within their industry, pharmaceutical companies must also consider the effects these challenges and potential solutions will have on their revenue, expenses, and capital structure. Potentially effective solutions must be quantified in terms of added value and Return on Investment (ROI).

There may be opportunities to generate additional income as a secondary outcome of integrating specific solutions throughout the existing E2E supply chain. These opportunities can include:

- increased sales due to customer satisfaction and loyalty,
- increased manufacturing capacity and efficiencies,
- branding opportunities, and
- data availability.

Also, added inventory visibility will generate ways to reduce expenses through:

- process improvement,
- theft reduction,
- returns management, and
- elimination of the need to purchase data from wholesalers.

There are also prospects to impact working capital through reducing inventory and accounts receivable.

### Drug Shortage in a Crises (COVID-19 Outbreak)

The fourth challenge is medical supply shortages. Shortages have profound adverse consequences: economic, clinical, and humanistic. The coronavirus outbreak is already starting to lead to drug shortages in the United States. In February 2020, the United States Food and Drug Administration (FDA) said it had identified the first drug shortage caused by the coronavirus outbreak's effect on the supply chain for pharmaceuticals. The FDA stated that the drug shortage is caused by manufacturing problems with the active pharmaceutical ingredient. This ingredient is central to antimalarials and antivirals which may be effective in treating COVID-19.

Also, in early February, 96% of community pharmacies said they were already experiencing a shortage of surgical masks, hand sanitizers, gloves, thermometers, and pulse oximeters used to monitor blood-oxygen levels, were becoming increasingly hard to come by in drug store chains and other retailers such as Walmart. A smart supply chain through the integration of Artificial Intelligence (AI) and data analytics will provide predictive analytic solutions that can help pharmaceutical managers to identify vulnerabilities and optimize their inventory and replenishment systems, thus ensuring adequate supply.

### Overall Patient Health

In addition to the risks within the commercial supply chain, patients also experience difficulty adhering to their prescribed medication regimen; in many cases abandoning their medications altogether. Patient compliance, or degree to which a patient correctly follows medication, is critical to proper treatment of many medical conditions. Medication non-adherence leads to 125,000 premature deaths each year and an estimated \$300 billion in United States healthcare costs (Jeff, 2018). By integrating patient use and consumption monitoring into the medical supply chain we can positively impact health.





## Section 1: Potential Solutions to Overcome Main Pharmaceutical Supply Chain Challenges

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### End-to-End (E2E) Traceability

The ideal E2E traceable value chain will provide many benefits and will add value to each node within the supply chain. The benefits of an E2E traceable value chain significantly address the pharmaceutical patient safety, patient health, product quality, product authenticity by reducing diversion and counterfeiting, profitability, and potential drug shortages (Figure 2).



**Traceability is the ability to identify the origin of a product to keep track of its locations and users as it moves along the supply chain. End-to-end (E2E) traceability is the key countermeasure to the challenges related to safety and security in many sectors, including healthcare, food and agriculture, transportation and pharmaceutical.**

- Trappey 2017 et al, Ding 2018, Aliakbarian 2019, Chiacchio et al. 2020



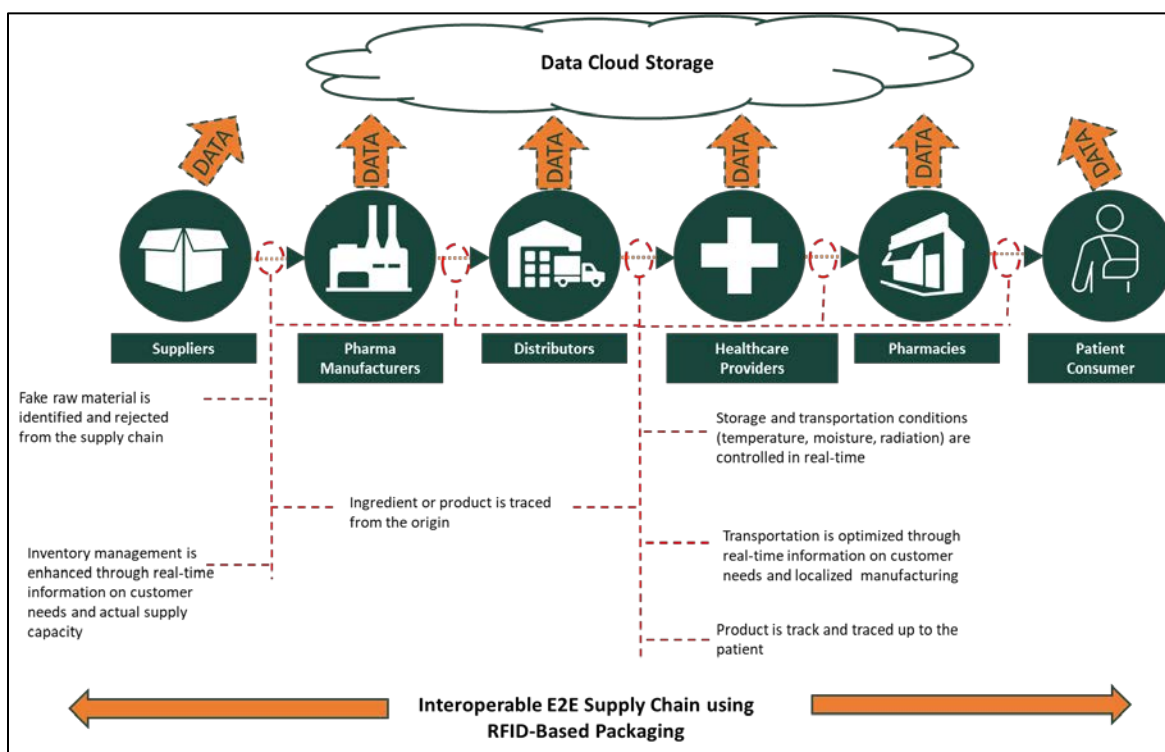


Figure 2. End-to-End Traceable Pharmaceutical Supply Chain and Potential Benefits

With E2E traceability, supply chain members can monitor the progress of the product as it leaves and arrives at the various nodes within the supply chain. They will be able to screen and monitor in real-time when a product is diverted, thereby enabling interception and risk remediation and elimination of counterfeits. Given enhanced visibility and traceability, every node in the supply chain can be confident in the authenticity of the product because they can track the journey of the product.

Also, detection is possible for products that did not originate from the manufacturer, were diverted during transport, were introduced or reintroduced at inappropriate times and locations, or reentered the supply chain after the product was identified to have been previously distributed. This new ability to detect would trigger alerts that the product may have been diverted, counterfeited, or otherwise tampered during the transportation and storage. If additional data provided by smart sensing and packaging indicates the quality of the product has been compromised and is no longer of intended quality or safe, a member of the supply chain would be able to intercept this damaged product before it is administered to the patient.

E2E traceability starts from the manufacturer and ends with the patient or health care provider. There is an easy way to establish the E2E at patient consumption through a smart dispenser utilizing Internet of Things (IoT).

### Internet of Packaging (IoP)

To provide E2E traceability and ensure that patients receive authentic medications, dispensers must be able to trace the individual product back to the originating manufacturer. For this to occur, the supply chain must allow the dispenser to be able to look back through the supply chain to confirm the product's authenticity. Enabling this system requires capturing this data stream and making it visible to dispensers and patients so that they can



have confidence in the effectiveness and quality of the medication. Many emerging technologies are now available to bring E2E traceable solutions to the medical industry, and many are in use in other industries.

The term "Internet of Things" was introduced by Kevin Ashton, of Procter & Gamble, who used the phrase to describe the role of Ultra-High Frequency Radio-Frequency Identification (UHF RFID) in making supply chains more efficient (Ashton, 2009). Internet of Packaging (IoP) is the application of Internet of Things (IoT) into packaging and could provide necessary visibility and traceability (Koelsch Sand, 2020). IoT is a complex network of physical and non-physical components in which electronic information (data) can be produced through different devices and shared over a network of components.

Wireless sensor networks, Near Field Communication (NFC), and UHF RFID technology are known as the major components of IoT. IoP includes emerging physical, electrical, and detection technologies integrated into packaging that combines with data analytics to monitor the condition of the material inside the package and its surrounding environment. The collection of these data in real-time ensures authenticity and product quality.

The use of RFID technology is evolving in the pharmaceutical industry. RFID technology has been shown to improve productivity enabled by automated planning and scheduling (Pacciarelli et al., 2009), to optimize inventory and eliminate shrinkage (Çakıcı et al., 2011; Zhang et al., 2018), and to optimize data quality (Van der Togt et al., 2017). Purdue (Oxycontin makers) and Pfizer (Viagra makers) are among the first pharmaceutical companies to start using HF RFID technology in their production lines. HF RFID (13.56MHz), an inductively coupled RFID technology, provides only short read distances. The main aim of adopting RFID technology is to serialize and prevent counterfeits through the tracking and tracing of products (Taylor, 2014). Pharmaceutical supply chains could leverage existing technologies already put into place through serialization and traceability requirements as indicated by International Standards Organization (ISO/DIS 12931) to secure the drug supply chain and combat the current drug shortage crisis that the nation is facing.

Today, it takes weeks or months for this kind of information to reach drug manufacturers, leading to shortages. If supply chain stakeholders could more easily share information about supply and demand, real-time signals could be shared to indicate regional upticks in demand for medicines. They would then be able to quickly pivot and rapidly increase the shipment of medicines to that region, allowing them to adequately meet patient health demands before the virus spreads even further. To accomplish this, drug manufacturers need to leverage advanced technologies, like IoT and artificial intelligence (AI), to share data signals with upstream suppliers of raw pharmaceutical materials and downstream partners like distributors and health care systems. This would allow supply chain leaders to proactively make fast, real-time decisions on inventory and medicine availability.

Technologies such as smart packaging with RFID tags combined with IoT solutions can be used to generate the data in real-time and directly communicate with pharmaceutical supply chain stakeholders.

## Cost Benefit

The benefits and ROI of implementing RFID-based smart packaging solutions into pharmaceutical and medical device supply chains depend on the several factors including type of RFID, labor costs and the value of real-time data accuracy. For example, active RFID tags use internal batteries to power their circuits and they also use their battery to broadcast radio waves to a reader, whereas passive or semi-passive tags rely on the reader to supply their power to broadcasting. Because active tags contain more hardware than passive ones, they are more

expensive. However active tags broadcast high frequencies from 850 to 950 MHz that can be read 100 feet or more away. Passive tags have significantly improved sensitivity and RFID readers have significantly improved performance. Passive UHF RFID tags and the associated high-performance readers are providing up to 40 feet of read distance to enable the accurate and reliable tracking of items in the supply chain at a lower cost versus RFID active tags.

Here are some of the benefits of RFID-based smart packaging:

- elimination of the need for labor effort on form filling,
- real-time data realization with high accuracy,
- avoidance of data transcription and missed item errors,
- enhanced inventory management through real-time information on customer needs and actual supply capacity, and
- cost reduction through improved control of stocks or assets.

All these benefits provide the foundation for building a solid business case for the use and integration of RFID-based packaging solutions into pharmaceutical and medical device supply chains.

## **Section 2: Develop a Smart Value Chain Platform to Secure a Drug Supply Chain in Emergencies: Case of an Antibiotic**

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### **Background**

A smart value chain looks holistically at the entire supply chain and focuses on delivering value to the end customer. Organizations operating with a smart value chain mindset are less likely to experience a disruption in their supply chains due to tighter integration with suppliers and shared objectives – delivering their product or service to the end customer as efficiently and effectively as possible.

It is considered practically impossible to completely isolate the different parts of a product supply chain to make it immune to counterfeiting, tampering, and contamination. Thus, there is a need for end-to-end trust verification for the entire value chain to enhance patient safety, patient health, product quality, and product authenticity by reducing diversion, counterfeiting, profitability, and potential drug shortages.

The Axia Institute, the value chain thought leader, is positioned to establish the framework and help implement the smart packaging solution to enhance traceability and secure the critical drugs supply chain during current COVID-19 emergency. The Axia Institute is working with two industrial partners eAgile and IntelliGuard to deliver an incumbent solution. eAgile is a leader in the market of IoT and RFID brand protection solutions that distribute standard or customized security printing, IoT and RFID products in UHF, HF, NFC, LF and dual frequencies across a wide variety of form factors including custom hardware and software solutions. IntelliGuard is a technology company using RFID, cloud-based software and data analytics to track and trace critical items in a complex

supply chain environment. They offer Intelligent Inventory Management Software Solutions powered by RFID such as Smart Cabinets that automatically track, control and monitor critical drug inventory levels and temperature.

## Cross-Functional Collaboration

The aim of this cross-functional collaboration is to develop a smart value chain platform to secure the drug supply chain during emergency situations such as the current COVID-19 outbreak that can:

- Reduce the shortage and increasing the availability of medications.
- Prevent drug counterfeit, tampering and diversion.
- Increase profitability, reduce the factory recalls, and manage customer returns.
- Generate predictive models for similar futuristic emergencies, including COVID-19 and Flu vaccine distributions.

Empiric antimicrobials such as Azithromycin have been considered for incubated patients with COVID-19 by the United States Department of Defense (DOD). We selected this medication for our case study, because of the sharp global increase in demand that will cause drug shortage.

The main objectives of this cross-collaborative proposal are (Figure 3):

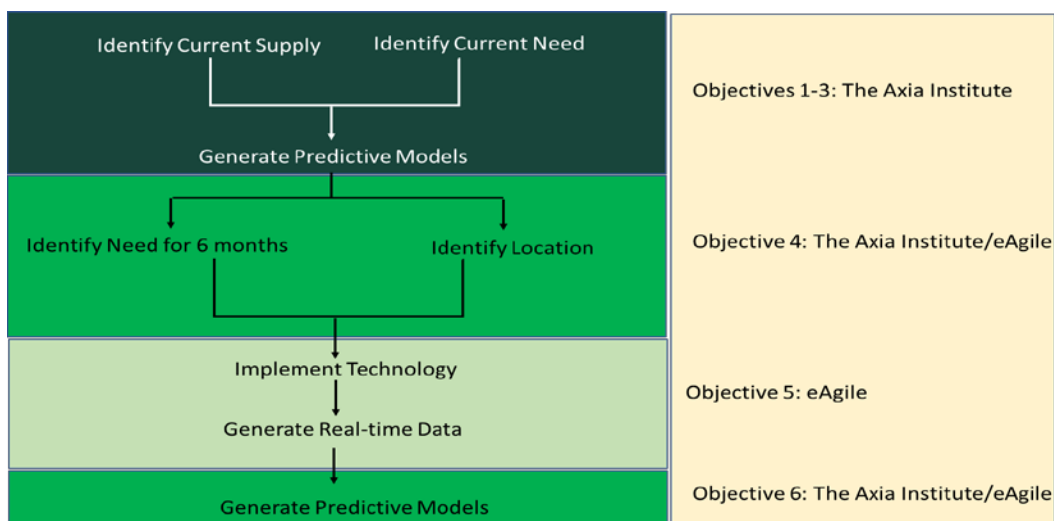


Figure 3. Proposed Objectives to Develop a Smart Value Chain Platform

1. Identify top global and national manufacturers for antibiotics such as Azithromycin, their current supply capacity, their supply chain approach to achieve active ingredients (AI) and distribution centers.
2. Identify the current demand for antibiotics such as Azithromycin in the United States through the interview with health care providers.
3. Develop an AI-based predictive model for the antibiotics such as Azithromycin demand for the next six months of the outbreak based on the results from previous objectives.

4. Identify 1 or 2 manufacturers in the United States to implement RFID-based smart packaging technology. The results from Objective 1-3 will be used to determine the need for the technology implementation (quantity and location).
5. Implement eAgile's RFID-based smart packaging technology to track and trace antibiotics such as Azithromycin packages. This will allow end-users to verify the contents of sealed containers to ensure the product is genuine, not part of a recall and within the expiration date.
  - a. This smart packaging solution reaches beyond supply chain security to create unique brand interaction and marketing opportunities by making smart products that link to consumers through smartphones and other connected devices.
6. Analyze big data and generate AI-based predictive models. Based on the real-time data collected from the previous objective, predictive algorithms will be developed to secure regional demands in the future for safe and secure distribution of vaccines.

Artificial intelligence combined with IoT will allow sharing the data signals with suppliers of raw materials and distributors, thus supporting fast decisions about inventory management.

## Section 2: Conclusion and Impact

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Through an E2E traceable supply chain enabled by smart packaging solutions, all members of this value chain can be confident in the quality and safety of the critical care products that ensure a higher level of patient safety. Manufacturing companies will also gain benefits through the integration of this E2E traceable value chain. They will have many opportunities to both generate income as well as more effectively manage their expenses.

An improved supply chain with accurate data sharing empowers authorities such as FDA to:

- develop required risk assessment plans,
- identify vulnerabilities, and
- develop plans to mitigate the identified vulnerabilities by integrating contingencies for emergency situations.

The results of this cross-functional approach could be adopted for other pharmaceutical products such as surgical anesthesia drugs, high blood pressure treatment medications, antivirals or any other critical drug in risk of supply chain disruption.

The results of this pilot study will be used to develop a value proposition for implementing technology and to calculate the potential returns on investment.



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