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Ensuring Product Quality in Irish Biologic and Biopharmaceutical Logistics through IoT-enabled Cold Chain Monitoring

By

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[redacted]

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CANDIDATE DECLARATION

Candidate Name: Nisha Manikantan Nair

I hereby declare that the dissertation entitled “Ensuring Product Quality in Irish Biologic and Biopharmaceutical Logistics through IoT-enabled Cold Chain Monitoring” submitted for the award of degree in MSc in Digital Transformation (Life Science) is a research work carried out by me under the supervision of Dr Martin Barr. I further declare that all sources used have been acknowledged by means of complete references.

SIGNED: NISHA MANIKANTAN NAIR

DATE: 19th May 2024

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LIST OF ABBREVIATIONS

IoT- Internet of Things

FDA- Food and Drug administration

WHO- World Health Organisation

TTSPP-Temperature Sensitive Pharmaceutical Product

RFID-Radio Frequency Identification

GPS-Global positioning System

GDPR-General Data Protection Regulation

IT-Information Technology

CSV-Comma Separated Value

MES-Manufacturing Execution System

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ABSTRACT

The fourth industrial revolution along with the advancement in digital technologies have revolutionized the realm of biologics and biopharmaceutical logistics. This dissertation embarks on a journey to explore the integration of Internet of things (IoT) enabled technologies in cold chain monitoring within the Irish biologic and biopharmaceutical logistics sector. The study focuses on ensuring the quality and safety of temperature-sensitive biologics and biopharmaceutical products like gene therapies, monoclonal antibodies, vaccines, diagnostic kits and reagents during storage and transportation till it reaches the end customer.

The study is relevant especially for a country like Ireland renowned for being one of the leading global hubs in biopharmaceuticals, medical device technology and digital health technology. The biologic and biopharmaceutical logistics industry of Ireland rely heavily on efficient and reliable cold chain monitoring to ensure the quality, safety, and efficacy of temperature-sensitive medications, vaccines, and biologics. The ever-increasing demand for vaccines, gene therapies, monoclonal antibodies, and biomedical products like diagnostic reagents and medical laboratory supplies post COVID-19 pandemic has made it important to maintain the optimal storage conditions throughout their transit within the supply chain.

Industry 4.0 technologies like the Internet of things (IoT) can be a game changer in the cold chain logistics through its capabilities in offering real-time monitoring of temperature and other environmental factors like humidity, pressure, etc. Through time-monitoring, anomalies in temperature and other environmental factors can be detected immediately and immediate measures can be taken to prevent any adversities, thus ensuring the safety and efficacy of the product.

This research further aims to emphasise the understanding of available IoT technologies having the potential to transform the biologic and biopharmaceutical cold chain, thus enhancing product quality and ensuring patient safety.

Keywords: Internet of Things (IoT), quality, biologics and biopharmaceutical logistics, cold chain, temperature-sensitive products, patient safety

1. INTRODUCTION

1.1. Overview

Throughout our history, mankind has always been dependent on technology. It all began with the first industrial revolution wherein steam power was used to mechanize production. Later in the second industrial revolution, electric power and assembly lines were used to make mass production possible. The third industrial revolution was all about automation using electronics and information technology to connect the world we are living in. At present we are witnessing the dawn of the fourth industrial revolution encompassing a fusion of technologies that blurs out the fine line between the physical, digital and biological sphere (Schwab, 2017). The fourth industrial revolution along with the advancement in digital technologies have catalysed the realm of biologics and biologic and biopharmaceutical logistics through optimized operational excellence and enhanced quality assurance. Efficient and reliable delivery of biologic and biopharmaceutical products is of utmost importance to safeguard public health. It stands especially true for a country like Ireland renowned for being one of the leading global hubs in biopharmaceuticals, medical device technology and digital health technology. With the ever-increasing demand for vaccines, gene therapies, monoclonal antibodies, and biologic and biopharmaceutical products like diagnostic reagents and medical laboratory supplies, it is crucial to maintain the optimal storage conditions throughout their transit within the supply chain.

The Irish biologic and biopharmaceutical logistics deals with activities related to transportation, storage and distribution of various products including medical devices, diagnostic tools, bio-pharmaceutical products, biologics, laboratory supplies, diagnostic kits and other healthcare-related products. Most of these products are sensitive to storage conditions and undergo the process of spoilage making it unfit/hazardous for use. Therefore, biologic and biopharmaceutical logistics rely heavily on efficient and reliable cold chain monitoring to ensure the quality, safety, and efficacy of temperature-sensitive medications, vaccines, and biologics. Challenges associated with preserving the product quality in transit, storage, and distribution of biopharmaceutical products and biologics pose a significant blockade for both healthcare providers as well as logistics stakeholders. The implementation of Internet of Things (IoT), specifically has emerged as a disruptive force shaping the future of biologic and biopharmaceutical logistics offering unprecedented capabilities in the management of cold-chain. Integration of IoT into cold-chain monitoring systems has emerged as a game changer in the overall management of biologic and biopharmaceutical cold-chain logistics from transit

to distribution. Through real-time visibility into the supply chain, identifying anomalies in environmental parameters of product and intervening at the right time to mitigate any risk, IoT-enabled sensors along with data analytics platforms and cloud computing infrastructures can help stakeholders monitor temperature fluctuations in real-time and address them before they turn into critical problems.

In the wake of COVID-19, there has been a drastic transformation in the biologic and biopharmaceutical logistics sector especially in the adoption of digital health technologies. There were an increasing number of vaccine related adversities globally during storage and transit, which could have been avoided with infallible cold-chain management (Gillespie *et al.*, 2023a). The pandemic really made us understand the importance of a resilient and agile supply chain in ensuring the integrity of biopharmaceutical products and biologics. Use of IoT enabled cold-chain monitoring could possibly limit the dependency on human resources and tackle errors and losses associated with it.

Despite the fact that integrating IoT technologies in cold chain monitoring has immense potential, one must not overlook the challenges it may pose during implementation. These challenges include issues pertaining to its interoperability, regulatory compliance and data privacy concerns to name a few. Moreover, the inherent complexities of biologic and biopharmaceutical logistics characterised by product integrity and safety, stringent quality and diverse stakeholders necessitates a multifaceted approach towards digital transformation especially in the use of IoT technologies.

This dissertation sheds light on use of IoT enabled cold chain monitoring highlighting its immense potential in ensuring product quality in Irish biologic and biopharmaceutical logistics. It helps monitor temperature and other environmental factors like pressure, humidity and detect anomalies in real-time and fluctuations. In contrast to traditional methods of cold chain monitoring like manual recording of temperature using thermometers, cold chain monitoring using IoT enabled sensors could track the excursions in temperature and other environmental factors in real time resulting in transparency in cold chain and prevent any spoilage by pre-emptive risk mitigation.

Against this backdrop, the dissertation aims to understand the current state of cold chain monitoring in Irish biologic and biopharmaceutical logistics and analyse available IoT technologies used in biologic and biopharmaceutical logistics for cold chain monitoring. It also shines light on the challenges faced in implementation of IoT technologies and its

environmental and socio-economic impacts. Furthermore, the dissertation offers insights into emerging trends in the adoption of IoT technologies of cold chain monitoring and provides recommendations for future improvements.

1.2 Research Aims and Objectives

a) To evaluate the current state of cold chain monitoring in Irish biologic and biopharmaceutical logistics

b) To identify and analyse the available IoT technologies used in biologic and biopharmaceutical logistics for cold chain monitoring in Ireland

c) To identify and analyse the challenges faced in implementing IoT enabled cold chain monitoring in Ireland

d) To evaluate the economic, environmental, and social impacts of implementing IoT-enabled cold chain monitoring systems in Ireland

e) To investigate emerging trends in the adoption of IoT technology for cold chain monitoring in Irish biologic and biopharmaceutical logistics and provide recommendations for the future improvements

1.3 Research Questions

a) What is the current state of adoption of IoT enabled technologies in cold chain transportation of temperature sensitive biologics, biopharmaceutical products, diagnostic kits, laboratory reagents and vaccines in Ireland?

b) What are the available IoT devices and technologies that can be used in cold chain monitoring of temperature sensitive biologics and biopharmaceutical products during transit and storage in Ireland?

c) What are the advantages of IoT enabled cold chain monitoring when compared to the conventional method?

d) What are the challenges faced for implementing IoT enabled cold chain monitoring?

e) How does the use of IoT technology in cold chain monitoring contribute to the overall efficiency of pharmaceutical transit processes?

2. LITERATURE REVIEW

2.1. Introduction to Biologic and Biopharmaceutical Logistics

2.1.1. Biologics and Biopharmaceuticals

In a study by Deiana et al., (2017), the term 'Biologics' is referred to as active components that are derived from biological sources natively or through biotechnology processes. They include a wide range of products such as vaccines, gene therapies, monoclonal antibodies, components of diagnostic kits, blood and blood components to name a few (Figure 1). With the increasing knowledge of scientists and researchers in the field of genetics and cell biology, more and more biologics are produced through genomics, proteomics, monoclonal antibody technologies, cell culture and microarray techniques (MORROW and Felcone, 2004). The first recombinant insulin 'Humulin' got its approval from FDA in the year 1982. Ever since, FDA has approved 91 more biologics produced from recombinant DNA technologies till 2013 to be used as therapeutics. These 91 biologics can be further classified into 3 groups as monoclonal antibodies, enzyme modulators and receptor modulators (Kinch, 2015).

Selected categories of biologic agent structure
Hormone (growth hormone, parathyroid hormone, insulin): A substance, usually a peptide or steroid, produced by one tissue and conveyed by the bloodstream to another to effect physiological activity, such as growth or metabolism.
Interferons: Proteins that are normally produced by cells in response to viral infection and other stimuli.
Interleukins: A large group of cytokine proteins. Most are involved in directing other immune cells to divide and differentiate.
Growth factor: A substance such as a vitamin B12 or an interleukin that promotes growth, especially cellular growth.
Monoclonal antibodies (MAbs): A single species of immunoglobulin molecules produced by culturing a single clone of a hybridoma cell. MAbs recognize only one chemical structure, i.e., they are directed against a single epitope of the antigenic substance used to raise the antibody.
Polypeptides: Peptides containing ten or more amino acids. Typically, a peptide consists of fewer than 50 amino acids, while a protein has more than 50 amino acids.
Proteins: Naturally occurring and synthetic polypeptides having molecular weights greater than about 10,000 (the limit is not precise).
Vaccine: An agent containing antigens produced from killed, attenuated or live pathogenic microorganisms, synthetic peptides, or by recombinant organisms. Used for stimulating the immune system of the recipient to produce specific antibodies providing active immunity and/or passive immunity in the progeny.

Figure 1: Different classes of Biologics (MORROW and Felcone, 2004)

According to (Rader, 2008) Biopharmaceuticals refers to pharmaceutical agents of biological nature but manufactured using biotechnological processes. However, what separates 'Biopharmaceuticals' from 'Biologics' is that the former could also be produced from sources other than extracting from the native biological source, like direct chemical synthesis or recombinant DNA technology. Some examples of the biopharmaceutical products include oligonucleotides and hybridoma based antibody production. (Walsh, 2002) in his paper discusses the difficulty in classification of many modern biotechnology-based pharmaceutical products using the traditional terminologies. That being said, most of the products of biologic or biopharmaceutical origin fall into the grey area and are considered 'Biopharmaceuticals'.

According to (Kesik-Brodacka, 2018), biopharmaceuticals were first introduced in the year 1982 and have revolutionised the healthcare system ever since through its ability to treat a wide variety of health conditions. It is considered to be a rapidly growing sector due to its high demands in the healthcare sector.

The Europe Pharmaceutical Market Size, 2021-2028 report suggests that the market for pharmaceuticals was valued at USD 282.75 billion in the year 2020 and is expected to grow at a compound annual growth rate of 5.4% from the year 2024 to 2028. Emergence of biologics and biosimilars along with a surge in R&D investments and healthcare expenditures can be attributed to this expected growth (Grand view research, 2021). The European Union was the first to commercialise biosimilars which by May 2019 have rolled out 59 biosimilars to be sold in Australia, Japan, Canada and South Korea. Another credit for the growth of the biopharmaceutical sector goes to the changing demographics. Aging population creates vast opportunities in the introduction of novel products and services to prevent lifestyle-associated diseases (Mika Naumanen, 2019).

2.1.2. Critical role of Logistics

The term "logistics" was coined in the year 1950s and is used as an umbrella term for all the planning, implementation and control of the flow of goods, services and related information from manufacturer to the customer in an efficient way. Although both 'logistics' and 'supply chain management' are closely related and sometimes used interchangeably, the former focuses on the physical movement of the goods from one location to another. Supply chain Management on the other hand primarily focuses on the supplier-customer relationship to optimise the effective flow of goods and services (Yildiz, 2023). Logistics is an important

subset of supply chain management and plays a crucial role in transportation of products to the end user.

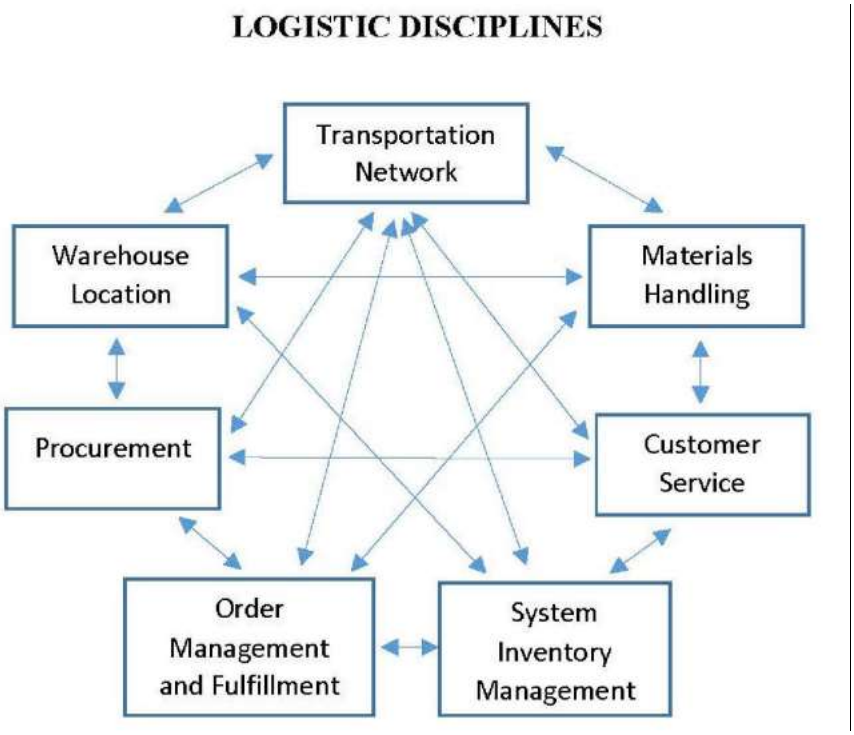

Figure 2: Logistic disciplines (Scott and Rutner, 2020)

However, logistics is not only about transportation networking, it also involves procurement, material handling, warehouse location, order management and fulfilment, system inventory management and customer service (Figure 2). Since all the disciplines shown in Figure 2 are interconnected, any disruption across the area could affect the entire logistics, thus disrupting the supply chain significantly (Scott and Rutner, 2020).

In the pharmaceutical sector, a wide array of products is sensitive to changing temperatures and requires low-temperatures during their transit and storage. These products are handled in a temperature-controlled manner right from the collection to their delivery using cold chain systems (Pajić *et al.*, 2024). Biologic and Biopharmaceutical cold chain logistics refers to management of biologics and biopharmaceutical products from site of production to the user point at recommended temperature to ensure its quality (Chatterjee and Pandey, 2003). These products are highly sensitive to temperature changes during their transport from manufacturer to the consumer. Therefore, the transport and storage of these products in transit is highly crucial for its safety and efficacy. Biologics and Biopharmaceutical industries often rely on cold chain logistics to manage their goods flow in a temperature-controlled way. These goods

range from insulin which are categorised under low-risk to high-risk products like life-saving vaccines (Mohsin and Yellampalli, 2017).

Cold chain logistics is crucial for maintaining the quality and efficacy of biologics during storage and transportation. Factors like temperature control, packaging materials, and environmental conditions are essential for preserving biologics' stability throughout the supply chain (Nadimuthu and Victor, 2022). Quality management systems for biological sample collection ensure standardization and efficiency, especially in large-scale studies. These systems maintain sample quality and compliance with protocols, enhancing the reliability of research outcomes. Risk assessment methods are also essential for identifying potential risks and implementing preventive measures. These methods evaluate factors such as temperature fluctuations, packaging integrity, and transportation conditions, enabling proactive measures to safeguard biologics' integrity during storage and transit. Maintaining a robust and reliable cold chain infrastructure is essential for upholding biologics' quality and effectiveness. Implementing quality management systems and risk assessment strategies can mitigate risks and ensure optimal conditions for biologic storage and transportation, ultimately safeguarding public health and research integrity (Peplies *et al.*, 2010).

2.2. Importance of product quality during Biologic and Biopharmaceutical logistics

The quality of pharmaceutical products is highly dependent on factors like quality of raw materials, manufacturing process, packaging, shipping and storage to name a few. Any challenges regarding either one of the factors could have a significant impact on the produced goods quality. Such situations could result in outcomes like lack of therapeutic effect, toxicity and mortality in patients, economic loss and lack of trust in the healthcare organization (Goyal and Gupta, 2021).

Product spoilage due to temperature excursions remains one of the key problems in the biopharmaceutical sector. (Kumar and Jha, 2017) provides a useful insight into the impact of storage environmental conditions affecting the quality of pharmaceutical products. The author further mentions environmental parameters during storage, especially temperature excursions due to natural or human errors, having the potential to impact the quality of pharmaceutical products significantly.

According to World Health Organization (WHO) Model Guidance (2011), temperature excursion is an event where a time temperature sensitive pharmaceutical product (TTSPP) is exposed to temperatures which are outside the permissible range approved for storage and transportation. It not only causes economic loss for the company but also turns out to be hazardous for the patients and subsequent regulatory actions. Biologic and biopharmaceutical products especially the biological products like vaccines and other injectables have shorter shelf-life and are extremely sensitive to storage conditions, therefore it is very important to monitor the temperature during the cold chain process (Shashi, 2022) .

(Haddud *et al.*, 2017) argues biologic and biopharmaceutical supply chain compared to other classic ones faces many critical challenges, one of the key challenges being related to temperature monitoring during cold chain management. Biologic and biopharmaceutical products and biologics, for example vaccines, gene therapies, monoclonal antibodies, diagnostic reagents and medical laboratory supplies work as intended only within a specified temperature as follows: Below +25°C (controlled temperature), +2°C to +8°C (temperature-sensitive products), -20 °C to -40 °C (negative temperature), and -70 °C (ultra-low temperature).

The COVID-19 pandemic has further made us understand the importance of maintaining product quality throughout the supply chain. With the implementation of mass vaccination on a global scale, there has been a pressure on the cold chain logistics to deliver the vaccines with utmost safety and efficiency. Figure 3 shows three of the COVID-19 vaccine candidates along with their storage conditions.

	Freezer temperature	**Refrigerator temperature**	**Max storage days**
Pfizer	- 70 degrees Celsius	N/A	30 days after opening the freezer
Modena	- 20 degrees Celsius	2-8 degrees Celsius	30 days in the refrigerator
Oxford-AstraZeneca	N/A	2-8 degrees Celsius	6 months in the refrigerator

Figure 3: COVID-19 vaccine candidates with their storage conditions (Antal *et al.*, 2021)

2.3. The Biologic and Biopharmaceutical cold chain logistics

2.3.1 Essential elements of cold chain

There are three essential elements of a cold chain: storage, transport, and temperature monitoring during processing and distribution (Singh *et al.*, 2020).

Cold storage: It consists of a cooling system enabling it to store the temperature-sensitive biologic and biopharmaceutical products at required temperature for a certain period of time.

Cold transport: Pharmaceutical companies pack the products in an insulated box which helps maintain the temperature during transportation.

Cold processing and distribution: During processing and distribution, it is crucial to meet the sanitary conditions especially during consolidating and de-consolidating the boxes, crates and pallets.

The reagents/kits used in medical diagnostics (eg: ELISA kits), in research (eg: antibodies) and for human interventions (eg: vaccines) remain viable and effective only when kept within a particular temperature. It will lose its viability and effectiveness if the temperature becomes too hot or too cold. Cold-chain breaches can lead to adverse drug reactions in patients. Minuto *et al*., (2010) have reported ketoacidosis in patients with diabetes when administered with frozen or thawed insulin. Thus, it is very important to have a system which monitors the temperature conditions of the product throughout the supply chain from storage to transportation and finally to the end customer by real-time monitoring. Such a system will allow medical practitioners and researchers to check the authenticity of the drug product if it is out of the temperature limits thus ensuring patient safety (Singh *et al*., 2020).

2.3.1 Challenges in cold chain management

The cold chain in biologic and biopharmacceutical logistics is very complex and sensitive and requires effective management based on its impact on public health. The key challenges in cold chain logistics include increased sensitivity of the products, its volume, ever growing regulations, gaps in infrastructure pertaining to temperature monitoring and location tracking throughout the cold chain (Mohsin and Yellampalli, 2017).

According to (Manish, 2022), current biologics and biopharmaceutical cold chain possess following constraints:

a. Poor visibility:

Most cold-chain inventories even today rely on traditional methods of data collection using temperature probes and humidity sensors before and after unloading of product. They lack effective systems for routine data collection, which is much more accurate and gives visibility in identifying the gaps and help with taking actions to tackle them (Ashok *et al.*, 2017).

b. Monitoring

Traditional cold chain also lacks effective monitoring of temperature, pressure and pressure periodically throughout the whole process. Periodic monitoring of above-mentioned parameters can actually ensure the safety and efficacy of the product (Biswas *et al.*, 2023).

c. Supply chain fragmentation

Involvement of multiple stakeholders from production to distribution results in interoperability between the systems. Along with limited transparency it can attribute to quality deviation and product loss

There is an immediate need for saving this crippling cold chain logistics through disruptive technologies like Internet of things (IoT), which helps to reduce the extent of human intervention (Mohsin and Yellampalli, 2017)

2.4. IoT-enabled cold chain monitoring technologies

The term IoT was coined in 1999 by Kevin Ashton, the founder of the Auto-ID research group at the Massachusetts Institute of Technology. It refers to the collective network of physical objects being connected to the internet. IoT has two entities, sensing entity and cloud entity which enables communication between each other. The sensing entity comprises sensors which collect data and the cloud entity gathers the collected data and stores them for decision making (Mohsin and Yellampalli, 2017).

According to (Hernández and Yamaura, 2017), using IoT in logistics, companies can monitor their assets easily and also increase visibility in their supply chain. In the biopharmaceutical industry, it is highly important to have an extremely specialised and compliant network for the transit and storage of products in an efficient manner while maintaining the integrity of the product. Haddud et al (2017) provides a useful insight into techniques like radio frequency

identification (RFID), sensors (wired or non-wired), mobile applications, and machine-to-machine systems for the process of decision-making in supply chain systems with minimal or no human intervention. Hasanat et al (2020) has proposed an IoT model on vaccine cold-chain monitoring wherein the model can provide information such as the information about the carrier, continuous sensing of temperature & humidity using sensors, location tracking of the carrier and also provide notifications if the sensor parameters are not met.

COVID-19 pandemic has been a catalyst and has highlighted the necessity to maintain optimum temperatures to prevent spoilage and loss of products. In his study, (Goodarzian *et al.*, 2023) aims to develop a real-time temperature recording framework using RFID, IoT and Statistical Process Control Charts which helps in identifying and addressing temperature excursions and any instability within the cold chain process. The framework also aims to take pre-emptive actions during temperature excursions in order to prevent spoilage of products during storage and transit.

2.4.1 Monitoring sensor

IoT-enabled sensors play a very important role in monitoring temperature and other environmental factors in the cold chain logistics of biologics and biopharmaceuticals. They provide real-time insights into critical parameters like temperature, humidity, pressure and gas levels. Through remote monitoring and data logging, they allow continuous surveillance of environmental conditions. By tracking the conditions during transportation and storage, they help safeguard the integrity of temperature-sensitive goods and ensure their efficacy. With advancements like RFID temperature sensors, peptide-based hydrogels for defrost sensing, and wireless sensor networks offer practical solutions for monitoring and managing temperature fluctuations and environmental conditions throughout the supply chain.

By leveraging IoT systems, real-time monitoring capabilities are enhanced, allowing for proactive anomaly detection and decision support options. This enables stakeholders to intervene promptly to prevent spoilage, reduce waste, and maintain medication and biological product efficacy. Continuous monitoring and data-driven insights mitigate the risk of product degradation and loss, improving operational efficiency and cost-effectiveness in cold chain management (Shafiq et al., 2019; Singh et al., 2020; Gillespie et al., 2023b).

2.4.2 Tracking sensors

GPS tracking is crucial in improving cold chain monitoring for biologics and biopharmaceuticals (Vivaldi et al., 2020). It provides real-time temperature and location monitoring, enabling remote surveillance of cold storage containers. This ensures product quality preservation during transportation and protects sensitive biologics from degradation. GPS data optimizes logistic distribution plans, improving coordination between central offices and vehicles, thus promoting transparency. Advanced technologies like smart environment sensing and RFID enable comprehensive tracking capabilities, enabling reliable courier operations with minimal labour requirements. Combining GPS tracking with wireless sensor networks, particularly Zigbee technology, allows cost-effective live monitoring of goods within the cold chain. This integration ensures safe, compliant transport, meeting international regulations, and optimizing efficiency and reliability in the cold chain logistics industry (Liu et al., 2022).

Additionally, GPS technology can help companies to track the exact location of the container throughout the distribution network. It could prevent theft or tampering of biopharmaceutical products. GPS technology not only ensures security but also ensures effective planning and timely delivery of the biologic and biopharmaceutical products (Pastrana, 2013; Klein and Stolk, 2018).

2.4.3 Integration with blockchain

Blockchain technology is another game changer in Pharma 4.0. By integrating blockchain technology, IoT devices can securely store and share data related to the quality and safety of temperature-sensitive biologics and biopharmaceuticals during cold chain. This helps reduce the risk of tampering and ensures unbreakable trust among the key stakeholders. (Meisami et al., 2023) in her research emphasize how block-chain based security architecture helps IoT ecosystems by ensuring the validity and reliability of the data stored in the system. (Hamzah et al., 2023) argues that blockchain technologies safeguards IoT technologies by creation of secure identities, communication channels and transactions, all of which makes the IoT technologies protect itself from cyber-attacks.

Furthermore, blockchain in cold chain logistics helps in real-time monitoring, quality evaluation, and provides transparency in the supply chain. Various studies have highlighted the

potential benefits of integrating IoT technologies with blockchain to create robust monitoring systems that guarantee the integrity of data, improve traceability, and enhance overall quality and safety management in cold chain logistics for temperature-sensitive products (Feng et al., 2020; Hu, 2022).

3. RESEARCH METHODOLOGY

3.1. Introduction

The systematic process through which a researcher carries out the research is defined as research methodology. It is an integral part of the dissertation which aligns the research tools and techniques to the underlying philosophy to ensure consistency. One of the most common methods of research method construction is the "research onion" model (as depicted in figure 4) proposed by Saunders in 2019. The research onion model has a systematic approach and has seven layers (philosophy, approach, methodological choice, strategy, time horizon and techniques), each of which serves as a basis for overall study. Accomplishing each of the layers, an effective methodology is made possible (Melnikovas, 2018).

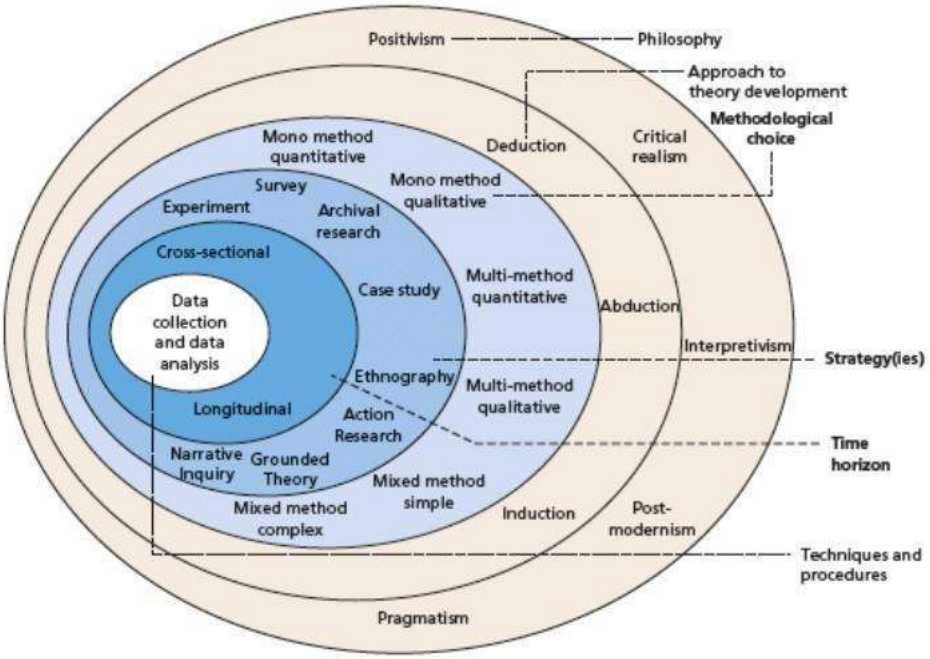

Figure 4: Research onion model by Saunders (Melnikovas, 2018)

3.2. Overview of Chapter

S. No	Research methodology	Chosen Action
1	Philosophy	Pragmatism
2	Research Approach	Abduction
3	Methodological choice	Mixed method research design
4	Research strategy	Online survey
5	Time Horizon	Cross-sectional
6	Technique	Questionnaire
7	Sampling technique	Purposive sampling

Table1: Primary research data collection

3.3. Research Philosophy

According to (Saunders *et al.,* 2019) research philosophy means having certain assumptions and beliefs at each and every stage throughout the research process. These beliefs and assumptions help the researcher in framing research questions, choosing proper methodology and how to interpret the findings. Research philosophy can be divided into five categories. They include positivism, interpretivism, critical realism, postmodernism and pragmatism. The present study uses pragmatism research philosophy.

Pragmatism

Pragmatism is one of the five philosophical approaches wherein the researcher strongly focuses on addressing the problems and providing practical solutions that could be adopted in the future. Pragmatists are driven by reality, and if a research question does not suggest a specific knowledge or method, they are open to work with different methods and knowledge. According to them, there are different ways of interpreting the world and there is no one method which enables us to see the complete picture (Saunders *et al.*, 2019). This research focuses on collecting practical experiences of logistics experts across the biopharmaceutical and biologics sector, drawing both qualitative and quantitative data to address all the objectives of the study. This justifies the use of pragmatism research philosophy in the present study.

3.4. Research approach

The research approach can be of three types: induction, deduction and abduction. The present study uses a deductive approach.

Deductive approach

Deductive research approach is often used in instances where the research begins with a theory, often obtained through literature review followed by designing of the research strategy to test it out (Saunders *et al.*, 2019). The title of the present study focuses on evaluating the effectiveness of IoT-enabled cold chain monitoring systems in ensuring product quality in the Irish biologic and biopharmaceutical sector. This itself suggests that there is existing evidence or expectation that IoT-enabled cold chain monitoring can positively impact the quality. Through collection of data through surveys the researcher tries to collect empirical evidence to test its alignment with the pre-existing theory.

3.5. Methodological choice

The methodological choice of research design can be qualitative, quantitative or mixed. The present study uses a mixed method of research design using both quantitative and qualitative approaches. The closed-ended (quantitative) questions to gather numerical data, is to help understand the current state of cold chain monitoring, IoT technologies and its efficacy. The open-ended (qualitative) questions help provide highly valued opinions on participant's experience, thoughts and opinions related to cold chain monitoring and IoT technologies.

3.6. Research strategy

Research strategy focuses on finding answers to all the research questions (Saunders *et al.*, 2019). The present study aims to address practical issues of the biologic and biopharmaceutical industry and seeks to provide practical solutions that could be adopted in the future. An online survey using both open-ended and closed-ended questions can help to gain a comprehensive understanding of the research problem and how to solve them. The quantitative methods (close-ended questions) can be used to gather data on the overall effectiveness of IoT-enabled cold chain monitoring systems in ensuring product quality, while qualitative methods (open-ended questions) can give insight on the perspective, challenges, and suggestions of key stakeholders.

3.7. Time horizon

Time horizon explains whether the study is carried out over a longer period of time or within the specific time frame. It is divided into two categories: Longitudinal and cross-sectional, where in the former represents research carried out over a longer period of time and the latter represents research carried out in a specific time frame (Saunders *et al.*, 2019). The present study was conducted as a part of an academic course where the primary research had to be done in four weeks. Therefore, the time horizon here is cross-sectional.

3.8. Data collection techniques

An online survey questionnaire consisting of both close-ended and open-ended questions was chosen to carry out the primary research. The survey questionnaire was generated through google forms and sent out to the target participants for the survey across Ireland. The target participants work in the following departments (but not limited to):

- **Cold Supply chain**: individuals responsible for overseeing the transportation and storage of biologic and biopharmaceutical products, including vaccines, biologics and other biopharmaceutical products.
- **Logistics:** companies often partner with third party logistic, for cold chain management of biologic and biopharmaceutical products, including vaccines, biologics and other biopharmaceutical products
- **IT**: individuals who can tell us more about the IoT technology and how it can be deployed.

The participants were contacted through email and LinkedIn. The survey questionnaire consisted of 11 questions related to the study, of which 5 were close-ended and remaining 6 were open-ended. A brief introduction was provided with the survey containing information related to the topic, purpose of study and the outcomes of the study. An estimated total of 80 survey forms were sent out to the potential participants through LinkedIn and email. Reminders and follow up messages and emails were sent out to the target participants for an improved response rate. Participants were asked for their consent for their valuable participation in the survey. The survey was closed with a total of 33 responses following 3 weeks of data collection. This brings the survey response rate to 41.25%.

3.9. Sampling technique

The sampling techniques can be of two types: probability sampling and non-probability sampling. The former is used when a small set of samples has an equal probability of being chosen and that it is representative of a population. On the other hand, in non-probability sampling, samples are chosen at random, keeping in mind the purpose of the study. In the present study, purposive non-probability sampling method is chosen wherein the participants are selected based on a specific criterion, stakeholders in Irish biologic and biopharmaceutical cold chain logistics.

3.10. Ethical Considerations

The research data was collected keeping in mind all the ethical considerations. The online survey questionnaire contained questions specific to the research topic and no personal questions were asked. Before collecting the primary data, ethical approval was obtained from the supervisor to make sure the questionnaire adheres to the ethical principles. A brief introduction was provided with the survey containing the information related to the topic, purpose of study and the outcomes of the study. Furthermore, it was informed to the participants that their participation is voluntary and all their responses will be kept strictly confidential as per the GDPR norms. Participants can choose to withdraw from the research at any point with no consequences. Also, at the beginning of the survey, two questions were put forth asking participant's consent to participate in the survey.

3.11. Data findings and analysis

Since the survey contains both qualitative and quantitative questions, a combination of descriptive statistics and thematic analysis will be used to analyse the gathered data. The quantitative data obtained from close-ended questions are analysed using descriptive statistics, while thematic analysis was performed on the qualitative data obtained from open-ended questions.

4. FINDINGS AND ANALYSIS

This chapter presents the analysis of findings from the survey responses received from the research participants. It tries to make sense of the mixed data (quantitative and qualitative) from different stakeholders in the biologics and biopharmaceutical sector in Ireland. For close-ended questions, descriptive statistics was used to analyse the quantitative data and for open-ended questions, thematic analysis was used to analyse the qualitative data.

The insights generated from the data was valuable in concluding the research study in ensuring product quality in Irish Biologic and biopharmaceutical logistics through IoT enabled cold chain monitoring. The survey began with a short introduction about the topic, purpose and significance of the study. It was following by asking first two questions whether the participant understands the purpose of the study, and if the participant is willing to participate in the study.

4.1. Understanding and Participation consent

Q.1 Do you understand the purpose of the study?

Answer: All the 33 participants (100%) understand the purpose of the study. This indicates the clarity of survey instructions.

Q.2 Do you agree to participate in the survey?

Answer: All the 33 participants (100%) agree to participate in the study. This demonstrates that the participants find the topic important and relevant, which is useful in obtaining relevant and meaningful data from the survey.

4.2. Demographics of the participants

The survey was generated through google forms and were distributed to key stakeholders in the Irish biologic and biopharmaceutical logistics including:

- Supply chain: planners, managers, coordinators
- Logistics: analyst, coordinators, managers
- Manufacturing: compliance & operations lead, operators
- Quality: pharmaceutical distribution manager, biotech operators
- IT: technical support – material management, lab IT & CSV professionals, MES analyst

A total of 80 potential participants from the above categories were approached via LinkedIn and email to participate in the study. 15 participants from each category were chosen for

achieving a strong viable data. Initial engagement of the participants was found to be low in the beginning week. In order to improve the response rate, reminder messages and follow-up emails were sent, which resulted in an increase in number of responses. The survey was closed following 3 weeks of data collection. Of the 80 potential participants, only 33 chose to participate in the study, thus bringing the response rate to 41.25%.

Q.3 How many years of experience do you have in the biologic and biopharmaceutical industry?

Answer: Regarding the experience of the participants, it ranges from 0 to over 10 years across the different job roles. Out of the total 33 participants, majority of the participants accounting to 48.5% (16) had experience ranging from 0 to 2 years, followed by 24.2% (8) of the participants with 3 to 5 years of experience in their current role. The remaining number of participants accounted for 12.1% (4) with experience or 6 to 10 years and 15.2% (5) with experience more than 10 years, as shown in table 2.

Years of experience	No. of Participants	Percentage (%)
0-2	16	48.5
3-5	8	24.2
6-10	4	12.1
More than 10	5	15.2
Grand total	33	100%

Table 2: Q.3 Years of experience in the biologic and biopharmaceutical industry

4.3. Confidence and satisfaction with current systems

Q.4 How satisfied are you with the accuracy and reliability of the data provided by your current cold chain monitoring systems?

Answer: The survey data (figure 5) suggests that the majority of respondents (64%) expressed their satisfaction or higher with the accuracy and reliability of the data provided by their current cold chain monitoring systems. However, 18% of the respondents were dissatisfied or very dissatisfied with the accuracy and reliability of the data provided by their current cold chain monitoring systems. Another 18% of the respondents were neutral about

the data provided by their current cold chain monitoring systems. This indicates that even though majority of the respondents find the current system to be effective, there is still room for improvement as indicated by the 36% who were either neutral, dissatisfied or very dissatisfied.

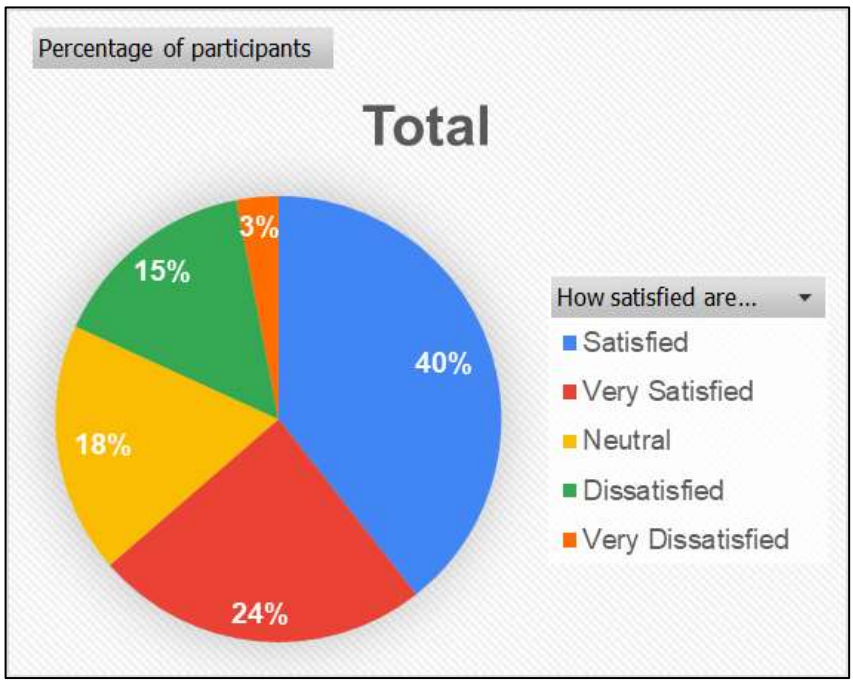

Figure 5: Q.4 Accuracy and Reliability of the data provided by current cold chain monitoring systems

Q.5 On a scale from 1 to 5, how confident are you that current quality control measures within your biologic and biopharmaceutical logistics operations meet regulatory requirements?

Answer: By looking at figure 6, it can be said that nearly half of respondents (17 respondents accounting 52%) were somewhat confident that the current quality control measures within their biologic and biopharmaceutical logistics operations meet the regulatory requirements. A total of 13 respondents (39%) were confident or highly confident that that the current quality control measures within their biologic and biopharmaceutical logistics operations meet the regulatory requirements. Only 3 of the respondents (9%) were not confident that the current quality control measures within their biologic and biopharmaceutical logistics operations meet the regulatory requirements.

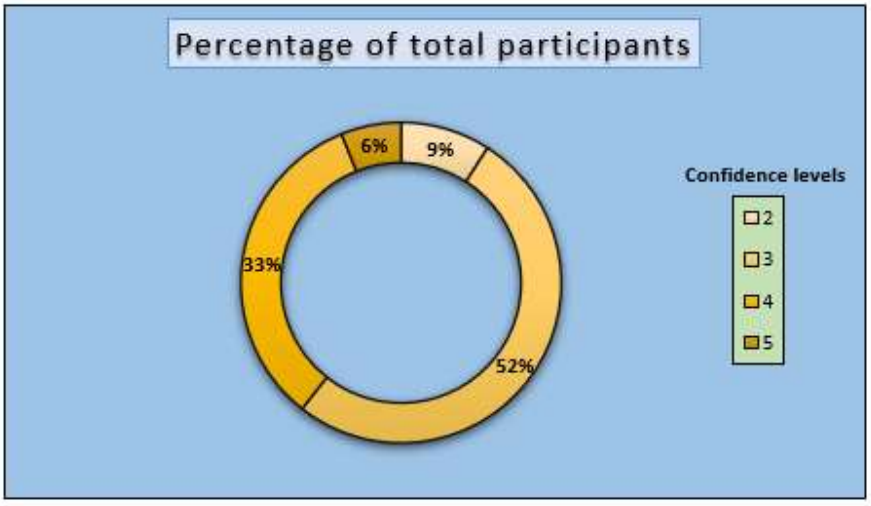

Figure 6: Q.5 On a scale from 1 to 5, how confident are you that current quality control measures within your biologic and biopharmaceutical logistics operations meet regulatory requirements?

Q.6 Are you currently utilizing IoT-enabled cold chain monitoring solutions in your biologic and biopharmaceutical logistics operations? (Yes / No)
If yes, please specify for what type of products

Answer: Of the total respondents, 64% answered 'No' to the above question. The remaining 36% respondents were asked to specify the type of product, for which they use the IoT-enabled cold chain monitoring solutions. The answers given by the respondents were grouped as shown in figure: as follows:

- Temperature sensitive injections like diabetic injections and subcutaneous injections for treating migraines – 6%
- Vaccines – 9%
- DNA kits, diagnostic kits, blood kits – 6%
- Gene therapies and Monoclonal Antibodies – 9%
- Temperature-sensitive biological products – 3%
- Diagnostic reagents – 3%

From the above-mentioned data (figure 7), it can be clearly understood that there are significant barriers which outweigh the potential benefits of IoT technologies in cold chain. For those who are currently using IoT-technologies, the majority are for high-value products

like vaccines, gene therapies and monoclonal antibodies (18%), reflecting the need for highly advanced technologies in maintaining their quality and integrity.

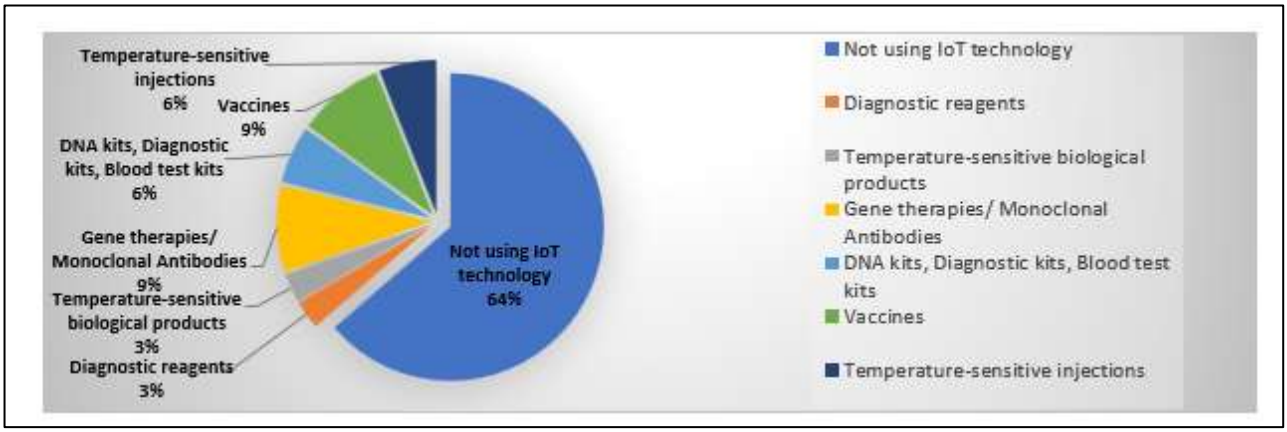

Figure7: Q.6 Are you currently utilizing IoT-enabled cold chain monitoring solutions in your biologic and biopharmaceutical logistics operations? If yes, please specify for what type of products.

4.4. Thoughts on effectiveness of IoT enabled cold chain

Q.7 Please rate the effectiveness of IoT-enabled cold chain monitoring solutions in ensuring product quality.

Answer: The participants were asked to rate the effectiveness of IoT-enabled cold chain monitoring solutions in ensuring product quality within a scale from excellent to poor. Of the total respondents, the majority rated the technology to be either good (39.39%), very good (24.24%) or excellent (9.09%). While nearly a quarter of the respondents (27.27%) rated the technology to be “fair”, none of the respondents rated the technology “poor”, see figure 8. This could indicate that IoT technologies in cold chain monitoring could be reliable and beneficial to the biologics and biopharmaceutical logistics.

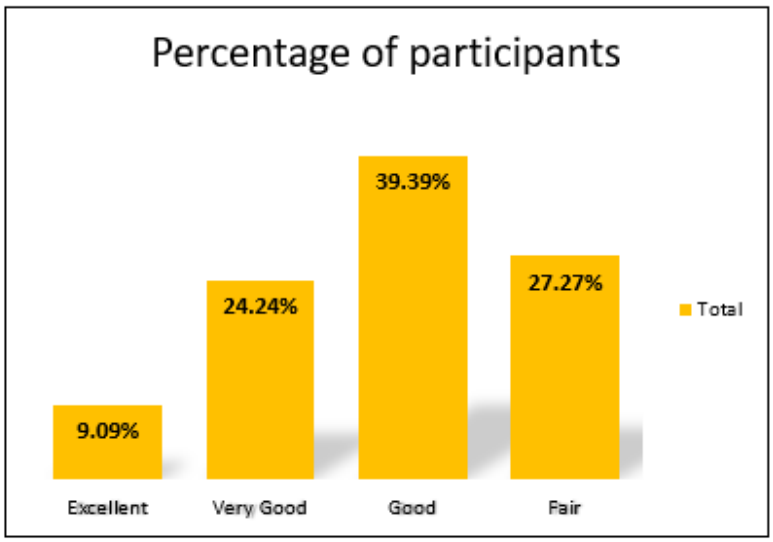

Figure8: Q.7 Please rate the effectiveness of IoT-enabled cold chain monitoring solutions in ensuring product quality.

4.5. Challenges and incidents

Q.8 How often do you encounter issues related to temperature excursions or other environmental factors that can impede affecting product quality during transportation or storage?

Answer: Participants of the survey were asked to mention how often do they encounter issues related to temperature excursions or other environmental factors that affect the product quality during transportation or storage. They were given four options to choose from: daily, weekly, monthly and rarely, as shown in the figure 9. Of the 33 respondents, a vast majority of 48.48% people chose the option “monthly”, followed by 27.27% people who chose the option “weekly”. This may suggest that the excursions in temperature or other environmental factors are common. The remaining 24.3% of people said that they rarely experience any encounter issues related to temperature excursions or other environmental factors, affecting the product quality during transportation or storage. Such a small proportion may indicate either the use of robust systems or the products that are less sensitive to temperature excursions or changes in other environmental factors.

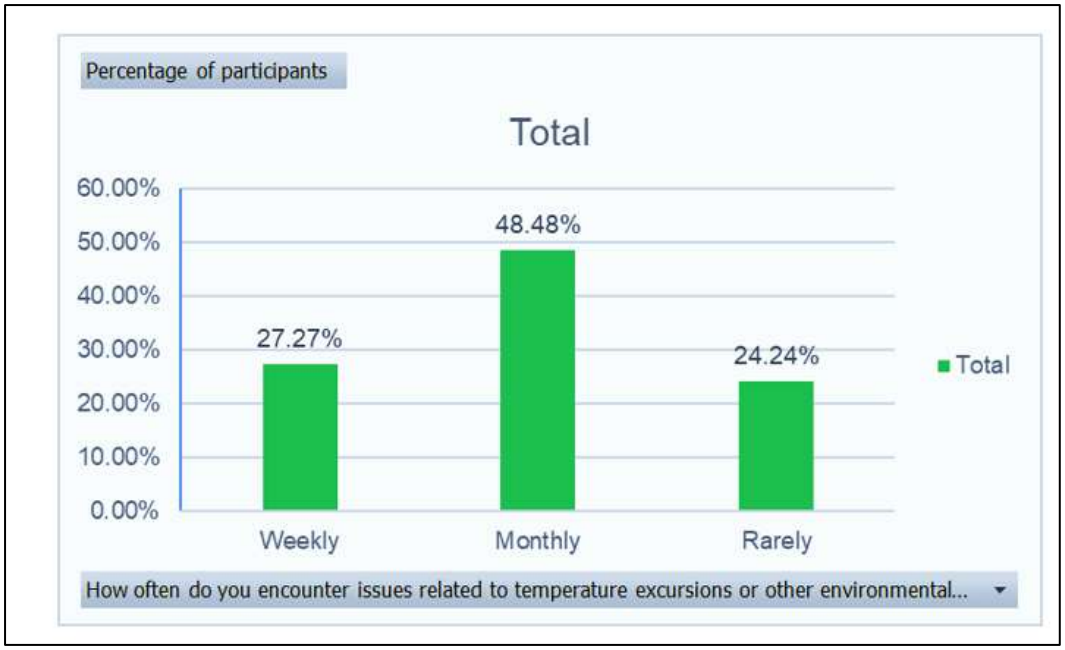

Figure9: Q.8 How often do you encounter issues related to temperature excursions or other environmental factors that can impede affecting product quality during transportation or storage?

Q.9 What are the main challenges you face in implementing IoT-enabled cold chain monitoring solutions in your biologic and biopharmaceutical logistics operations?

Answer: The above question was asked as an open-ended question. Participants were asked to write down the challenges they face in implementing IoT-enabled cold chain monitoring in their present biologic and biopharmaceutical logistics operations. The results obtained were grouped and classified as shown in figure 10. It can be concluded that the most challenging factor in the implementation of IoT-enabled cold chain monitoring is the cost (20%), followed by data security (18%). Other than cost and data security, respondents also raised concerns such as compatibility issues in integrating with the existing technologies (12%), network and connectivity issues during transportation through remote areas (12%), the need for upskilling the workforce to keep up with the new technology (10%) and technical problems (8%). A small proportion of respondents also identified challenges related to interoperability between the stakeholders (6%), regulatory compliance issues (6%), issues in scalability (4%) and reliability of the generated data through IoT technologies (4%).

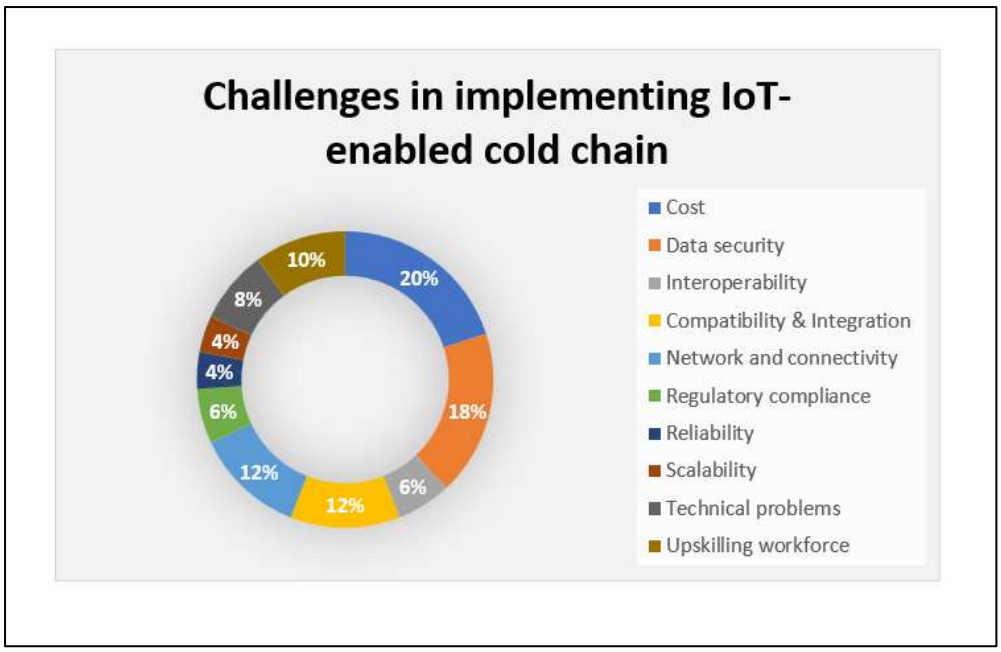

Figure10:Q.9 Challenges in implanting IoT-enabled cold chain monitoring

Q.10 Can you describe a recent incident where temperature or other environmental factors were compromised as part of your supply chain?

Answer: Out of the total 33 participants, only 51.52% chose to answer this question (see figure 11). Of this the major reasons were temperature excursions during delays in transit (21.21%) and equipment/power failure (24.24%). A small proportion of the respondents mentioned improper handling due to inadequate training (3.03%) and loss of internet connectivity during transit (3.03%).

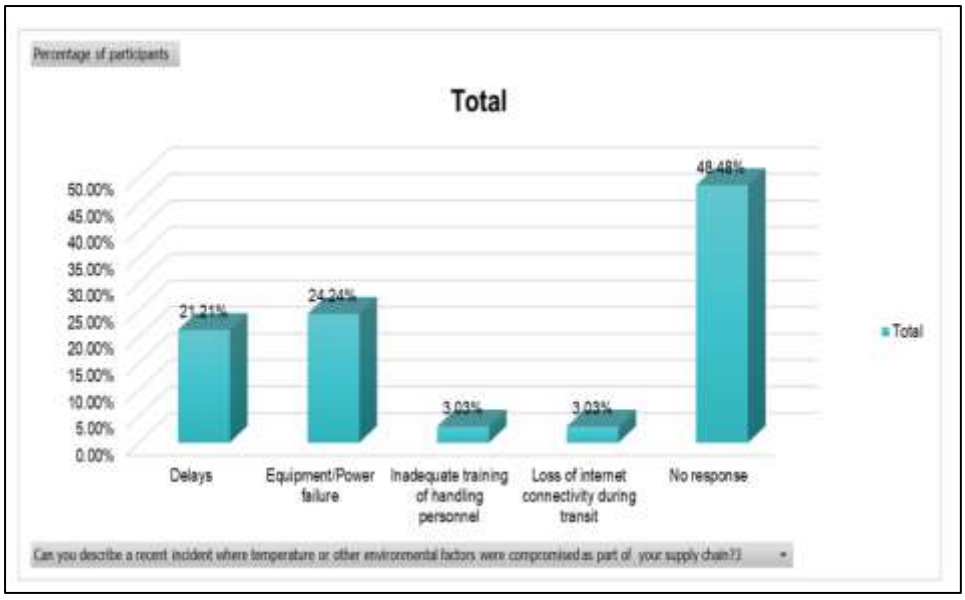

Figure11: Q.10 Recent incidents

4.6. Requirements and essential features

Q.11 What features or capabilities do you believe are essential in an IoT-enabled cold chain monitoring solution for biologic and biopharmaceutical logistics?

Answer: By looking at the figure 12, it can be concluded that majority of respondents (26%) believe the most essential feature of IoT-enabled cold chain monitoring solution for biologic and biopharmaceutical logistics is 'real-time monitoring". This is followed by GPS tracking (15%), data security and automated alerts (11% each), ease of integration with existing systems (10%), predictive analytics (7%), user-friendly interface and sustainability (4% each), battery back-up, durability and remote access (3% each), scalability and compatibility (1%).

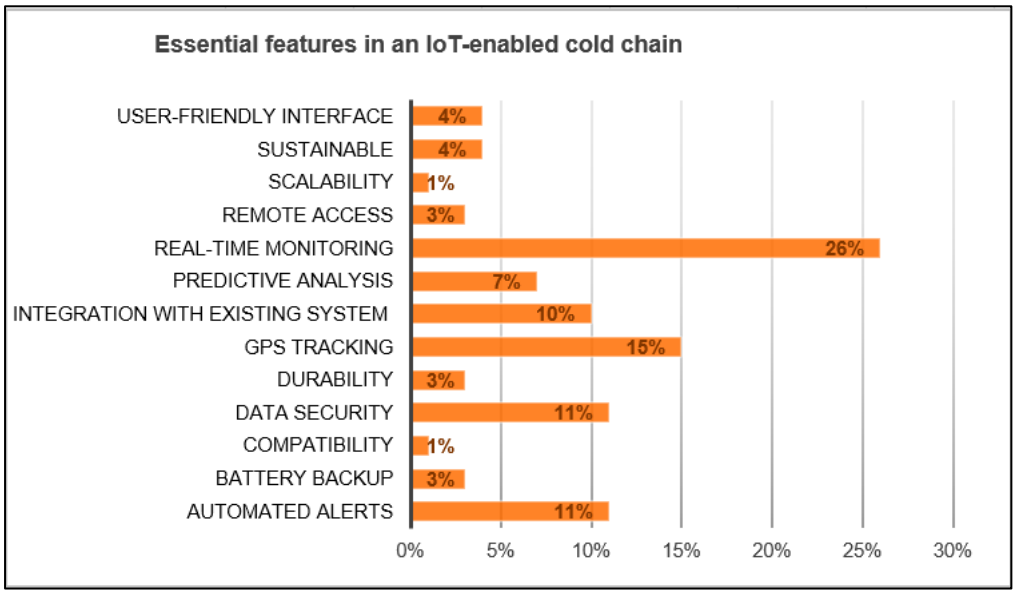

Figure12: Q.11 Essential features

4.7. Regulatory and Industry perspectives

Q.12 How do you perceive the role of regulatory authorities in ensuring the quality and safety of biologic and biopharmaceutical products throughout the supply chain?

Answer: The above question was an open-ended question. By performing a thematic analysis, it has been reached to a conclusion that the role of regulatory authorities can ensure quality and safety of biologics and biopharmaceuticals by performing regular risk assessment and monitoring, establishing standards, conducting audits and enforcing compliance.

4.8. Future outlook and benefits

Q.13 In your opinion, what are the potential benefits of integrating IoT technology into biologic and biopharmaceutical logistics operations?

Answer: As shown in figure 13, the possible benefits of integrating IoT technologies into biologic and biopharmaceutical logistics operations include:

- Quality and efficiency (as agreed by 18% of the respondents)
- Visibility (as agreed by 18% of the respondents)
- Patient safety (as agreed by 16% of the respondents)
- Transparency (as agreed by 16% of the respondents)
- Traceability (as agreed by 16% of the respondents)
- Risk reduction (as agreed by 11% of the respondents)
- Cost savings (as agreed by 4% of the respondents)
- Competitive advantage (as agreed by 2% of the respondents)

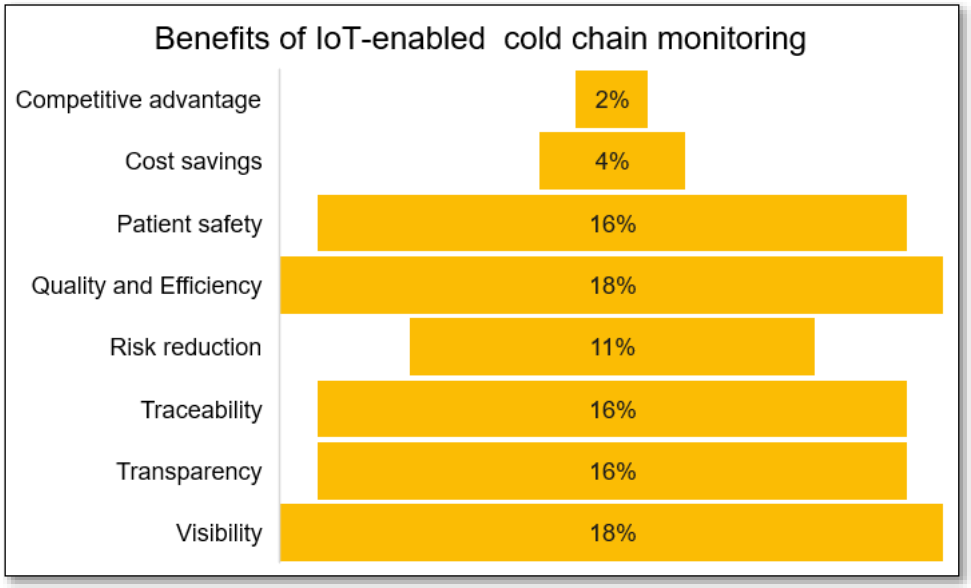

Figure 13: Q.12 Benefits of IoT-enabled cold chain monitoring

Q.14 How do you envision the future of cold chain monitoring in the industry, particularly with advancements in IoT technology?

Answer: According to all the respondents, with advancements in the IoT technologies, respondents see the future of cold chain monitoring becoming more predictive and integrated. Real-time

analytics and machine learning will enable proactive interventions to prevent temperature issues. Blockchain may enhance data transparency, bolstering regulatory compliance and trust. This promises a more efficient and resilient biologic and biopharmaceutical logistics system to meet growing demands.

5. CONCLUSIONS AND RECOMMENDATIONS

Cold chain monitoring is very crucial and important step in Irish biologic and biopharmaceutical logistics. It not only ensures product quality and patient safety, but also helps the biologic and biopharmaceutical industry to flourish. Let us try to discuss our research questions and objectives, provide conclusions and then proceed to recommendations.

5.1. Answers to the research questions

Research Question 1: What is the current state of adoption of IoT enabled technologies in cold chain transportation of temperature sensitive biologics, biopharmaceutical products, diagnostic kits, laboratory reagents and vaccines in Ireland?

Even in the Industry 4.0 era, majority of the biologic or biopharmaceutical companies in Ireland is still following the conventional method of cold chain logistics. Only a fraction of the companies is into harnessing the digital potential of Industry 40 through IoT-enabled cold chain monitoring. This is sad especially for a country like Ireland, which is considered a global hub for the biopharmaceuticals. However, willingness of companies to adopt IoT in future can change the entire landscape of biologics and biopharmaceutical logistics in Ireland.

Research Question 2: What are the available IoT devices and technologies that can be used in cold chain monitoring of temperature sensitive biologics and biopharmaceutical products during transit and storage in Ireland?

The available IoT technologies in biologic and biopharmaceutical logistics for cold chain monitoring include temperature sensors, humidity sensors, GPS tracking, RFID tags, smart packaging, integration with block chain technology to name a few. These existing technologies can help in monitoring the animalities in temperature and other environmental factors, tracking the shipment using GPS in remote areas, knowing the complete parameters of the shipment along with visibility into the inventory and supply chain, and protection of data privacy and security.

Research Question 3: What are the advantages of IoT enabled cold chain monitoring when compared to the conventional method?

IoT technologies in cold chain have huge benefits. These include increased visibility into the supply chain, better transparency for various stakeholders, traceability of the shipments, enhanced quality, efficiency and better patient safety, to name a few. Apart from this IoT technologies have a better competitive advantage and return of investments in the long run.

Research Question 4: What are the challenges faced for implementing IoT enabled cold chain monitoring?

Adoption of IoT technologies in cold chain monitoring can be quite challenging. The main reason could be the unwillingness towards a change. However, apart from that there are few other factors as demonstrated by the present study which biologic and biopharmaceutical logistics across Ireland face while deciding whether or whether not to implement IoT enabled cold chain monitoring. These challenges include: cost of implementation, concerns regarding data security and privacy, concerns regarding compatibility in integrating with existing systems, network and connectivity issues during transportation, need for upskilling the workforce, difficulty in interoperability between the stakeholders, issues in scalability. The primary challenges are cost and data privacy, if addressed them first, there will be much faster adoption of IoT technologies in cold chain monitoring in Ireland.

Research Question 5: How does the use of IoT technology in cold chain monitoring contribute to the overall efficiency of pharmaceutical transit processes?

By implementing IoT enabled cold chain monitoring systems in Ireland, spoilage of products can be prevented, which in turn benefit the stakeholders economically and also ensures safety of the patients. It also offers visibility into the supply chain, bridge the gap between the fragmented supply chain and provide predictive analysis for operational excellence.

5.2. Conclusion

Objective 1: To evaluate the current state of cold chain monitoring in Irish biologic and biopharmaceutical logistics

There was no literature to be found which discusses the current state of cold-chain monitoring in Irish biologic and biopharmaceutical logistics. However, the study presents meaningful insights from the biologic and biopharmaceutical logistics personnels in Ireland who gives us a better understanding of the present state of cold chain monitoring.

Objective 2: To identify and analyse the available IoT technologies used in biologic and biopharmaceutical logistics for cold chain monitoring in Ireland

The literature identifies some of the technologies currently in use across various biologic and biopharmaceutical industries across the globe, however it doesn’t mention about the technologies used in Ireland. Through survey it was made understand that IoTs in Irish cold chain monitoring of biologic and biopharmaceutical industries is still in budding stages and not

widely adopted, there is hope that in near future companies will be more willing to incorporate them.

Objective 3: To identify and analyse the challenges faced in implementing IoT enabled cold chain monitoring in Ireland

Both literature and the survey identify few common challenges faced while implementing IoT technologies in cold chain monitoring. However, literature tells nothing about the scenario of Ireland, the survey complements this aspect and both together provide a meaningful insight into this topic. It can be said that in Ireland, the cost of implementing IoT enabled cold chain technologies and concerns about the security and privacy of the data is the main challenge.

Objective 4: To evaluate the economic, environmental, and social impacts of implementing IoT-enabled cold chain monitoring systems in Ireland

As backed by the literature, the study gives insights into the economic, environmental, and social impacts of implementing IoT-enabled cold chain monitoring systems in Ireland. By minimizing the occurrence of product spoilage through better monitoring practices, IoT technologies can prevent economic losses to the company. Reduction of waste and better energy efficiency by IoT technologies can promote sustainability and eco-friendliness. The social impact includes better patient safety.

Objective 5: To investigate emerging trends in the adoption of IoT technology for cold chain monitoring in Irish biologic and biopharmaceutical logistics and provide recommendations for the future improvements

The research findings along with the literature suggests that the emerging trends in adoption of IoT technologies for cold chain monitoring in Irish biologic and biopharmaceutical logistics focuses on two main areas which are “predictive analytics” and “integration with blockchain technologies”. The former help in improved decision making and automating the system while the latter ensures the safety and security of the data generated.

5.3. Recommendations

The study recommends several steps that can be taken to improve the current rate of adoption of IoT technologies in cold chain monitoring in Irish biologic and biopharmaceutical logistics:

1) Collaboration between government bodies and biopharmaceutical companies

The Irish government can help the biologic and biopharmaceutical companies to overcome the cost barrier of implementation by providing subsidies, tax incentives and grants. This will result in widespread adoption of IoT technologies.

2) Investing in employee training programs

Through upskilling the existing workforce, making them familiar to the technology can have a positive impact on the willingness in adoption of IoT technologies.

3) Establishing compliance assistance:

Compliance assistance can be provided to assist companies in implementation, operation and meeting all the regulatory requirements related to IoT-enabled cold chain monitoring.

4) Enhanced data privacy and security

Encouraging companies to integrate block chain technology and take other advanced security measures to improve transparency throughout the supply chain.

5) Taking pilot initiatives

Pilot programs can be run to understand the feasibility and benefits pf IoT in cold chain monitoring.

6. REFERENCES

Antal, C. *et al.* (2021) 'Blockchain Platform For COVID-19 Vaccine Supply Management'. *IEEE Open Journal of the Computer Society*, 2, pp. 164–178. DOI: 10.1109/OJCS.2021.3067450.

Ashok, A., Brison, M. and LeTallec, Y. (2017) 'Improving Cold Chain Systems: Challenges and Solutions'. *Vaccine*, 35(17), pp. 2217–2223. DOI: 10.1016/j.vaccine.2016.08.045.

Biswas, K. *et al.* (2023) 'A Reliable Vaccine Tracking and Monitoring System for Health Clinics Using Blockchain'. *Scientific Reports*, 13, p. 570. DOI: 10.1038/s41598-022-26029-w.

Chatterjee, S. and Pandey, K.G. (2003) 'Thermoelectric Cold-Chain Chests for Storing/Transporting Vaccines in Remote Regions'. *Applied Energy*, 76(4), pp. 415–433. DOI: 10.1016/S0306-2619(03)00007-2.

Deiana, S., Gabbani, T. and Annese, V. (2017) 'Biosimilars in Inflammatory Bowel Disease: A Review of Post-Marketing Experience'. *World Journal of Gastroenterology*, 23(2), pp. 197–203. DOI: 10.3748/wjg.v23.i2.197.

Feng, H. *et al.* (2020) 'Evaluation on Frozen Shellfish Quality by Blockchain Based Multi-Sensors Monitoring and SVM Algorithm During Cold Storage'. *IEEE Access*, 8, pp. 54361–54370. DOI: 10.1109/ACCESS.2020.2977723.

Gillespie, J. *et al.* (2023) (3) 'Real-Time Anomaly Detection in Cold Chain Transportation Using IoT Technology'. *Sustainability*, 15(3), p. 2255. DOI: 10.3390/su15032255.

Goodarzian, F. *et al.* (2023) 'Designing an Integrated Responsive-Green-Cold Vaccine Supply Chain Network Using Internet-of-Things: Artificial Intelligence-Based Solutions'. *Annals of Operations Research*, 328(1), pp. 531–575. DOI: 10.1007/s10479-022-04713-4.
Goyal, P. and Gupta, V. (2021) *Building Quality in Pharmaceutical Products*.

Grand view research. (2021) *Europe Pharmaceutical Market Size Report, 2021-2028*. Available at: https://www.grandviewresearch.com/industry-analysis/europe-pharmaceutical-market-report (Accessed: 8 May 2024).

Haddud, A. *et al.* (2017) 'Examining Potential Benefits and Challenges Associated with the Internet of Things Integration in Supply Chains'. *Journal of Manufacturing Technology Management*, 28(8), pp. 1055–1085. DOI: 10.1108/JMTM-05-2017-0094.

Hamzah, A.K. *et al.* (2023) 'Ensuring Trust and Security in IoT Systems through Blockchain Integration'. In *2023 Third International Conference on Secure Cyber Computing and Communication (ICSCCC)*. 2023 Third International Conference on Secure Cyber Computing and Communication (ICSCCC). pp. 298–303. DOI: 10.1109/ICSCCC58608.2023.10176600.

Hasanat, R.T. *et al.* (2020) 'An IoT Based Real-Time Data-Centric Monitoring System for Vaccine Cold Chain'. In *2020 IEEE East-West Design & Test Symposium (EWDTS)*. 2020

IEEE East-West Design & Test Symposium (EWDTS). pp. 1–5. DOI: 10.1109/EWDTS50664.2020.9225047.

Hernández, A. and Yamaura, M. (2017) 'Cold Chain Management with Internet of Things (IoT) Enabled Solutions for Pharmaceutical Industry'.
Hu, X. (2022) 'Cold Chain Logistics Model of Agricultural Products Based on Embedded System and Blockchain'. *Production Planning & Control*, 0(0), pp. 1–12. DOI: 10.1080/09537287.2022.2101939.

Kesik-Brodacka, M. (2018) 'Progress in Biopharmaceutical Development'. *Biotechnology and Applied Biochemistry*, 65(3), pp. 306–322. DOI: 10.1002/bab.1617.

Kinch, M.S. (2015) 'An Overview of FDA-Approved Biologics Medicines'. *Drug Discovery Today*, 20(4), pp. 393–398. DOI: 10.1016/j.drudis.2014.09.003.

Klein, K. and Stolk, P. (2018) 'Challenges and Opportunities for the Traceability of (Biological) Medicinal Products'. *Drug Safety*, 41(10), pp. 911–918. DOI: 10.1007/s40264-018-0678-7.

Kumar, N. and Jha, A. (2017) 'Temperature Excursion Management: A Novel Approach of Quality System in Pharmaceutical Industry'. *Saudi Pharmaceutical Journal*, 25(2), pp. 176–183. DOI: 10.1016/j.jsps.2016.07.001.

Liu, K. *et al.* (2022) 'Highly-Efficient Cold Energy Storage Enabled by Brine Phase Change Material Gels towards Smart Cold Chain Logistics'. *Journal of Energy Storage*, 52, p. 104828. DOI: 10.1016/j.est.2022.104828.

Manish. (2022) *E36220611522*. *International Journal of Engineering and Advanced Technology (IJEAT)*. Available at: https://www.ijeat.org/portfolio-item/e36220611522/ (Accessed: 10 May 2024).

Meisami, Sajad. *et al.* (2023) 'Combining Blockchain and IoT for Decentralized Healthcare Data Management'. *International Journal on Cryptography and Information Security*, 13(1), pp. 35–50. DOI: 10.5121/ijcis.2023.13102.

Melnikovas, A. (2018) 'Towards an Explicit Research Methodology: Adapting Research Onion Model for Futures Studies'. *Journal of Futures Studies*, 23, pp. 29–44. DOI: 10.6531/JFS.201812_23(2).0003.

Mika Naumanen. (2019) *Trends in European Clusters: Results from the 2019 European Panorama, Trends and Priority Sectors Reports Published | European Cluster Collaboration Platform*. Available at: https://clustercollaboration.eu/eu-initiatives/trends-european-clusters-results-2019-european-panorama-trends-and-priority (Accessed: 8 May 2024).

Minuto, N. *et al.* (2010) 'Diabetic Ketoacidosis Caused by Exposure of Insulin to Low Temperature'. *Diabetes Technology & Therapeutics*, 12(9), pp. 745–746. DOI: 10.1089/dia.2010.0055.

Mohsin, A. and Yellampalli, S.S. (2017) 'IoT Based Cold Chain Logistics Monitoring'. In *2017 IEEE International Conference on Power, Control, Signals and Instrumentation Engineering (ICPCSI)*. 2017 IEEE International Conference on Power, Control, Signals and Instrumentation Engineering (ICPCSI). pp. 1971–1974. DOI: 10.1109/ICPCSI.2017.8392059.

MORROW, T. and Felcone, L.H. (2004) 'Defining the Difference: What Makes Biologics Unique'. *Biotechnology Healthcare*, 1(4), pp. 24–29.
Nadimuthu, L.P.R. and Victor, K. (2022) 'Environmental Friendly Micro Cold Storage for Last-Mile Covid-19 Vaccine Logistics'. *Environmental Science and Pollution Research*, 29(16), pp. 23767–23778. DOI: 10.1007/s11356-021-17584-2.

Pajić, V., Andrejić, M. and Chatterjee, P. (2024) 'Enhancing Cold Chain Logistics: A Framework for Advanced Temperature Monitoring in Transportation And'. 3, pp. 16–30. DOI: 10.56578/mits030102.

Pastrana, E. (2013) 'Protein GPS'. *Nature Methods*, 10(8), pp. 696–697. DOI: 10.1038/nmeth.2588.

Peplies, J. *et al.* (2010) 'Quality Management for the Collection of Biological Samples in Multicentre Studies'. *European Journal of Epidemiology*, 25(9), pp. 607–617. DOI: 10.1007/s10654-010-9481-1.

Rader, R.A. (2008) '(Re)Defining Biopharmaceutical'. *Nature Biotechnology*, 26(7), pp. 743–751. DOI: 10.1038/nbt0708-743.

Saunders, M. *et al.* (2019) '"Research Methods for Business Students" Chapter 4: Understanding Research Philosophy and Approaches to Theory Development'. In pp. 128–171.

Schwab, K. (2017) *The Fourth Industrial Revolution*. Crown.

Scott, R. and Rutner, S. (2020) 'Scheduling and Delivery Logistics of Bio-Perishable Goods: A Review Of Literature And Research Options'. *Journal of Transportation Management*, 31(1). DOI: 10.22237/jotm/1593576300.

Shafiq, Y. *et al.* (2019) 'A Reusable Battery-Free RFID Temperature Sensor'. *IEEE Transactions on Antennas and Propagation*, 67(10), pp. 6612–6626. DOI: 10.1109/TAP.2019.2921150.

Shashi. (2022) *E36220611522. International Journal of Engineering and Advanced Technology (IJEAT)*. Available at: https://www.ijeat.org/portfolio-item/e36220611522/ (Accessed: 16 May 2024).

Singh, R., Dwivedi, A.D. and Srivastava, G. (2020) (14) 'Internet of Things Based Blockchain for Temperature Monitoring and Counterfeit Pharmaceutical Prevention'. *Sensors*, 20(14), p. 3951. DOI: 10.3390/s20143951.

Vivaldi, F. *et al.* (2020) 'A Temperature-Sensitive RFID Tag for the Identification of Cold Chain Failures'. *Sensors and Actuators A: Physical*, 313, p. 112182. DOI: 10.1016/j.sna.2020.112182.

Walsh, G. (2002) 'Biopharmaceuticals and Biotechnology Medicines: An Issue of Nomenclature'. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, 15(2), pp. 135–138. DOI: 10.1016/s0928-0987(01)00222-6.

WHO. (2011) *TRS 961 - Annex 9: Model Guidance for the Storage and Transport of Time and Temperature Sensitive Pharmaceutical Products*. Available at: https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport (Accessed: 12 February 2024).

Yildiz, T. (2023) *Logistics and Supply Chain Management: Fundamentals and Strategies*.