Cold Chain Management with Internet of Things (IoT) enabled solutions for Pharmaceutical Industry

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Summary: This research presents how IoT enabled solutions can be used to minimize the wastage risk of pharmaceuticals due to temperature excursions. The context of this work is based on a pharmaceutical company in a developing country. Limited technologies, unreliable temperature monitoring devices and human errors are the primary causes for temperature excursions. By applying the framework for envisioning implication of IoT (Phadnis 2017), it's observed IoT enabled solutions are beneficial to improve the risk mitigation for temperature excursions. Especially future technologies which we defined as "Progressive IoT" such as 5G wireless network, device miniaturization, AI and Machine to Machine (M2M) will make the risk of temperature excursions reduce extensively in the pharmaceutical cold chain.

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KEY INSIGHT

- Temperature excursions in cold chain result from human error and technical limitation.
- Internet of Things (IoT) has great possibility to mitigate the risk for cold chain.

Introduction

The production value of the global pharmaceutical industry reached approximately USD 1 trillion with 2.8% growth rate in 2014 (IFPMA, 2017).

Biotechnology and the pharmaceutical industry (biopharma) are continuing their discovery and development of medicines to treat diseases and have successfully developed numerous therapies for the treatment of autoimmune, allergic, infectious diseases, as well as cancer. Worldwide prescription drug and over-the-counter (OTC) sales by biotechnology continues to increase and will reach USD 337 billion in 2022, and total sales of top 15 therapy areas including oncology, anti-diabetes, etc. reached USD 420 billion (EvaluatePharma, 2016).

Biologics, which are temperature-sensitive medicines are potentially exposed to temperature excursions throughout their storage and delivery process. World Health Organization (WHO) Model Guidance (2011) defines temperature excursion as an event in which a time-temperature sensitive pharmaceutical product is exposed to temperatures outside the permissible ranges approved for storage and transportation.

According to the Green Book (2013) , "The cold chain, is a term used to describe the cold temperature conditions in which certain products need to be kept during storage and distribution. Maintaining cold chain integrity ensures that vaccines are transported and stored according to the manufacturer's suggested temperature range of +2˚C to +8˚C until the point of administration."

To mitigate the risk of temperature excursions, pharmaceutical manufacturers and logistics companies implement devices or systems for transport from manufacturing location to final destinations.

Despite extensive efforts, risk mitigation in the cold chain does not seem satisfactorily effective in the prevention of temperature excursions.

There are options to mitigate risks of temperature excursions. The Internet of Things (IoT) provides the possibility of having programmed sensors that can automatically send alerts if the pharmaceutical products storage is out of a specified temperature range and can assure quality & efficacy (Cognizant, 2017).

With IoT, real-time monitoring provides timely warning to operators to check temperatures in storage areas as well as tracking of accumulated temperature excursions that have exceeded the allowed temperature ranges to maintain the effectiveness and viability of the medicine.

Research Objective

Pharma X, a Swiss multinational pharmaceutical company involved in the production and distribution of a variety of medicines and one of the largest pharma companies in the oncology sector, is interested to know how the Internet of Things can help their supply chain, and specifically the temperature monitoring to increase the visibility in the last-mile delivery.

This research is motivated by the statement "20% of temperature-sensitive pharmaceutical products are damaged during transport due to a broken cold chain (interrupted series of storage and distribution activities that does not maintain the desired low-temperature range)" (Geoff, 2015).

This research seeks to capture the supply chain process of Pharma X and how with their actual process, by the implementation of an IoT enabled solution they can improve cold chain efficiency and mitigate the risk of possible temperature excursions throughout the distribution process. Thus, the critically important question to be answered is:

How can IoT solutions be used to minimize the wastage risk of pharmaceuticals due to temperature excursions?

Literature Review

Cold Chain and Pharmaceutical Industry

Adequate temperature monitoring in cold chain has become inevitable as small variations in temperature can impact the shelf life and value of products.

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Pharmaceutical products need to be handled within the permissible ranges, and in case of any break in the cold chain, the medicines would be exposed to temperature excursions. WHO Model Guidance (2011) defines the temperature excursion as an event in which a time-temperature sensitive pharmaceutical product is exposed to temperatures outside the permissible ranges approved for storage and transportation.

Exceeding the ranges allowed for a substantial period leads to the generation of impurities that appear as a result of product degradation. Distribution is a significant activity of the integrated supply-chain management of pharmaceutical products. Pharmaceuticals must be placed under strict requirements for temperature, and according to Brzozowska et al.(2016) the quality of product distribution largely impacts the safety of patients' health and life.

Maintenance and monitoring of the temperature of vials and vaccines throughout the whole supply chain are of critical priority to ensure their effectiveness. Proper maintenance and monitoring of temperatures also allow for the detection of any failure of equipment and lapses of procedures.

To reduce the risk of temperature excursions, precise information gathering about Time and Temperature History (TTH) is a critical factor and is also valuable in terms of decision making. Ketzenberg et al. (2015) state that TTH significantly affects product shelf life and if actively managed can reduce uncertainty in the management of the product.

Currently, to maintain a high quality of TTH, there are a variety of methods for monitoring and recording temperature described by WHO (2015) and UNICEF guidelines (2014) such as chemical-based indicators, temperature loggers, electronic freeze indicators, integrated digital thermometers, etc.

Many researchers tried to understand the vaccine mismanagement and identified the main factors that caused the supply chain problems such as product packaging, shipping, local transport, handling of vaccine at the clinic, failure to follow proper vaccine storage procedures, patients' knowledge for vaccines usage, temperature monitoring and power outage. These challenges can be categorized as human error, infrastructure, and temperature control.

According to Sarley et al. (2017), the ultimate measure of success for any supply chain transformation is the increased visibility and availability of vaccines at the last-mile. Many challenges while maintaining the integrity of the processes might be faced in the last-mile delivery, and the efficacy of pharmaceutical products must not be compromised. With emerging technologies, these issues can be addressed and the increase of solutions meeting the cost challenge.

Internet of Things

The principle idea of the IoT is that virtually every physical thing can also become a computer that is connected to the Internet (ITU, 2005) The internet of things represents a vision in which the internet extends into the real world embracing everyday objects and not the result of single novel technology (Mattern & Floerkmeier, 2009).

Even though the term "Internet of Things" and the literature is still nascent, many available definitions can be found.

"IoT is simply the point in time when more "things or objects" were connected to the Internet than people." (Evans, 2011)

IoT according to Xu, He, and Li (2014) includes four main essential layers such as sensing, networking, service, and interface.

Even though the definitions are different, they broadly have many similarities that can be understood according to the following categories: sensors captured data as data gathering function, network traversed data as data sharing functions and stored data for decision making.

The benefits of implementing IoT in the supply chain is the increase of visibility and how companies can monitor their assets through this technology. For the pharmaceutical industry, for example, the requirements of cold chain require highly specialized and compliant networks to move products efficiently, while protecting the integrity of the medicine. Also, regulatory compliance, product quality, inventory, end-to-end supply network visibility, etc. are also a considerable concern for the industry (Pharma Logistics IQ, 2017).

Daily millions of tons of temperature sensitive goods are produced, transported, stored and distributed worldwide. For these products, temperature monitoring is the key point in cold chain operations and the most important factor in the avoidance of temperature changes which affects the properties of the products (Ruiz-García & Lunadei, 2010).

Methodology

The methodology was based on three main topics: Cold Chain, Pharmaceutical Industry and Internet of Things.

After analyzing the literature review, three challenges were identified from the cold chain and the pharmaceutical industry: human error, technology, and temperature control.

To further comprehend these challenges, 10 semi-structured interviews were held, first with Pharma X and then with System Integrator, Freight Forwarder and a Humanitarian Medical Organization.

Pharma X, throughout the interviews, shared that they do not experience temperature excursions, the outcome was the process mapping and the good cold chain management practices that could be as an example for other organizations to maintain the integrity of the medicines.

The purpose of the rest of the interviews was to understand the challenges these interviewees were facing in the cold chain management day to day. Human Error, Technology, Temperature control, Infrastructure and Business challenges were identified.

The next step was to benchmark the existing technologies that could address these challenges, but only human error, technology, and temperature control challenges can be addressed. Infrastructure and business challenges can't be addressed due to the scope of the research. The business challenges have potential for future work and integration systems in the near future.

Finally, an existing framework was applied to the pharmaceutical industry, and based on the previous information of technology mapping created the need

to expand the definition of the Internet of Things with the conventional and progressive IoT.

Results

Literature and semi-structured interviews show the needs and challenges of the pharmaceutical industry. Technical mapping shows the limitation of exciting technologies to prevent temperature excursions. An IoT framework for global supply chain performance is applied (Phadnis, 2017) to explore the effect of IoT capabilities on the performance of pharmaceutical cold chains. This framework has three components, data gathering, data sharing and decision making.

Data gathering:

In the pharmaceutical cold chain, ideally the information such as TTH, light, humidity, GPS, or shock is captured for each vial. Due to the size of the existing devices, it is difficult to attach an IoT device to a secondary package.

Data sharing:

The data can be shared instantly via several communication technologies such as RFID, NFC, BLE etc. In the future, new mobile network technologies such as LTE-M and LTE-NB will play a significant role in sending data from IoT devices.

Decision Making:

Decision making can be proactive monitoring and be taking counter actions before having temperature excursions. In the future, machines or system itself can make a decision to send messages to warn the temperature exclusions in advance.

IoT technology can overcome the challenges of the cold chain but most of the technologies to improve supply chain performance is not existing technologies but future technology. Thus, proposed herein is the categorization into two types of IoT, (1) as conventional and (2) as progressive. The concepts addressed to get full benefits of IoT are, those that result in risk mitigation of temperature excursion, invisible hardware, instant connection and machine-centric concepts Fleisch (2010). The purpose of defining IoT at a deeper level is to articulate more precisely the difference between IoT just connected to the Internet and ubiquitous computing (Weiser, 1991)

Figure 1 depicts the conceptual model of the difference between conventional IoT and progressive IoT. Risk of temperature excursions will be mitigated when companies apply progression IoT to their cold chain process.

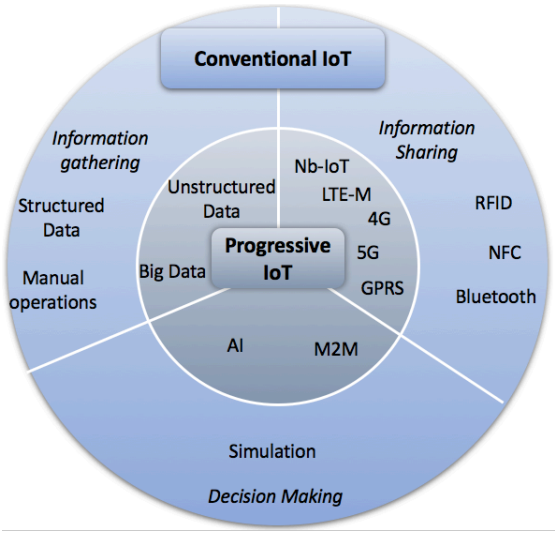

Figure 1. Conventional and Progressive IoT

Conclusion

There are three challenges (technology, temperature control and human error) identified as potential candidates to be resolved by an IoT enabled solution. As challenges are examined and mapped to technical features, it's observed that the existing technologies cannot be met to resolve the challenges and future technologies will have a possibility to resolve them.

Hence, we built up the propositions for IoT implementation (Immediate, Within 1-2 years, Beyond) and identify the impact of each of the challenges identified. (Table 1) In "beyond" period, companies can attach IoT devices to secondary package and upload the data for temperature, GPS, humidity, shock etc. instantly via 5G/LTE-M mobile network anywhere and anytime. AI and M2M can support decision making and counteractions without human intervention. Consequently, we concluded that new IoT technologies that we defined as Progressive

Table 1. Potential Implementation for IoT Enabled Solutions and Impact

Challenges: Technology | Temperature Control | Human Error

	Information Gathering		Information Sharing		Decision Making	
	Attached to	Target Data	Technology	Target Location	Proactive Alert	Counter Action
Immediate	Pallet	TTH ☆	4G, NFC, RFID, BLE	Storage	Manual	Operators
Within 1-2 years	Pallet	TTH, GPS ☆	LTE-M, LTE-NB, NFC, RFID, BLE ☆	Storage / Delivery ☆	Combination of Manual and AI ☆	Operators
Beyond	Secondary Package	TTH, GPS, Humidity, Shock etc.	5G ☆☆☆	Storage / Delivery	AI ☆☆☆	M2M ☆☆☆

IoT will improve cold chain management in terms of data gathering, data sharing and decision-making performance.

Limitations and future work

In this study, we tried to articulate IoT characteristics to identify the nature of IoT and apply it to the pharmaceutical industry for risk migration of medicine wastage due to temperature excursion, but some limitations are observed.

First, infrastructure is the primary limitation, especially for developing countries. The new wireless network such as LTE-M and 5G will start rolling out in developed countries, and there is a dilemma that areas of a high possibility of temperature excursions also face the possibility of weak infrastructure. Second is security issues. IoT implementation can make devices connect anytime from anywhere without borders. Third is device management. Companies require to manage lots of devices and dispose of them properly. These limitations need to be considered for IoT implementation.

AI and M2M are the related topics for IoT enabled solutions as the future work. AI is a promising technology of forecasting temperature excursions and setting up the threshold of sending alert messages. M2M can eliminate human errors and accelerate automation for the entire process of cold chain with IoT enabled implementation. We recommend AI, and M2M to be researched jointly with IoT implementation to mitigate the risk of temperature excursions.

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