Griffith College

An Evaluation of Orthopaedic Knee Implant FDA Recalls (From Manufacturing to Market release): 2019-2023

By

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[redacted]

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Griffith College Dublin

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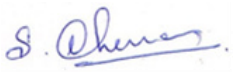
CANDIDATE DECLARATION

I, **Thennarasu Selvaganapathi** certify that the information presented in this study is true. I confirm that the Innopharma Griffith College academic integrity standards were followed in the conduct of this study. The study's findings are unique and derived from my own research. Every source utilized in this research, including books, journals, websites, and articles, is cited, and no one else's work has been plagiarized.

Thennarasu Selvaganapathi

Student's signature: 

Date: 19th May 2024

Dr. Aine Behan PhD

Supervisor's signature:

Date:

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Finally, I want to express my gratitude to my friends, partner, and family for their unwavering support.

ABSTRACT

Background: In recent years, the medical device sector has been positioned for consistent expansion, with worldwide yearly sales predicted to increase by more than 5% annually, reaching close to $800 billion by the year 2030 (van den Heuvel *et al.*, 2018). In parallel to this growth, there is ongoing debate around the need for increased regulations and higher standards for medical device manufacturers, particularly as recalls have not decreased in frequency. The orthopaedic devices sector represents nearly 20% of the medical devices available on the global market and 16% average of these devices undergo recalls. Nonetheless, there exists a gap in the literature around investigations on orthopaedic knee implant recalls. (DeRuyter *et al.*, 2023)

This study aims to evaluate FDA recalls associated with orthopaedic knee implants, seeking to comprehend current orthopaedic knee implant recall's trends and the reasons behind these recalls, and to determine the effectiveness of the current manufacturing quality standards and regulatory systems.

Methods: A quantitative monomethod was utilized, involving the distribution of an online survey to subject matter experts on recalls within the orthopaedic implant industries. The survey, administered via Microsoft Forms, comprised of 18 questions, encompassing both closed- and open-ended formats assessing the factors contributing to orthopaedic knee implant device recalls and the effectiveness of the current system and to provide suggestions and recommendations regarding Orthopaedic manufacturing standards, regulatory frameworks, and other relevant areas.

Responses from a total of 71 participants were collected and data analysis undertaken to investigate the reasons behind recalls, contributors to these recalls, and the efficiency of the current manufacturing standard and regulatory system. Secondary research was also undertaken to detect prevailing trends in the recall of orthopaedic knee implant devices. Data was sourced from the FDA database, specifying the years 2019 to 2023, and filtered for details such as manufacturer, approval process, implant type, recall classification, recall dates, reasons determined by the manufacturer, quantity affected, and more. These data points were then analyzed utilizing histograms to visualize the frequency of recalls across each year.

Findings: FDA recall data has shown a significant increase in the number of recalls involving orthopaedic knee implants in recent years from different manufacturers. This increasing trend in recalls has raised concerns from both the medical community and among patients as they rely on these implants to regain mobility and improve their quality of life. These recalls, often attributed to issues such as manufacturing defects, material failures, or design flaws, underscore the challenges faced by manufacturers in ensuring the reliability and safety of these critical medical devices. Survey responses further highlight key factors contributing to orthopaedic recalls as perceived by participants. Manufacturing defects stand out as the primary concern, with a majority of respondents identifying them as the main contributors to orthopaedic recalls. This underscores the importance of addressing issues within the manufacturing process, including production errors, design flaws, and lapses in quality control, to uphold the reliability and safety of orthopaedic

devices. Additionally, some respondents point to a lack of stringent FDA regulation as a significant factor contributing to orthopaedic recalls. This suggests apprehensions regarding the adequacy of regulatory oversight and enforcement, potentially resulting in compromises in product safety and quality standards. The response underscores the necessity for more robust regulatory measures to mitigate risks associated with orthopaedic devices.

Conclusions: The research findings emphasize the urgent need for a comprehensive and proactive approach to managing recalls of orthopedic knee implants, highlighting the deficiencies in the current system. Stakeholder feedback reveals diverse opinions on the necessary changes in the medical device landscape. Some stakeholders are satisfied with the current system when properly followed and advocate for no changes. However, others suggest improvements such as eliminating the predicated equivalent approval process, establishing a dedicated recall committee to review and refine the approval process as needed, and improving alignment between different international Quality Management System (QMS) standards, including ISO 13485 and FDA regulations. Additionally, stakeholders recommend integrating principles from ISO 14971 into QMS requirements to help manufacturers systematically identify, assess, and mitigate risks throughout the product lifecycle. Strengthening collaboration with small and medium-sized enterprises (SMEs) is also suggested, as suppliers often do not adhere to QMS certifications. Emphasis is placed on incorporating risk management ISO 14971 principles into QMS requirements, enhancing post-market surveillance, clinical evidence requirements, and regulatory measures, particularly in competitive and dynamic industries.

Key words: Orthopaedic, Knee implants, medical device recalls, regulation.

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List of Abbreviations

CAGR- Compound Annual Growth Rate
CFR- Code of Federal Regulations
EMA- European Medicines Agency
EUDAMED- European Union Database on Medical Devices
EU- European Union
FDA- Food and Drug Administration
IVDR- In Vitro Diagnostic Regulation
MDD- Medical Device Directives
MDR- Medical Device Regulations
PMCF- Post-Market Clinical Follow-up
PMN- Pre-Market Notification
R&D – Research and development
MFG- Manufacturing
CFR - Code of Federal Regulations Title 21(CITE: 21CFR820)
QMS- Quality System Regulations
510K - Premarket Notification
PMA - Pre-Market Approval
GDPR - General Regulation for the Protection of Data
SME – Subject matter expert
Current system* - (Medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30 and Sub-clause 4.4 of ISO 9001, ISO 14971:2019- Medical devices Risk Management and regulatory framework).

1 CHAPTER

1.1 Introduction:

There is a higher propensity for danger to patient safety when medical devices malfunction. Recalls of orthopaedic devices account for more than 20% of all devices on the market, ranging from 12% to 20% over a ten-year period. This makes orthopaedic the specialty with the highest number of recalled devices. From January 1, 2008, to December 31, 2018, a total of 904 hip and knee arthroplasty devices were approved. Among these, 485 (53.7%) were hip devices and 419 (46.3%) were knee devices. Out of the total, 179 devices (19.8%) were recalled, with 94 hip devices (19.4%) and 85 knee arthroplasty devices (20.3%) being recalled during this period of study (DeRuyter *et al.*, 2023).The objective of this dissertation is to evaluate orthopaedic knee implant recalls, identifying the underlying factors contributing to these recalls and see if improvements can be made.

This study also aims to provide significant insights into orthopaedic knee implant recalls and see if there is a gap in current system and an improvement can be made on overall quality of orthopaedic knee implant devices by investigating multiple factors such as device design, software design, manufacturing procedures, process control, regulatory control, and post-market surveillance.

1.2 Purpose of the research:

This research aims to assess the reasons behind product recalls of orthopedic knee implants by examining common factors contributing to these recalls within the orthopedic knee implant industries. It involves gathering insights from subject matter experts employed in orthopedic knee implant industries. The study covers various orthopedic knee implant products, including femoral components, tibial components, polyethylene implants, inserts, sleeves, spacers, and others. It seeks to analyze factors such as design flaws, material problems, manufacturing defects, regulatory compliance, approval processes, human factors, and post-market monitoring etc.

The purpose of this research is to look at industry data that captures the key metrics around recall efficacy, timeliness, and the impact on patient safety and product quality. Based on these developments, this thesis will evaluate the existing industry situation for medical device recalls.

1.3 Research Objectives:

Objective #1: Investigate main factors that are contributing to orthopaedic knee implant device recalls. (Survey data collection)

Objective #2: Discover if current system* is effective or improvement is required. (Survey data collection)

Objective #3: Identify current trend of orthopaedic knee implant device recalls. (FDA database collection)

1.4 Research Questions:

Question#1: What are the factors which are contributing to orthopaedic implant recalls?

Question#2: Is the current system* in place effective or does it need improvement?

Question#3: What is the current recall trend in orthopaedic knee implant products?

*(Medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30 and Sub-clause 4.4 of ISO 9001, ISO 14971:2019- Medical devices Risk Management and regulatory framework)

1.5 Scope and limitations of the research:

Scope: This study aims to pinpoint the main reasons behind the prevailing recall patterns in Orthopaedic knee implant products. It focuses solely on knee implants within the Class III Orthopaedic category and does not encompass other orthopedic products or classes. The research examines various aspects such as design flaws, material issues, manufacturing defects, regulatory compliance, approval processes, human factors, and post-market monitoring specifically related to knee implants.

Limitations: One primary limitation of this study is its small sample size, primarily due to the constraints of the dissertation timeline. The research period may not allow for a comprehensive examination of a large number of cases. Bias and varying viewpoints may arise among participants offering feedback, as data collection involved multiple departments, including Quality Engineering, Regulatory Affairs, Manufacturing, Research and Development, Validation Engineering, Product Compliance, Clinical Engineering, and others.

1.6 Research Significance:

The research aims to assess recent patterns in orthopedic knee implant recalls determining the effectiveness of the current system in ensuring product quality and patient safety. Moreover, it seeks to uncover and comprehend the causes behind these recalls, a detailed examination of root causes. Understanding why a device failed or posed risks offers manufacturers valuable insights to rectify design flaws, manufacturing problems, or other contributing factors leading to recalls and regulatory agencies like the FDA depend on research outcomes to evaluate the safety and efficacy of medical devices.

1.7 Dissertation Outline:

The dissertation will be organized into five chapters.

Chapter #1- Provides an overview of the research study. This includes the purpose of the research and study background, research objectives and research questions. Furthermore, it describes the scope and limitations of the study, significance of the study and overall structure of the Dissertation.

Chapter #2 – Represents the literature review of the study, which gives brief introduction of chapter providing background of medical device recalls, FDA regulation framework,

Chapter #3 – It gives a quick overview of the research approach before presenting the research onion and the study's research technique. Research philosophies, methodological selection, approach, strategies, time horizon, and research techniques make up the research onion. It stands for the general strategy employed for the investigation. This chapter will provide an explanation and justification of the method selected for each layer of the research onion. The chapter also discusses the research study's ethical ramifications. There will also be a quick explanation of data analysis in this part.

Chapter #4 - This comprises the data findings and analysis, which will show the information collected from primary research. The information gathered from qualified participants who have prior experience working in the medical device industries will be part of the core data gathering design. The participant is employed as a 'Quality Engineer, R&D engineer, Sustaining engineer, Regulatory specialist, Clinical Engineer, Product compliance officer, Manufacturing engineer, Validation engineer and other roles' in a top ranking multi-national medical device company. By means of these assessments, the research study will illustrate how effective the current system is and see if an improvement is required or not.

Chapter #5 – The conclusion draws the results from the survey to provide insights applicable to the Orthopaedic Knee implant industry. It provides recommendations for the industry & regulatory framework based on these findings. Additionally, references are listed, and supplementary materials such as the survey questions, raw data from the primary research are included.

2 CHAPTER

Literature review

Review of Orthopaedic Knee implant recalls, Causes, Trends and Impacts

2.1 Introduction:

The introduction outlines the importance of ensuring the safety of orthopaedic knee implant products and the serious consequences that recalls can have on patients and healthcare systems. It emphasizes the various factors contributing to recalls, trends within the orthopaedic knee implant industry, and the impacts on patient safety. Orthopaedic knee implant recalls profoundly affect patient safety, healthcare providers, and the entire medical device industry. This literature review aims to comprehensively explore the existing knowledge base concerning orthopaedic knee implant product recalls, with a focus on their causes, trends, and broader consequences. By analyzing information from relevant studies, reports, and regulatory documents, this review aims to identify common themes, gaps in literature and potential areas for enhancing the current orthopaedic knee implant device system.

2.2 Medical Devices and the role of the FDA in Medical Device regulation and compliance:

In this section, we examine into the realm of medical devices, exploring their definition and significance within the healthcare landscape and roles of FDA overseeing medical devices in the United States. The FDA serves as the principal regulatory authority responsible for ensuring the safety, effectiveness, and quality of medical devices available in the market.

What is a Medical Device:

As per section 201(h) of the FD&C Act (21 USC 321(h)) provides that the term "device" means:

an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which are:

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. (Commissioner, 2021)

Roles of FDA in Medical Device regulation & compliance:

The FDA (U.S. Food and Drug Administration) plays a crucial role in protecting and promoting public health by regulating and supervising a wide range of products, including pharmaceuticals, medical devices, biologics, food, dietary supplements, and veterinary products. The FDA's regulatory framework is designed to ensure the safety, efficacy, and security of these products. (Ramakrishna *et al.*, 2015)

The below Figure-1 depicts the medical device supply chain, which is a highly regulated supply chain with numerous stakeholders catering to various consumer groups. The FDA regulates this industry because medical devices play a vital role in the provision of healthcare. (Thirumalai and Sinha, 2011)

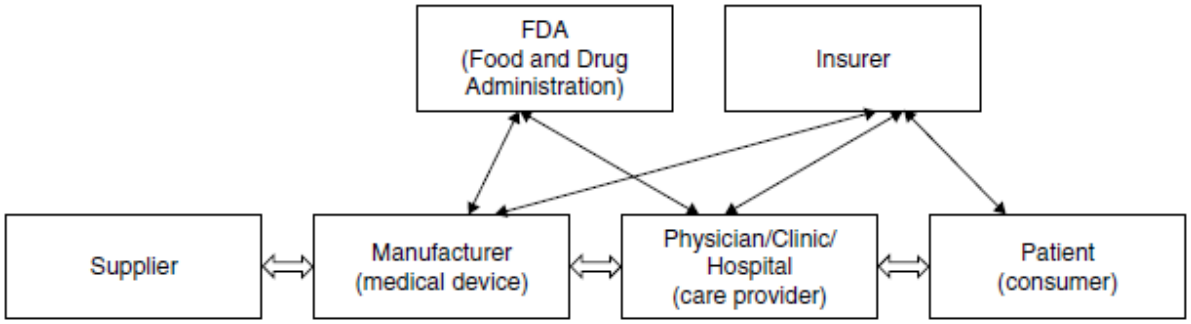


Figure 1:Medical device supply chain. (Thirumalai and Sinha, 2011)

FDA has classified medical device in to three classes based on risk category as shown in below table 1: Class I, Class II & Class III.

Device Class	**Risk Level**	**Controls**	**Device Example**
Class I	Low Risk	General Controls Example: • Labelling • 510k • QMS	Walking stick Bandage Examination Gloves Sunglasses
Class II	Moderate Risk	General Controls Special Controls: Examples: • Special labelling •Mandatory performance standard • Guidelines	Syringe Powered Wheelchair Acupuncture needle. Condoms
Class III	High Risk	General Controls Special Controls Premarket Approval (PMA)	Orthopaedic Knee implants, Automated external defibrillator

			Replacement heart valves Pacemaker HIV diagnostic test Implants.

Table 1: FDA Controls

Medical devices are typically approved through two methods: the premarket approval (PMA) process and the 510(k) premarket notification process. The PMA process has proven to be more expensive and time-consuming as it requires clinical evidence for authorization. On the other hand, the 510(k) premarket notification is an accelerated process that omits medical devices from the clinical trial requirements as long as the device is "substantially equivalent" to an alternatively utilized medical device. (Purnama and Drago, 2019)

The regulatory controls are applied based on medical device risk category as shown in Table-2

	General Controls	**Special Controls**	**Premarket Controls**
Class I	✓	X	X
Class II	✓	✓	X
Class III	✓	✓	✓

Table 2: Control requirements based on risk classifications.

The table-3 below provides overview of FDA different regulatory controls. (Ramakrishna *et al.*, 2015)

Regulatory controls	**Descriptions**
General controls	General controls are regulatory requirements authorized by the FD&C (Federal Food, Drug, and Cosmetic Act Act), under section 501, 502, 510, 516, 518, 51]9, and 520, and they apply to all medical devices, unless exempted by regulations.
Special controls	Special controls are regulatory requirements for Class II devices, for which general controls alone are insufficient to provide reasonable assurance of the safety and effectiveness of the device. Special controls are usually device-specific and include: performance standards, post market surveillance, patient registries, special labeling requirements, premarket data requirements, and guidelines.
Class I/II exemptions	Most Class I devices and a few Class II device are exempt from 510(k) requirements subject to the limitations on exemptions. However, these devices are not exempt from other general controls. A few Class I devices are additionally exempt from the GMP requirements with the exception of complaint files and general record keeping requirements.
Premarket notification (510(k))	A Class I, II, III device intended for human use, for which premarket approval (PMA) is not required, must submit a 510(k) to FDA unless the device is exempt from the 510(k) requirements. A 510(k)

	is a premarket submission to FDA to demonstrate that the device to be marketed is at least safe and effective, that is, substantially equivalent, to a legally marketed device that is not subject to PMA.
Premarket approval (PMA)	PMA is an FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. PMA is the most stringent type of device marketing application. required by the FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device.

Table 3: FDA Approval Pathways

2.3 Device recalls & regulation applies to Orthopaedic company:

The orthopaedic devices are regulated by the Food and Drug Administration (FDA) under the Center for Devices and Radiological Health (CDRH). Firms must adhere to regulations regarding device classification, premarket approval (PMA), 510(k) clearance, and Good Manufacturing Practices (GMP). The company must comply with following standards in order to release product into market. (Ramakrishna *et al.*, 2015)

Medical device standards for Orthopaedic products:

- 21CFR Part 820 – FDA Medical device standard
- FDA 21 CFR 820.30 - Design control
- ISO13485 – International quality management system (QMS)
- ISO 14971:2019- Medical devices Risk Management and regulatory framework

2.3.1 What is medical device recall:

When a company learns that there is a problem with one of their medical devices, it proposes a correction or a removal depending on where the action takes place.

Correction - Addresses a problem with a medical device in the place where it is used or sold.

Removal - Addresses a problem with a medical device by removing it from where it is used or sold.

FDA uses the term “recall” when a manufacturer takes a correction or removal action to address a problem with a medical device. Recalls occur when a medical device is defective, when it could be a risk to health, or when it is both defective and a risk to health.

A medical device recall does not always mean that we must stop using the product or return it to the company. A recall sometimes means that the medical device needs to be checked, adjusted, or fixed. If an implanted device (for example, an artificial hip) is recalled, it does not always have to be explanted from patients. When an implanted device has the potential to fail unexpectedly, companies often tell doctors to contact their patients to discuss the risk of removing the device compared to the risk of leaving it in place. (FDA, 2021)

Examples of types of recalls:

- Inspecting the device for problems.
- Repairing the device.
- Adjusting settings on the device.
- Re-labelling the device.
- Destroying device.
- Notifying patients of a problem.
- Monitoring patients for health issues.

2.3.2 Type of Medical device recall classes:

Recalls are classified by severity as shown in table 4. Class I recalls involve products that could cause serious health problems or death. Class II recalls involve products that may cause temporary or reversible health problems, while Class III recalls are less likely to cause health problems. Orthopaedic devices are recalled due to manufacturing defects, design flaws, or inadequate labelling and several other reasons which could pose risks to patients. (Health, 2021)

Recall Class	FDA Definition	Examples
1	Device will likely cause serious adverse health consequences or death	Device design, Process control, Labelling etc
2	Device may cause temporary or reversible adverse health consequences	Metal on metal hips: Possible sterility compromise in packaging
3	Device is not likely to cause serious adverse health consequences.	Incorrect identification codes.

Table 4: FDA Recall classes

2.4 Orthopaedic medical device market overview:

Orthopaedic medical devices have proven highly effective in enhancing mobility, alleviating discomfort, and enhancing the well-being of countless individuals annually. This success is evident in the global market, where orthopaedic devices have consistently held a significant share of sales, approximately dominating the 8.5% of market share by 2022 as shown in table 5. The global orthopaedics devices market was valued at $38.7 billion USD in 2017 (Awasthi and Stanick, 2022) and is estimated to grow with a CAGR of 5.2% ever year as shown in table-5. The rise of cutting-edge technologies like robotic surgeries, ortho-biologics, smart sensor-equipped devices, implants, and 3D printing methods, in parallel with a predicted increased incidence of orthopedic disorders such as osteoporosis, arthritis and sports injuries, will play a major role in driving market expansion.

SEGMENT	WW SALES ($BN)		CAGR	MARKET SHARE		CHG. (+/-)
	2017	2022	% Growth	2017	2022	
IVD	62.2	77.6	+4.5%	14.2	13.2	-0.9
Cardiology	50.1	69.9	+6.9%	11.4	11.9	+0.5
Diagnostic Imaging	43.1	53.9	+4.6%	9.8	9.2	-0.6
Orthopedics	38.7	49.8	+5.2%	8.8	8.5	-0.3
Ophthalmology	29.1	39.7	+6.5%	6.6	6.8	+0.2
General & Plastic Surgery	22.8	31.2	+6.5%	5.2	5.3	+0.1
Endoscopy	20.1	28.8	+7.5%	4.6	4.9	+0.3
Drug Delivery	20.7	27.6	+5.9%	4.7	4.7	0-0
Dental	14.4	20.0	+6.8%	3.3	3.4	+0.1
Wound Management	14.4	19.0	+5.6%	3.3	3.2	-0.1
Diabetic Care	12.5	18.2	+7.9%	2.8	3.1	+0.3
Nephrology	12.3	16.4	+5.8%	2.8	2.8	0-0
General Hospital and Healthcare Supply	12.0	14.4	+3.7%	2.7	2.5	-0.3
Neurology	8.5	13.0	+9.0%	1.9	2.2	+0.3
ENT	9.0	12.5	+6.8%	2.0	2.1	+0.1
Others (Wound care management, Healthcare IT, etc.)	68.6	93.5	+6.4%	15.7	16	+0.3
Total	438.2	585.4	6%			

Table 5: Worldwide MedTech sales by segments: Top 15 segments (2017 & 2022):(Awasthi and Stanick, 2022)

2.4.1 Orthopaedic knee implant or Total knee arthroplasty (TKA) market:

In the last four decades, there has been a substantial increase in the variety of implants accessible on the market, Total knee arthroplasty (TKA) has gained widespread recognition as an extremely effective and economical remedy for advanced degenerative knee joint conditions, offering notable benefits such as pain alleviation, enhanced functionality, and overall improvement in quality of life. Initially introduced to clinical settings in the 1970s, Orthopaedic knee implant has since evolved into one of the most frequently conducted inpatient surgical interventions in the United States. According to data from the Millennium Research Group, the number of TKA procedures in the US grew 2.9% in 2012 to 734,100 procedures. 80% of these procedures were primary TKA, 8% were uni-condylar replacements, 10% were revision TKA, and 2% were patello-femoral replacement.

2.4.2 Knee Joint Overview:

2.4.2.1 Knee Joint:

The knee is well-suited to handle the forces and pressures it faces. However, everyone's knee structure is a bit different, but they all work together in a complex way. The knee is made up of bones like the femur, tibia, patella, and fibula, along with ligaments, tendons, muscles, and joint capsule. These parts don't work alone; they team up for different knee functions. The knee has several parts: the inner and outer parts, the kneecap area, and the upper part where the tibia and fibula meet. Ligaments help keep the knee stable in all directions. In our daily activities, the knee bears a lot of our weight and moves in different ways, like bending and straightening, twisting, and moving side to side. It's like a hinge joint but with some gliding and rolling movements. The knee can move in six different ways: bending and straightening, twisting in and out, and tilting sideways. It can also move forward and backward and side to side, and it can be compressed or stretched. All these movements work together to let the knee do what it needs to do. (Hirschmann and Müller, 2015) Knee joint has six degrees of freedom, 3 rotational movements and 3 translation movements as shown in Fig-2.

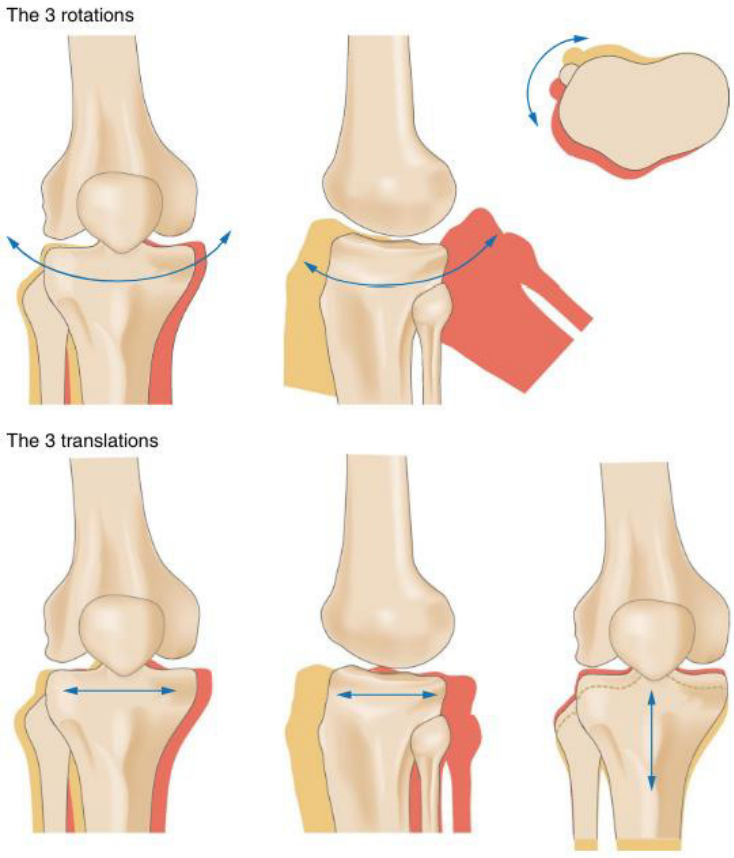


Figure 2: Knee six degree of freedom.((Hirschmann and Müller, 2015)

2.4.2.2 *Knee Implant Device:*

Knee implants are a surgical technique used to replace biological parts in order to lessen pain and restore knee functionality, is typically recommended for individuals who experience severe knee pain, stiffness, and reduced mobility due to conditions such an osteoarthritis, Rheumatoid Arthritis, traumatic arthritis, other knee conditions like severe fractures of the knee joint, knee deterioration due to poor blood supply. This is an invasive device mainly used to treat osteoarthritis, rheumatoid arthritis, traumatic arthritis where both compartments of the knee are affected by replacing affected condyles and this surgical procedure is called Knee Replacement. The knee implant has three major compartments:

Figure 3: Knee implant components.(Pande and Dhatrak, 2021)

(a) Femoral element (b) Tibial insert (bearing) (c) Tibial element (baseplate) (d) Inserted total knee arthroplasty.(Pande and Dhatrak, 2021)

	Osteoarthritis	**Rheumatoid arthritis**	**Traumatic arthritis**
Definition	It is a joint disease that gets worse over time; does not cause swelling in joints (not inflammatory)	It is an inflammatory condition (causes joint swelling) in which the immune system mistakenly attacks the tissue that lines and cushions the joints.	It is from an injury which leads to a condition called avascular necrosis: blood supply to the ball portion (the femoral head) of the thighbone is cut off.

Table 6 : Orthopaedic Knee related disease

When someone's knee is significantly impacted by arthritis or injury, everyday activities like walking or climbing stairs become difficult. The individual may experience pain while sitting, walking, or even lying down. To alleviate pain and regain a normal lifestyle, the patient may require total knee replacement surgery, as depicted in the figure below. (Left side picture in Fig-4) Severe osteoarthritis and (right side picture in Fig-4). The worn-out cartilage affected by arthritis and the original bone have been surgically removed and replaced with metal implants on both the

femur and tibia. A plastic spacer has been inserted between these implants to provide smooth movement.

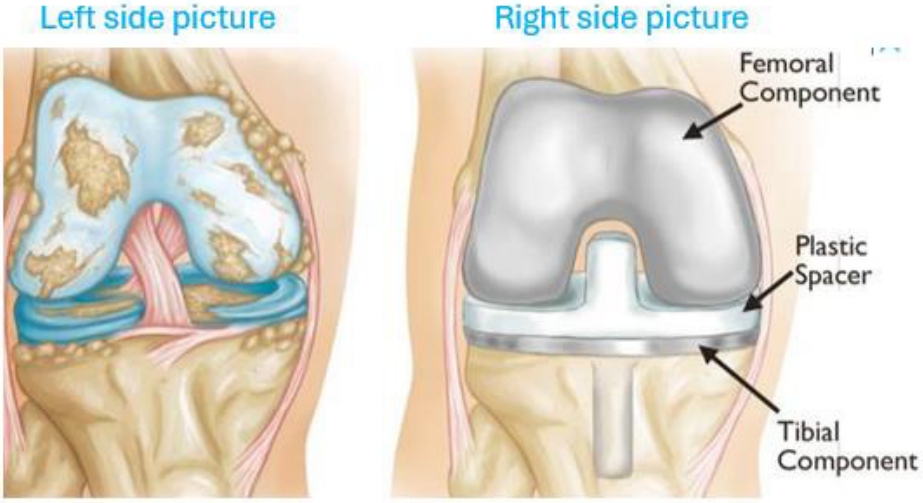


Figure 4: Knee implant device. (Orthoinfo, 2024)

2.5 Orthopaedic Product Market recalls:

Between November 2002 and December 2012 (Day *et al.*, 2016), a total of 1641 companies issued 20,093 recalls. Among the top 20 companies with the highest number of recalls during this decade, six were top orthopedic device manufacturers. These six companies were responsible for 19% of all recalls during this period. Within the ten-year timeframe, the top 20 companies accounted for 46% of all recalls (9,226 recall events), with orthopedic devices comprising the largest portion at 41%, followed by general hospital devices (25%), diagnostics (21%), cardiovascular (9%), anesthesia (2%), and radiation oncology (2%) as shown in fig-5. (Day *et al.*, 2016)

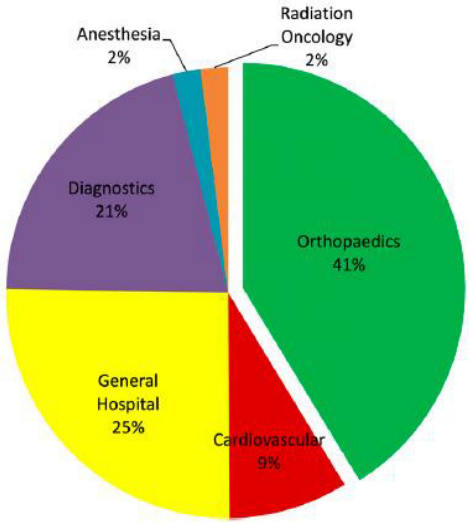


Figure 5: Orthopaedic product recall percentage. (Day et al.*, 2016)*

2.5.1 Causes of Orthopaedic Product recalls:

Four factors, comprising the manufacturer, regulatory oversight by the FDA, the hospital setting, and environmental & societal factors, contribute to medical device recalls. (Wang *et al.*, 2022) Manufacturers have control over the design and production of medical devices, and any issues arising during pre-market activities like labeling errors can prompt a recall. Hospitals, where medical devices are primarily utilized, face risk of device-related adverse events. To effectively prevent such issues, regulatory oversight by the FDA must diligently oversee all aspects from design to application. These interconnected elements—manufacturing, regulation, and usage require careful attention, as any oversight could trigger a recall. Furthermore, environmental factors such as regulations governing environmental practices impact the materials utilized in orthopedic implants. Alterations in material composition or sourcing can affect the performance or safety of implants, potentially resulting in recalls if not thoroughly evaluated. Similarly, societal factors like lifestyle preferences, occupations, and demographic characteristics can also influence the wear and tear experienced by orthopedic implants. These four factors may also influence the application of these elements (Fig-6).

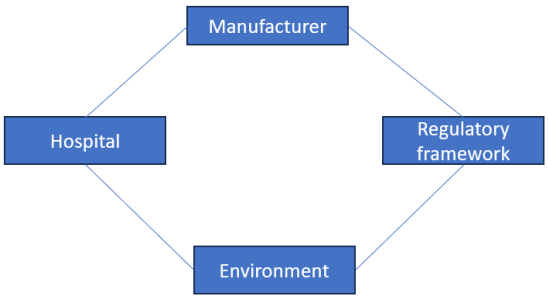


Figure 6: Factors contributing to Orthopaedic recalls. (Wang et al.*, 2022)*

1.Manufacturer-determined reasoning for recall:

The reason behind orthopaedic device recalls by manufacturers were categorized into seven groups based on the stage of the production cycle linked to the issue. These categories are as follows: "device design" if flaws in the design or raw materials led to implant failure; "manufacturing" if the device was produced outside specified parameters, resulting in nonconforming implants; "processing" if the device failed quality control measures or errors occurred during post-production processes; "packaging" if the product lacked adequate protective measures, was improperly packaged, or mislabeled; "sterility" if the product was inadequately sterilized or lacked documentation of sterilization; "software" if there were programming issues with the device; and "marketing" if the product was distributed without sufficient premarket approval or with misleading information for consumers. From 2015 to 2019, (Vajapey and Li, 2020) packing errors accounted for 33% of all orthopedic device recalls, with manufacturing errors and defective device designs each comprising 24% of all recalls. Software problems and marketing-related recalls were the least frequent causes, each accounting for 2% of recalls (Fig- 7).

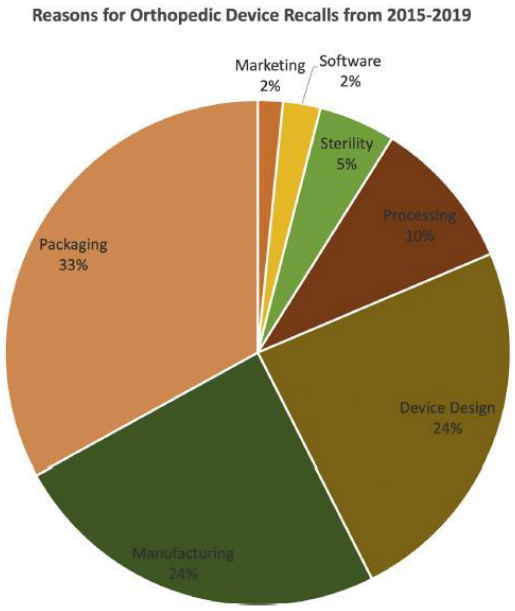


Figure 7: Manufacturer recalls in pie charts. (Vajapey and Li, 2020)

2.FDA-determined reasoning for recall:

Fig- 8 shows that between January 1, 2007, and December 31, 2017, a total of 6,758 orthopedic devices were approved: 5,833 (86.3%) through the 510(k) premarket notification process and 925 (13.7%) through the PMA process. Of the 300 knee arthroplasty devices recalled, 267 (89.00%) were approved via the 510(k) process, while 33 devices (11.00%) were approved through the PMA process. (Pellerin *et al.*, 2020) & (Pellerin *et al.*, 2018)

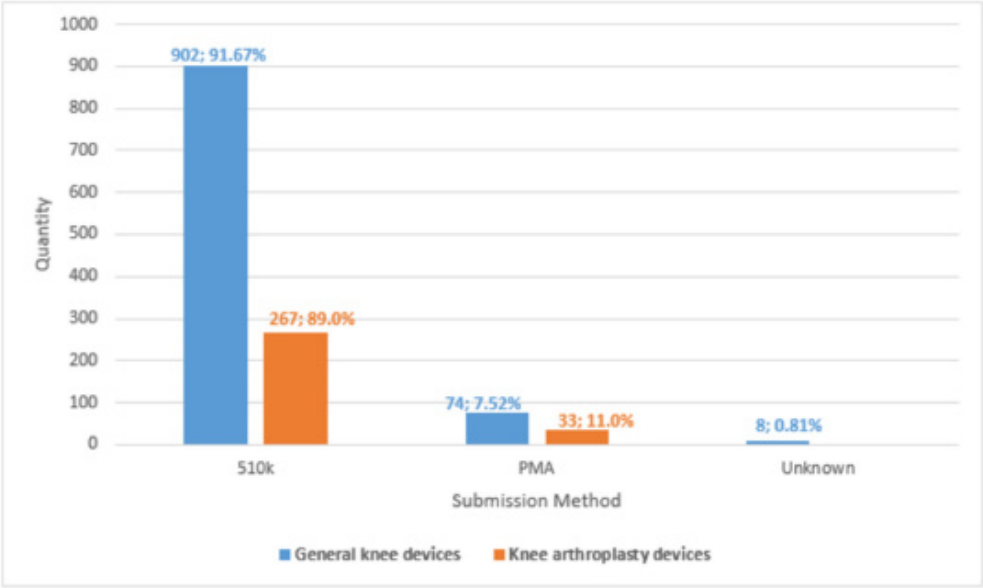


Figure 8: Orthopaedic recalls by FDA Approval pathway. (Pellerin et al.*, 2020)*

2.6 Current trend in Orthopaedic knee implant recalls:

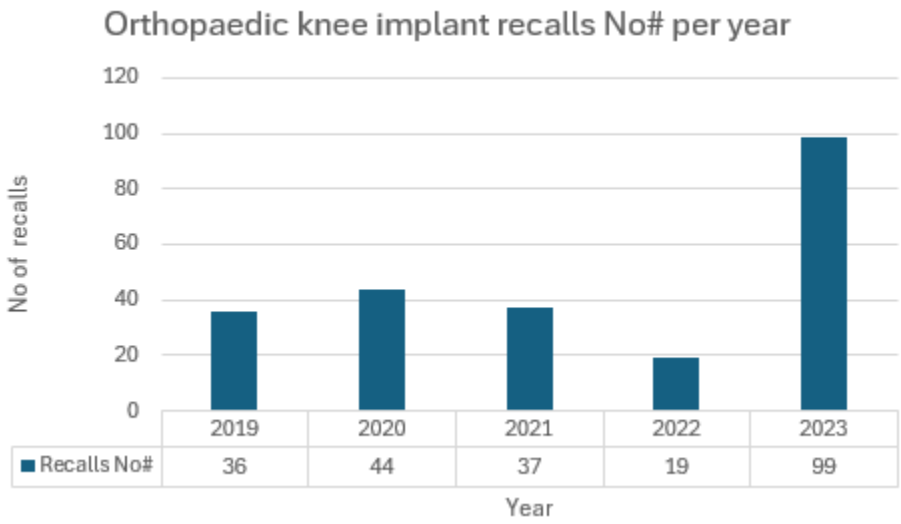


Figure 9: Current trend in Orthopaedic knee implant recalls.

The data on orthopaedic knee implant recalls from 2019 to 2023 reveals a notable trend of fluctuation over the years as shown in Fig-9. In 2019, the number of recalls stood at 36, showing a slight increase to 44 in 2020. The following year, 2021, saw a marginal decrease to 37 recalls. However, a significant drop occurred in 2022, with only 19 recalls recorded, representing the lowest number within the observed period. Interestingly, 2023 witnessed a dramatic spike, with the number of recalls surging to 99, marking the highest recall count in the five-year span. This sharp increase raises concerns about potential issues in manufacturing, regulation, or clinical practices during that year. This data indicates an overall increasing trend in recalls, especially in the recent years, suggesting a need for closer examination of the factors contributing to this rise. The substantial variations, particularly the spike in 2023, highlight the importance of implementing more robust quality control measures and possibly revisiting regulatory standards to ensure patient safety and product reliability. The above data was collected from FDA website in recall navigation page using "Orthopaedic" keywords and filtered out to last 5 years. (FDA, 2024)

2.7 Impact of Orthopaedic knee implant recalls on Patient Safety and Healthcare:

Orthopedic knee implant recalls can have significant negative impact for patients, ranging from physical discomfort to emotional distress and financial burden. Patients who have undergone knee implant surgery rely on these devices to alleviate pain, improve mobility, and enhance their quality of life. When a knee implant is recalled due to issues such as defects in design, materials, or manufacturing, patients may experience a range of adverse effects. Here are some potential impacts on patients due to orthopaedic recalls:

Knee implant Revision Surgeries: One of the most direct and immediate impacts is the potential need for revision surgeries. If a recalled orthopaedic knee implant or device is already in use,

patients may have to undergo additional surgical procedures to replace or correct the faulty product. (HSS, 2020)

Physical Discomfort and Pain: Patients with recalled orthopaedic knee implants may experience physical discomfort and pain associated with the defective device. This can affect their quality of life and mobility until the issue is addressed through revision surgery**.** (Drugwatch, 2023)

Complications and Adverse Events: Faulty orthopaedic knee implant devices may lead to complications and adverse events, such as infections, implant failure, or tissue damage. These issues can result in additional healthcare interventions and prolonged recovery periods for affected patients. (Drugwatch, 2023)

Emotional and Psychological Impact: Dealing with the news of a recall and the prospect of additional knee implant surgeries can have emotional and psychological impacts on patients. Anxiety, stress, and concerns about the success of revision procedures can affect the mental well-being of affected individuals. (HSS, 2020)

Financial Burden: Orthopaedic knee implant recalls can impose a financial burden on patients. Additional surgeries, medical treatments, and rehabilitation may result in increased healthcare costs, and patients may face expenses related to lost wages during recovery.(Orthoinfo, 2024)

Disruption of Daily Life: Patients undergoing revision surgeries may experience a disruption in their daily lives. Recovery periods, physical therapy, and rehabilitation can impact the ability to work, participate in regular activities, and maintain social engagements. (Orthoinfo, 2024)

Delayed Treatment: In some cases, patients may experience delays in receiving necessary orthopaedic treatments and interventions due to the recall. This delay can lead to prolonged pain, impairment, and a reduced quality of life for affected individuals. (Drugwatch, 2023)

Loss of Trust in Healthcare Providers and Manufacturers: Orthopaedic knee implant recalls may erode trust in healthcare providers and the manufacturers of the recalled products. Patients may question the safety and reliability of orthopaedic knee implant devices, leading to a loss of confidence in the healthcare system. (Drugwatch, 2023)

Long-Term Health Consequences: Depending on the severity of complications associated with the recalled orthopaedic knee implant devices, patients may face long-term health consequences. Chronic pain, mobility issues, and compromised joint function are examples of potential long-term effects. (HSS, 2020)

In summary, orthopedic knee implant recalls can profoundly impact patients, affecting their physical health, emotional well-being, financial stability, and trust in the healthcare system. Healthcare providers, regulatory agencies, and manufacturer’s product reputation.

2.8 Gaps in literature and Research Needs:

While there are numerous studies about orthopaedic product recalls, there is no specific study available with regards to orthopaedic knee implant recalls. So, it becomes apparent that there is a notable absence of a comprehensive literature review evaluating orthopaedic knee implant recalls from manufacturing to market release. Furthermore, there is a lack of studies that systematically examine the root causes and contributing factors leading to knee implant recalls. Secondly, no study available to evaluate current orthopaedic knee implants system is effective. Therefore, this study is going to bridge the gap by evaluating orthopaedic knee implants recalls from manufacturing to market release examining the root causes and contributing factors leading to knee implant recalls and effectiveness of current orthopaedic knee implants system and see if any improvements are required in manufacturing standard and regulatory framework. Through the utilization of an online survey questionnaire, insights will be gathered from subject matter experts employed in orthopaedic knee implant companies, thereby facilitating a comprehensive analysis to determine if any enhancements are necessary in manufacturing standards and regulatory frameworks.

3 CHAPTER

Research Methodology

3.1 Introduction:

The research methodology was outlined using the research onion framework. It was introduced by Saunders et al. in 2009. The research onion concept underlined the need for researchers to systematically progress through various stages of research, starting from the broad and general aspects to the specific and detailed elements. The layers of the research onion typically include philosophical assumptions, research approaches, research strategies, time horizons, data collection methods, and data analysis techniques. Each layer builds upon the previous one, guiding researchers in making methodological choices that align with their research objectives and philosophical perspectives. The research onion provided a structured framework for researchers to plan, conduct, and report their research effectively.

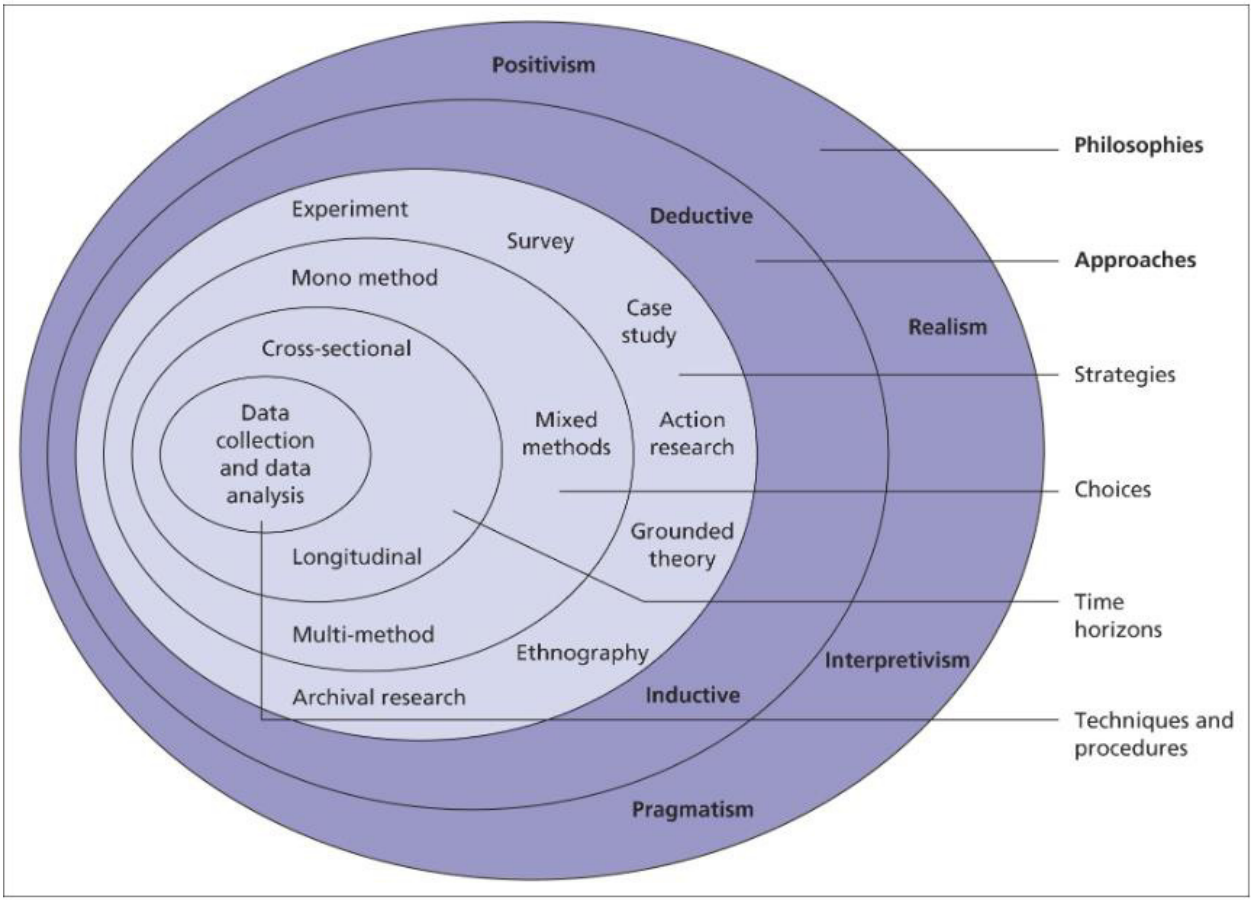


Figure 10: Research Onion (Source: Saunders et al. 2019)

3.2 Conceptual framework:

The following Table 7 explains the choice for each layer.

Research Methodology	Selective Action	Choice for this thesis
Philosophy	Interpretivism	Interpretivism was used as philosophical approach that emphasizes the subjective understanding and interpretation of orthopaedic knee implant subject matter expert's experiences and perceptions.
Approach	Inductive	The research is inductive: specific observations are made with the survey and the researcher aims to generalize the answers for the entire Orthopaedic knee implant industry.
Methodological choice	Mono method Quantitative	Mono method was used: a survey questionnaire. Mono method was more suitable where one data collection method is well aligned with the research objectives, questions.
Research Strategy	Online Survey-Microsoft form	The research involves conducting a survey, which falls under the category of "survey research." And the data collected from individuals by asking them a series of questions, typically through questionnaire.
Time Horizon	Cross-Sectional	Since the data was collected only once without any planned follow-ups, the research adopts a cross-sectional time horizon.
Technique	Questionnaire	18 Questionnaire which consists of 12 closed questions and 6 open questions.
Sampling technique	Probability Sampling	Probability sampling is a method used in research to select a sample from a larger population in such a way that each member of the population has a known chance of being included in the sample.

Table 7: Primary Data collection method

3.3 Research Strategy: Gathering of Primary Data

A survey questionnaire comprising 18 questions was distributed to Orthopaedic knee implant industry subject matter experts (SMEs).

The questionnaire was organized into following sections: The survey began with five initial questions aimed at obtaining participants' agreement and understanding of the survey. Following this, two questions focused on identifying the type of organization and the specific products participants work with. The remaining questions targeted around factors contributing to orthopaedic knee implant device recalls and the effectiveness of the current system. Lastly, the survey concluded with a series of open-ended questions inviting participants to provide suggestions and recommendations regarding Orthopaedic manufacturing standards, regulatory frameworks, and other relevant areas.

The survey required around 5~10 minutes to complete.

The survey questions are attached in Appendix A – Survey Questions.

A mono-method approach was used for the research strategy, which included quantitative data analysis. A survey was conducted with qualified participants who have prior experience working in the Orthopaedic knee implant industries ranging from less than 2 years (23%) 2 to 5 years (31%) and greater than 5 years (46%). The participants were employed as a 'Quality Engineer, R&D engineer, Sustaining engineer, Regulatory specialist, Validation engineer, Packaging engineer, Clinical Engineer, Manufacturing engineer, Product compliance officer' in a top ranking multi-national Orthopaedic knee implant medical device company. These participants were targeted as they are involved in the full life cycle of Knee implant products.

The survey design consists of 18 questions with both open and closed-ended questions. It was created on Microsoft Forms and was distributed online through Email, LinkedIn, WhatsApp's, Instagrams, Regulatory Affairs Professionals Society (RAPS). The survey was structured to gather additional information from individuals specifically with experience in the Orthopaedic sector. The format of the closed-ended questions in the survey was 'Yes or No' where the participants can provide one answer, or in the form of multiple-choice questions, where all options that apply can be selected. The open-ended questions allowed for the participants to type their opinion or perspectives into the open space provided.

3.4 Sampling techniques:

Both probability and non-probability sampling were used in the sampling process. When a researcher uses statistical analysis to infer information about a broader population from a smaller sample, they frequently employ probability sampling. On the other hand, with non-probability sampling, sample size cannot be determined using statistical analysis. It is employed when researchers are unable to select a random sample from the target population. This study used probability sampling with a simple random sample technique, which gives every member of the population an equal chance of being chosen for the sample.

The optimal sample size of 61 was determined using the survey monkey website calculator (Fig-11). The global orthopaedic knee implant expert population size is estimated roughly 100 Subject matter experts (SME) globally based on their experience level from orthopaedic knees implant

manufacturing companies existed in the global market. this sample size was deemed sufficient. However, the researcher received feedback from 71 respondents. To maintain a confidence level of 95% and a margin of error of 8%, adjustments were made due to the global nature of the study being conducted within a short timeframe, potentially introducing sampling errors. Consequently, the margin of error was increased from 5% to 8%.

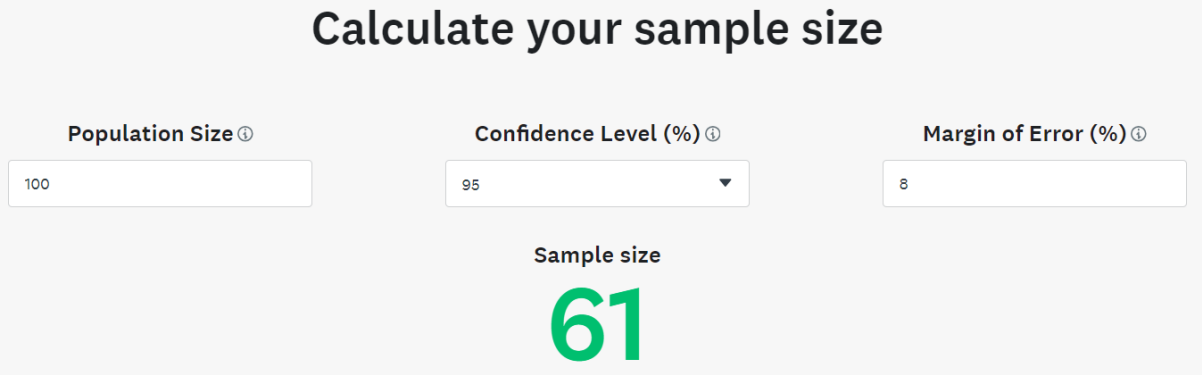


Figure 11: Sample size calculator.

3.5 Ethical considerations:

The researcher ensured that the online questionnaire survey solely focused on the research topic and did not capture any personal information. All survey questions were written in clear and understandable English. Prior to distributing the survey, ethical approval was sought from a supervisor designated by Inno Pharma Griffith College as part of the ethical consideration process (Refer to section-7 Appendix). Participants were assured that their data would only be used for research purposes and that their responses would be treated with the utmost confidentiality in compliance with GDPR regulations. Participation in the study was entirely voluntary, and consent from participants was obtained using questions 1 and 2 for general consent, questions 3, 4, and 5 to gather information on participants' experiences, the types of products, and industries they were involved in, and questions 6 and 7 to obtain details on their department and familiarity with medical device recalls. Questions 8 to 18 were designed to gather data on the factors contributing to orthopaedic knee implant device recalls and to assess the effectiveness of the current system (reference to Section 7 - Appendix)

3.6 Techniques used in data Analysis:

In this research paper, quantitative data obtained from an online survey questionnaire underwent thorough analysis. The researcher employed descriptive statistics to analyze this quantitative data, utilizing Microsoft Excel as the primary analytical tool. Specifically, descriptive statistics were utilized to gain insights into the characteristics of the data, such as higher portion of categories and frequency distributions. For research objective 3, an example bar chart was generated to examine frequencies, such as the number of recalls in specific years. This visualization allowed for a clear understanding of recall patterns over time to assess factors influencing orthopedic knee implant device recalls. On the other hand, for research objectives 1 and 2, pie charts were utilized to depict

the distribution of responses and highlight the proportion of various categories within the dataset. These pie charts facilitated the visualization of higher percentages within the data collected for these research objectives, providing a concise representation of the findings. Overall, using descriptive statistics and visualization techniques such as bar charts and pie charts, the researcher effectively analyzed the quantitative data obtained from the online survey questionnaire, contributing to a comprehensive understanding of the research objectives.

Hypothesis testing for statistical significance:

Given that the data is quantitative and primarily involves numerical data on categorical variables, the chi-square goodness-of-fit test was utilized to determine if the observed frequencies in the categorical data align with the expected frequencies according to a specific hypothesis. This statistical tool was employed in the survey research to evaluate whether the distribution of responses to survey questions matches the hypothesized distribution. (Turney, 2022)

What is the Chi-square goodness-of-fit test?

The chi-square goodness-of-fit test assesses whether the observed frequencies in a single categorical variable correspond to the expected frequencies based on a particular hypothesis.

To examine if the observed frequencies significantly differ from the expected distribution, the chi-square goodness-of-fit test was applied to the following questions using Minitab under the specified hypothesis conditions:

H0: The observed frequencies match the expected frequencies (participants have no preference).

HA: The observed frequencies do not match the expected frequencies (participants have a preference)

The above hypothesis condition was concluded by comparing the chi-square value to the critical value as stated below.

Chi-square Test value $\chi 2$ > Critical Value (χ 2 critical) – Reject Null hypothesis.

Chi-square Test value $\chi 2$ < Critical Value (χ 2 critical) – Accept Null hypothesis.

Survey questions that contain categorical variables:

8. Based on your experience, what do you think main contributors for Ortho-recalls?

- [ ] Manufacturer defects
- [ ] Lack of strict FDA regulation
- [ ] Lack of Clinical study
- [ ] Hospital
- [ ] Other

9. Do you think the current system (Medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30 , ISO 14971:2019- Medical devices Risk Management and Regulatory framework- 510K & PMA Approval) in place effective?

- ( ) Yes
- ( ) No
- ( ) Maybe

10. Do you think the current system (Medical Device Quality System Regulations)-21CFR Part 820, Design control- FDA 21 CFR 820.30 , ISO 14971:2019- Medical devices Risk Management and Regulatory framework- 510K & PMA Approval)) in place has some gaps and needed improvement?

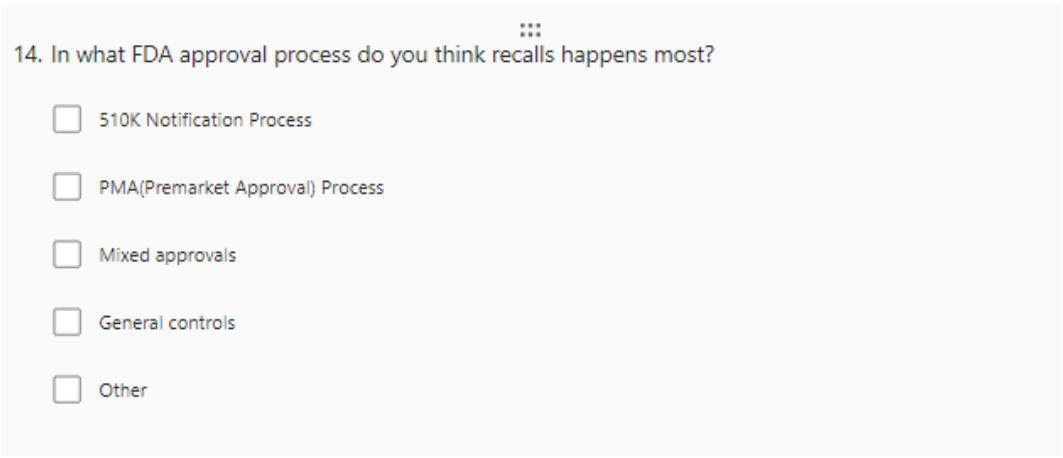
- ( ) Yes
- ( ) No
- ( ) Maybe

11. What area do you think Manufacturer should focus in order to prevent recalls?

- [ ] Device design
- [ ] Process design
- [ ] Process control
- [ ] Labelling error
- [ ] Packaging
- [ ] Material mix up
- [ ] Software
- [ ] Sterility
- [ ] QMS Standard
- [ ] Other

12. What area do you think Manufacturer recalls happens most?

- [ ] Device design
- [ ] Process design
- [ ] Process control
- [ ] Labelling
- [ ] Packaging
- [ ] Sterility
- [ ] Software
- [ ] Material mix up
- [ ] Other



The results of the chi-square goodness-of-fit test for the survey questions (8 to 14) are presented in Chapter 4, specifically in sections 4.1.1 to 4.1.7.

4 CHAPTER

Findings and Analysis

4.1 Result: Introduction to survey findings

The survey conducted using Microsoft Forms targeted qualified participants with prior experience in the Orthopaedic knee implant industry, with representation from various experience levels, including less than 2 years (23%), 2 to 5 years (31%), and greater than 5 years (46%). These participants held diverse roles within top-ranking multinational Orthopaedic knee implant medical device companies, encompassing positions such as Quality Engineer, R&D Engineer, Sustaining Engineer, Regulatory Specialist, Validation Engineer, Packaging Engineer, Clinical Engineer, Manufacturing Engineer, and Product Compliance Officer as shown in below table 8. These individuals were selected due to their involvement in the full lifecycle of knee implant products. The survey received responses from a total of 71 participants from all over the world, with the majority of respondents holding positions in Regulatory Affairs Specialist (20%), Quality Engineering (17%), and Product Development Engineering (10%). Other roles represented included Product Compliance, Research & Development Engineering, Manufacturing Engineering, Clinical Engineering, Validation Engineering, and Sustaining Engineering. These findings indicate a diverse and knowledgeable participant pool with significant expertise on various aspects of orthopaedic knee implant manufacturing and regulation.

Serial No#	Roles	Frequency	Percentage
1	Regulatory affairs specialist	14	20%
2	Quality Engineering	12	17%
3	Product Development Engineering	7	10%
4	Product Compliance	6	8%
5	Research & Development Engineering	7	10%
6	Sustaining Engineering	3	4%
7	Manufacturing Engineering	8	11%
8	Clinical Engineering	4	6%
9	Validation Engineering	4	7%
10	Packaging engineer	1	1%
11	Supplier engineering	1	1%
12	NPI, New Product Introduction	1	1%
13	Others	2	3%
	Total	71	100%

Table 8: Participant's background.

The survey was also completed by Regulatory affairs specialist, Quality engineering specialist, Product development engineering, Product compliance, Research and development engineering, Sustaining engineering, Manufacturing engineering, Clinical engineering, Validation engineering, Packaging engineer, Supplier engineering, new product introduction engineering and other consultants. Their familiarity with the notion of recalls and their professional expertise in the

orthopaedic knee implant medical device industries led them to participate in the study. Every department or position has a distinct set of experiences and information to offer. Limiting orthopaedic knee implant recall research to a small subset of experts could obscure the various viewpoints and insights from people working in different areas. As a result, information for the research thesis was gathered from various roles (Fig-12) within the Orthopaedic knee implant medical device industry.

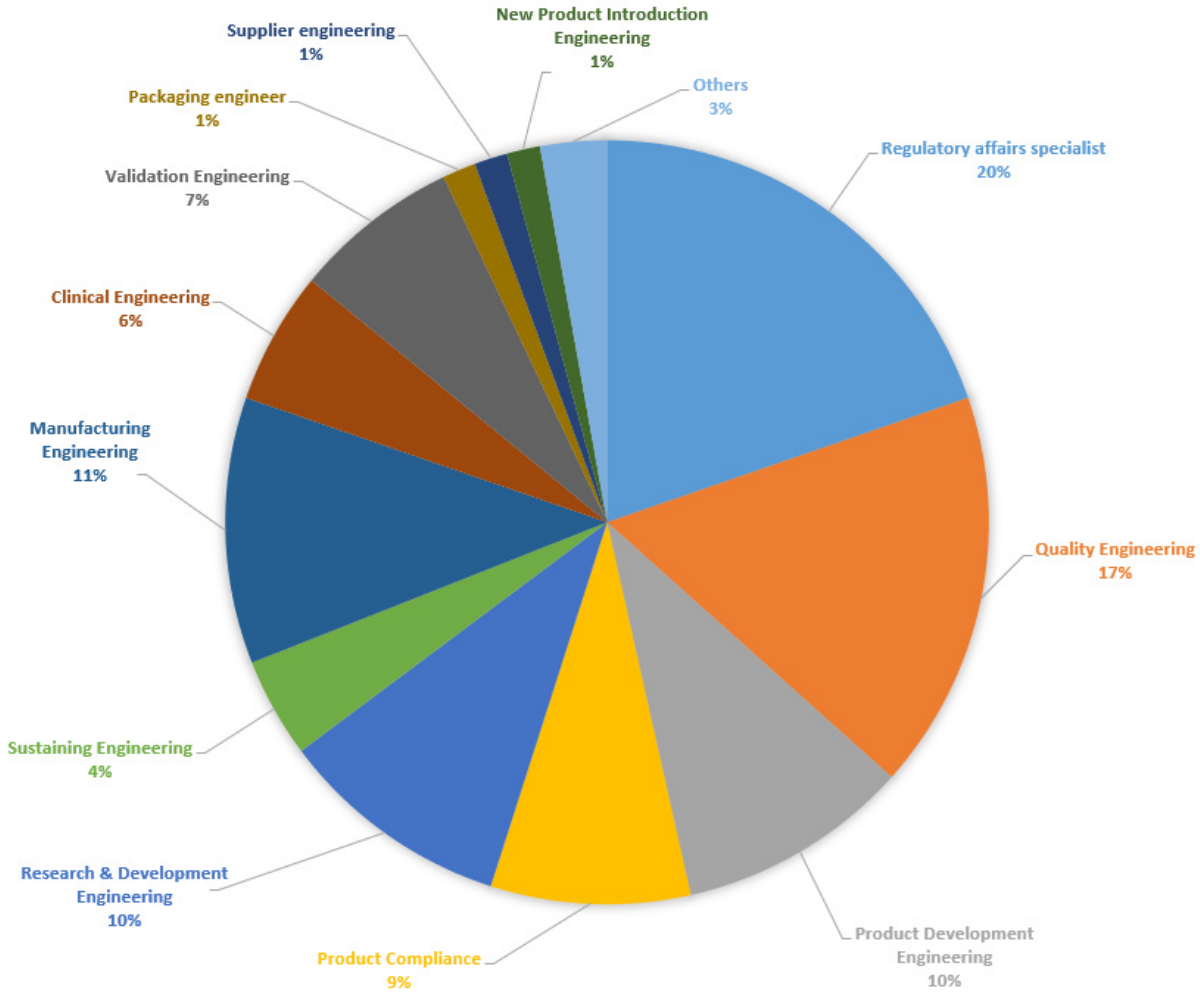


Figure 12: Participant's Background.

The findings of the survey indicate that the majority of participants (46%) possessed extensive experience exceeding five years within the medical device sector. Following this, 31% reported having two to five years of experience, while 23% had less than two years of experience (Fig-13).

Given the correlation between work experience and knowledge in orthopaedic knee implant recalls, participants with greater tenure in the field were more likely to contribute to the survey.

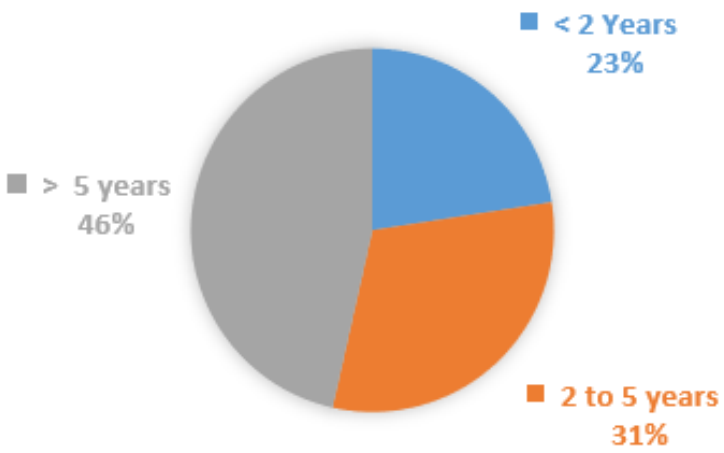


Figure 13: Participant's experience.

Furthermore, to effectively address research questions, participants were asked about their knowledge of orthopaedic medical device recalls. All 71 surveyed participants responded positively, demonstrating a high level of awareness concerning recalls in the orthopaedic knee implant industry. These results highlight the necessity of considering the participants' knowledge and awareness levels when interpreting survey responses and forming conclusions.

4.1.1 Analysis: Factors contributing to orthopaedic knee implant recalls

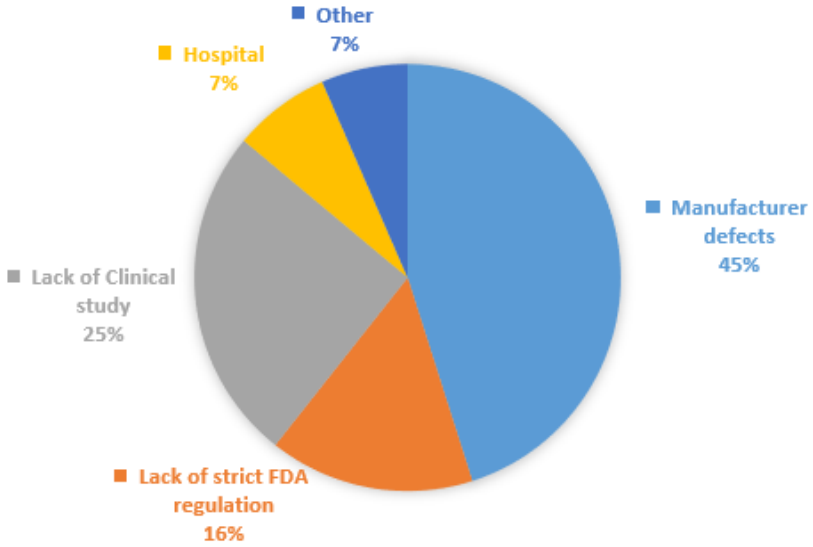


Figure 14: Main contributors of Orthopaedic knee implant recalls.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
Manufacturer defects	55	0.2	24.4	38.3754
Lack of strict FDA regulation	19	0.2	24.4	1.1951
Lack of Clinical study	31	0.2	24.4	1.7852
Hospital	9	0.2	24.4	9.7197
Other	8	0.2	24.4	11.0230

Chi-Square Test

N	DF	Chi-Sq	P-Value
122	4	62.0984	0.000

Figure 15: Chi square test result- Minitab.

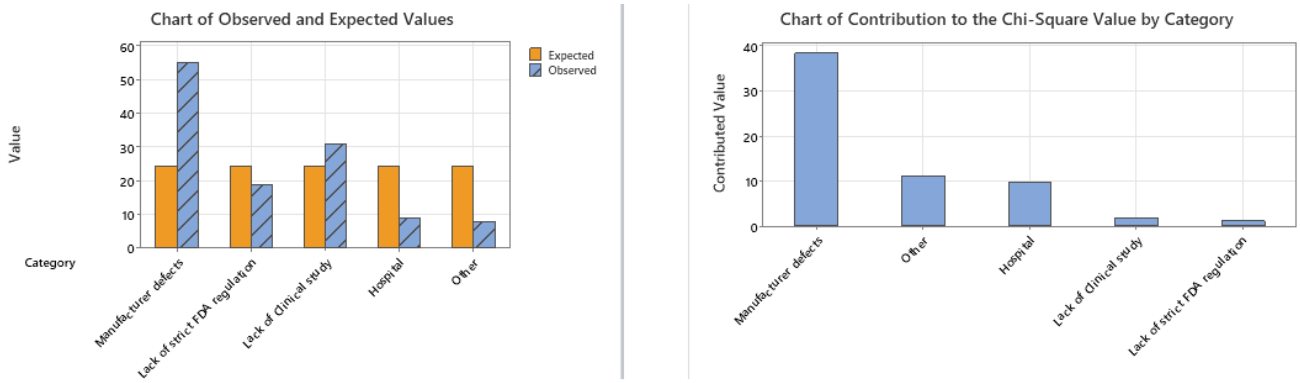


Figure 16: Observed & Expected value graph.

The above Fig-15 shows Chi-square Test value χ 2 = 62.09

Critical values of chi-square (right tail)

Significance level (α)

Degrees of freedom (*df*)	.99	.975	.95	.9	.1	.05	.025	.01
1	-------	0.001	0.004	0.016	2.706	3.841	5.024	6.635
2	0.020	0.051	0.103	0.211	4.605	5.991	7.378	9.210
3	0.115	0.216	0.352	0.584	6.251	7.815	9.348	11.345
4	0.297	0.484	0.711	1.064	7.779	9.488	11.143	13.277
5	0.554	0.831	1.145	1.610	9.236	11.070	12.833	15.086

Figure 17: Chi square table.

Critical Value (χ 2 critical) = 9.488 for Degree of freedom (df) = 5-1 = 4, confidence level = 0.05

Since the calculated chi-square statistic (62.09) is much greater than the critical value (9.488), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

The data highlights several key contributors to orthopaedic knee implant recalls as perceived by respondents as shown in Fig-14, Manufacturer defects emerge as the primary concern, with 45% of respondents identifying them as the main contributors to orthopaedic recalls. This emphasizes the significance of addressing issues within the manufacturing process, such as production errors, design flaws, and quality control lapses, to ensure the reliability and safety of orthopaedic devices. Furthermore, lack of strict FDA regulation is identified by 16% of respondents as a significant factor contributing to orthopaedic recalls. This suggests concerns regarding the adequacy of regulatory oversight and enforcement, potentially leading to lapses in product safety and quality standards. The need for stronger regulatory measures to mitigate risks associated with orthopaedic devices is underscored by this response. Additionally, lack of clinical study emerges as another noteworthy contributor to orthopaedic recalls, with 25% of respondents highlighting the importance of robust clinical research in evaluating device efficacy and safety. This suggests that inadequate clinical data may compromise the understanding of device performance, potentially leading to unforeseen complications and recalls. Hospital-related issues, identified by 7% of respondents, also contribute to orthopaedic recalls, highlighting the importance of vigilant monitoring and reporting mechanisms within healthcare institutions to identify and address device-related issues promptly. Lastly, other factors, identified by 7% of respondents, suggest additional complexities within the orthopaedic device landscape contributing to recalls. While not explicitly specified, these factors may include various issues such as material selection, labelling errors, packaging issues, and post-market surveillance challenges.

Overall, the data underscores the multifaceted nature of contributors to orthopaedic recalls, emphasizing the need for comprehensive efforts to address manufacturing defects, strengthen regulatory oversight, conduct robust clinical studies, enhance hospital monitoring, and mitigate other contributing factors to ensure the safety and effectiveness of orthopaedic devices.

4.1.2 Analysis: Manufacturer recalls- Identifying high risk recalls area

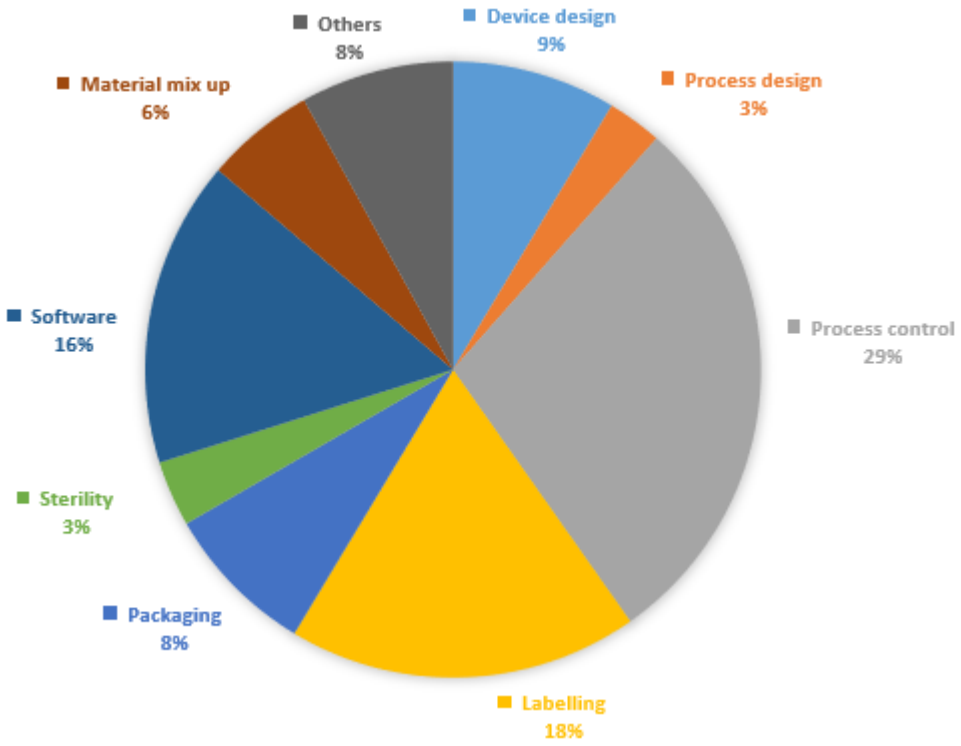


Figure 18: Most Recall Manufacturing area.

The findings from the survey provide valuable insights into the areas where manufacturer recalls are most prevalent, as perceived by respondents illustrated in Fig-18. Process control emerges as a primary concern, with 28% of respondents highlighting its significance. This underscores the critical importance of implementing robust quality control measures throughout the manufacturing process to prevent defects and ensure the safety and reliability of orthopaedic devices. Effective process control mechanisms can help identify and address issues promptly, thereby minimizing the risk of recalls. Additionally, labelling errors are identified as a major area where manufacturer recalls occur, with 18% of respondents emphasizing its importance. Ensuring accurate and clear product labeling is crucial to prevent confusion or misinterpretation by healthcare professionals or patients, thereby mitigating the risk of adverse events and recalls. Software-related issues also feature prominently, with 15% of respondents highlighting their significance. This underscores the importance of ensuring the reliability and security of software systems integrated into orthopaedic devices, as software vulnerabilities or malfunctions can compromise device performance and patient safety. Moreover, device design and packaging issues are identified by 8% of respondents respectively, suggesting the need for thorough design validation and verification activities and robust packaging practices to prevent design flaws and protect product integrity. Sterility issues and material mix-ups are also highlighted by 3% and 6% of respondents respectively, emphasizing the importance of maintaining sterile conditions throughout the manufacturing process and ensuring proper material management to prevent contamination and associated risks. Lastly, other factors, identified by 8% of respondents, suggest additional complexities within the manufacturing process contributing to recalls. While not explicitly specified, these factors may include various

issues such as supplier-related problems, manufacturing process variability, and inadequate quality management systems.

Overall, the data underscores the importance of addressing process control, labelling errors, software-related issues, device design, packaging practices, sterility maintenance, and material management to minimize the risk of manufacturer recalls and uphold product quality and safety standards in the orthopaedic knee implant device industry.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
Device design	15	0.111111	19.3333	0.9713
Process design	5	0.111111	19.3333	10.6264
Process control	50	0.111111	19.3333	48.6437
Labelling	32	0.111111	19.3333	8.2989
Packaging	14	0.111111	19.3333	1.4713
Sterility	6	0.111111	19.3333	9.1954
Software	28	0.111111	19.3333	3.8851
Material mix up	10	0.111111	19.3333	4.5057
Others	14	0.111111	19.3333	1.4713

Chi-Square Test

N	DF	Chi-Sq	P-Value
174	8	89.0690	0.000

Figure 19:Chi square test result- Minitab.

The above Fig-19 shows Chi-square Test value χ 2 = 89.06

Critical Value (χ 2 critical) = 15.51 for Degree of freedom (df) = 9-1 = 8, confidence level = 0.05

8	1.646	2.180	2.733	3.490	13.362	15.507	17.535	20.090

Figure 20:Chi square table.

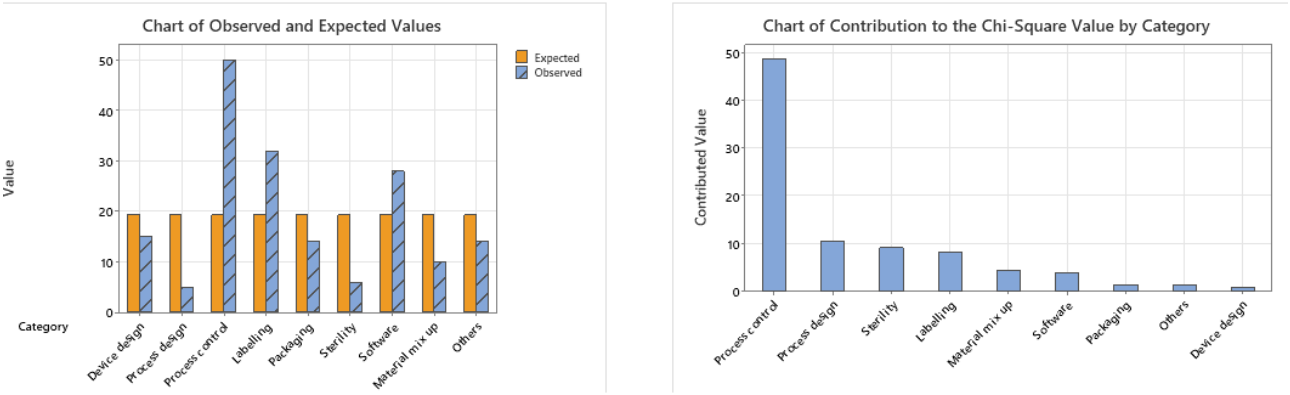


Figure 21:Observed & Expected value graph.

Since the calculated chi-square statistic (89.06) is much greater than the critical value (15.51), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

4.1.3 Analysis: Suggestion on manufacturer to minimize recalls

The findings highlight several key areas that need attention from manufacturers to prevent recalls, as emphasized by respondent feedback illustrated in Fig-22. A significant number of respondents, counting 27%, underscore the critical importance of process control. This indicates that rigorous control and monitoring of manufacturing processes are essential in preventing defects and ensuring product quality and safety. Additionally, respondents emphasize the significance of adhering to Quality Management System (QMS) standards, with 24% of respondents stressing the need for robust QMS implementation. This underscores the importance of establishing comprehensive quality management processes to maintain consistency and compliance throughout the manufacturing process.

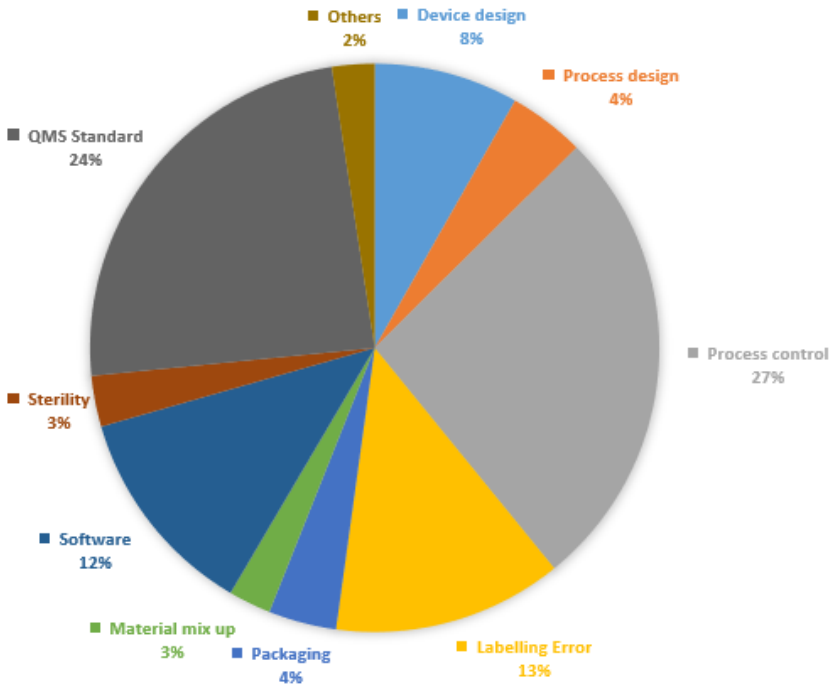


Figure 22: The area that Manufacturer needs to focus on

Furthermore, attention to device design emerges as another crucial area, with 8% of respondents indicating its importance. This underscores the need for thorough design validation and verification activities to identify and rectify potential design flaws that could compromise product functionality and safety. Similarly, software-related issues are highlighted by 12% of respondents, emphasizing the importance of ensuring the reliability and security of software systems integrated into medical devices. Labelling errors, packaging issues, and material mix-ups are also identified as areas requiring attention to prevent recalls, with 13%, 4%, and 3% respondents respectively highlighting these concerns. Ensuring accurate and clear product labelling, robust packaging, and proper material management are essential to minimize the risk of errors and ensure product integrity. Additionally, respondents identify sterility as a critical aspect, with 3% of respondents emphasizing the importance of maintaining sterile conditions throughout the manufacturing process to prevent contamination and associated risks.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

The below Fig-24 shows Chi-square Test value $\chi 2 = 150.44$

Critical Value (χ 2 critical) = 16.92 for Degree of freedom (df) = 10-1 = 9, confidence level = 0.05

9	2.088	2.700	3.325	4.168	14.684	16.919	19.023	21.666

Figure 23:Chi square table.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
Device design	17	0.1	20.7	0.6614
Process design	9	0.1	20.7	6.6130
Process control	55	0.1	20.7	56.8353
Labelling Error	27	0.1	20.7	1.9174
Packaging	8	0.1	20.7	7.7918
Material mix up	5	0.1	20.7	11.9077
Software	25	0.1	20.7	0.8932
Sterility	6	0.1	20.7	10.4391
QMS Standard	50	0.1	20.7	41.4729
Others	5	0.1	20.7	11.9077

Chi-Square Test

N	DF	Chi-Sq	P-Value
207	9	150.440	0.000

Figure 24:Chi square test result- Minitab.

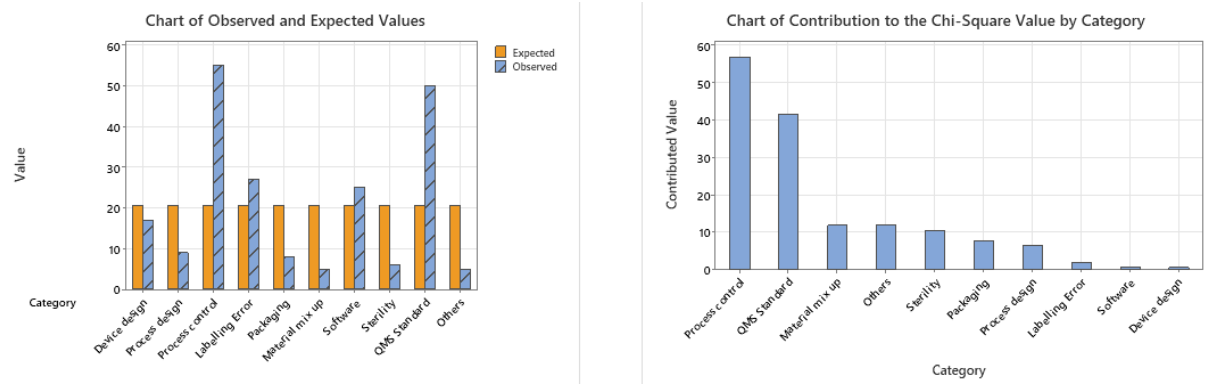


Figure 25: Observed & Expected value graph.

Since the calculated chi-square statistic (150.44) is much greater than the critical value (16.92), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

Overall, the data suggests that manufacturers should prioritize enhancing process control, adhering to QMS standards, ensuring robust design and software validation, addressing labelling and packaging concerns, maintaining sterility, and mitigating material mix-ups to prevent recalls and uphold product quality and safety standards.

4.1.4 Analysis: FDA Approval pathway contributes to recalls

The findings shed light on the FDA approval processes and the frequency of recalls as perceived by respondents participating in this research study illustrated in Fig-26. The data underscores significant concerns regarding the 510K Premarket Notification Process, with a substantial

majority of 39% individuals identifying it as the stage where recalls occur most frequently. This indicates a potential issue with the clearance of medical devices through this pathway, which relies on demonstrating substantial equivalence rather than extensive clinical data, potentially raising questions about the adequacy of safety assessments. Moreover, the identification of mixed approvals by 17% of respondents as a notable area for recalls suggests possible challenges or inconsistencies in the regulatory approach, particularly for devices subject to multiple approval pathways. This finding highlights the need for clearer guidelines and standardized procedures to ensure consistent and robust oversight. The recognition of general controls as another significant stage for recalls by 20% of respondents raises concerns about systemic issues within the regulatory framework applicable to all medical devices. Addressing these issues is crucial to prevent recurrent recall events and enhance overall patient safety.

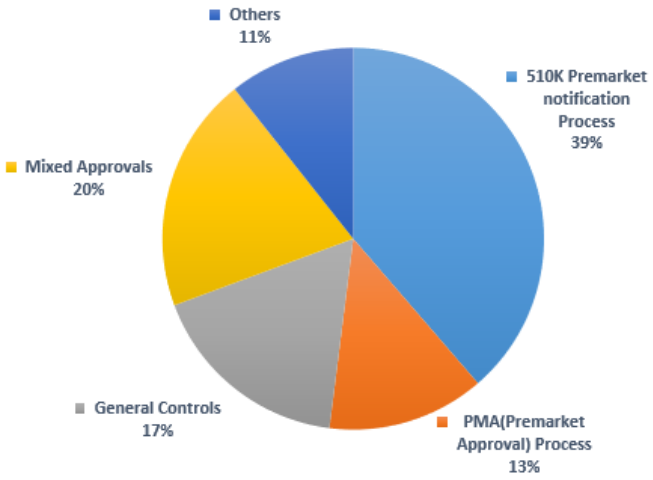


Figure 26: Recalls on different regulatory approval pathway process.

Conversely, a smaller proportion of respondents, counting 13%, pinpoint the PMA (Premarket Approval) Process as the stage where recalls occur most frequently. This finding may indicate that the rigorous requirements of the PMA process, which demand comprehensive clinical data for high-risk devices, generally result in fewer recalls compared to the 510K pathway.

Furthermore, the acknowledgment by 11% of respondents of other areas where recalls are common underscores the complex and multifaceted challenges inherent in the FDA approval process. This highlights the necessity for a holistic approach to regulatory reforms and interventions aimed at strengthening oversight and safeguarding patient safety across the entire medical device approval lifecycle.

In conclusion, these findings emphasize the urgent need for targeted interventions and regulatory reforms to address the identified concerns and enhance the effectiveness of the FDA approval process. Strengthening oversight and ensuring rigorous safety assessments are essential to minimize the occurrence of recalls and uphold patient safety standards.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

The below Fig-28 shows Chi-square Test value $\chi 2 = 18.27$

Critical Value (χ 2 critical) = 9.49 for Degree of freedom (df) = 5-1 = 4, confidence level = 0.05

4	0.297	0.484	0.711	1.064	7.779	9.488	11.143	13.277

Figure 27: Chi square table.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
510K Premarket notification Process	29	0.2	15	13.0667
PMA(Premarket Approval) Process	10	0.2	15	1.6667
General Controls	13	0.2	15	0.2667
Mixed Approvals	15	0.2	15	0.0000
Others	8	0.2	15	3.2667

Chi-Square Test

N	DF	Chi-Sq	P-Value
75	4	18.2667	0.001

Figure 28: Chi square test result- Minitab.

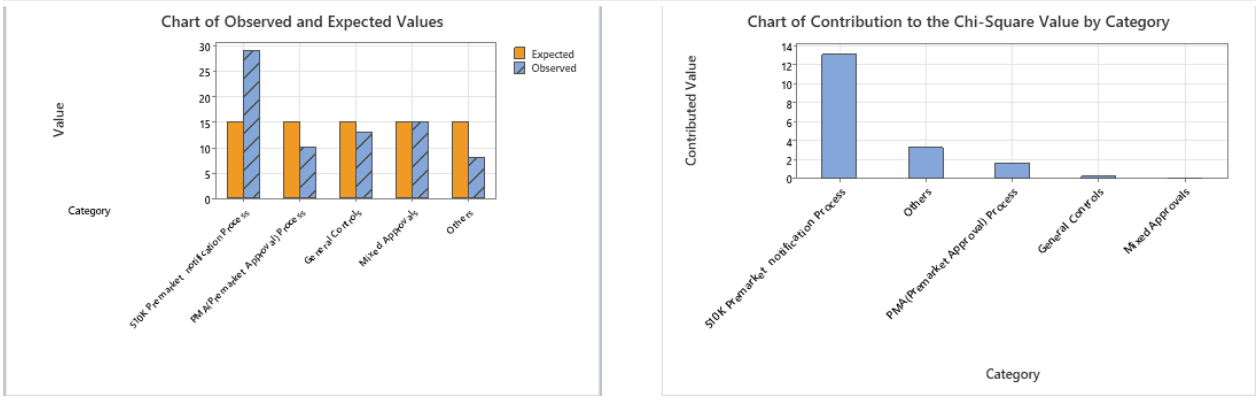


Figure 29: Observed & Expected value graph.

Since the calculated chi-square statistic (18.27) is much greater than the critical value (9.49), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

4.1.5 Analysis: Suggestion of FDA Approval pathways

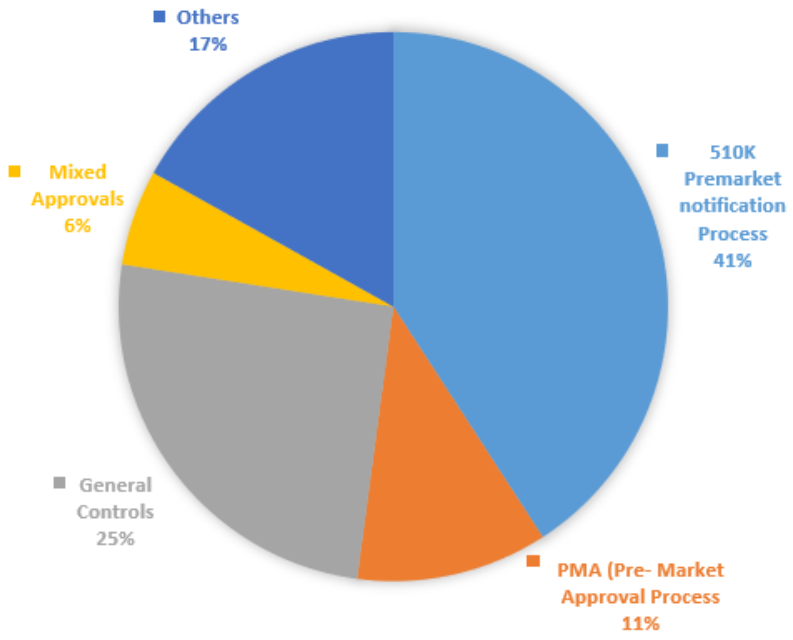


Figure 30: Suggestion on Regulatory approval pathways.

The findings offer valuable perspectives on areas (Fig-30) within the FDA regulatory framework that require tighter regulations to prevent future recalls, reflecting the collective opinions of respondents and highlighting key areas of focus. Foremost among the identified areas for enhancement is the 510K Premarket Notification process, which a substantial proportion of 41% of respondents emphasize as needing tighter regulations. This underscore concerns regarding the current efficacy of requirements for demonstrating the safety and effectiveness of devices cleared through this pathway. The emphasis on tighter regulations suggests a pressing need to reassess the criteria for substantial equivalence and to enhance scrutiny to ensure robust safety standards are met prior to market clearance. Furthermore, 25% of respondents believe strengthening general controls, which constitute the foundational regulatory requirements for all medical devices. Strengthening general controls is seen as imperative for addressing systemic issues and enhancing overall compliance with regulatory standards, potentially mitigating recall risks stemming from fundamental regulatory lapses. Moreover, 11% of respondents underscore the significance of tightening regulations surrounding the PMA process, particularly for high-risk medical devices. This underscores the importance of stringent requirements for demonstrating safety and effectiveness through comprehensive clinical data, aiming to mitigate risks associated with novel or high-risk devices and minimize the likelihood of recalls. However, a smaller subset of respondents, totalling 6%, point to the necessity for improvements in mixed approvals, indicating potential gaps or inconsistencies in the regulatory approach for devices subject to multiple approval pathways. Addressing these concerns is essential to ensure a consistent and robust

regulatory framework that effectively evaluates the safety and efficacy of devices with diverse approval pathways. Lastly, 17% of respondents identify additional areas for regulatory enhancement, suggesting a diverse array of concerns or perceived shortcomings within the current FDA regulatory framework. These findings underscore the complex challenges faced by regulatory authorities in striking a balance between fostering innovation and ensuring patient safety. Targeted interventions aimed at strengthening the regulatory framework are crucial to mitigate recall risks and uphold patient safety standards within the orthopaedic knee implant domain.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

The below Fig-32 shows Chi-square Test value χ 2 = 26.82

Critical Value (χ 2 critical) = 9.49 for Degree of freedom (df) = 5-1 = 4, confidence level = 0.05

4	0.297	0.484	0.711	1.064	7.779	9.488	11.143	13.277

Figure 31: Chi square table.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
510K Premarket notification Process	29	0.2	14.2	15.4254
PMA (Pre- Market Approval Process	8	0.2	14.2	2.7070
General Controls	18	0.2	14.2	1.0169
Mixed Approvals	4	0.2	14.2	7.3268
Others	12	0.2	14.2	0.3408

Chi-Square Test

N	DF	Chi-Sq	P-Value
71	4	26.8169	0.000

Figure 32: Chi square test result- Minitab.

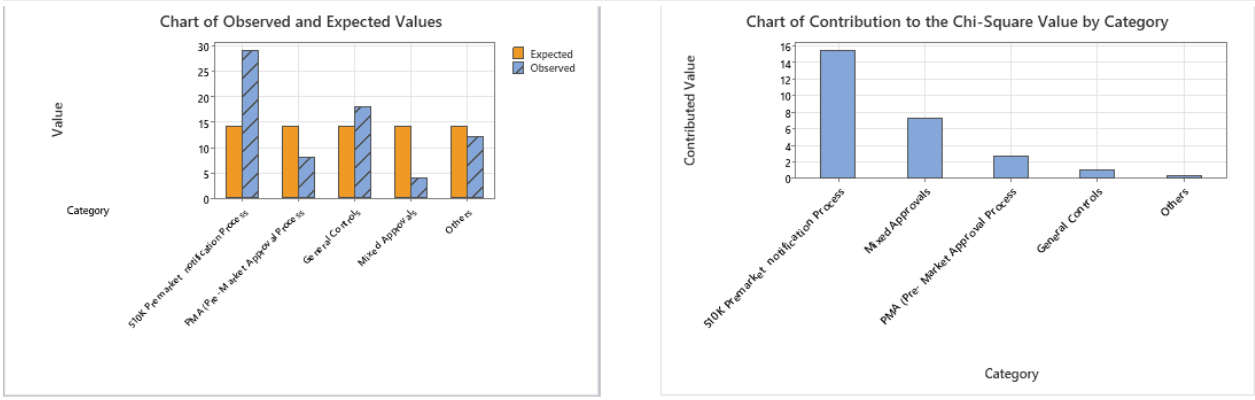


Figure 33:Observed & Expected value graph.

Since the calculated chi-square statistic value (26.82) is much greater than the critical value (9.49), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

4.1.6 Analysis: Effectiveness of current system on orthopaedic knee implant

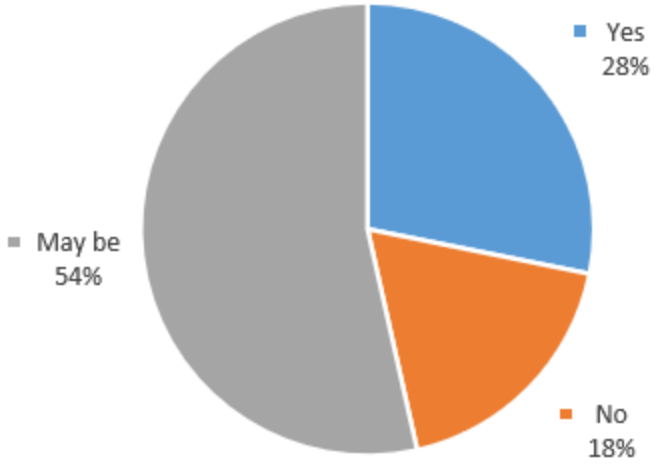


Figure 34: Current system effectiveness.

The data suggests a mixed sentiment (Fig-34) regarding the effectiveness of the current regulatory framework and standards governing medical device manufacturing. While 28% of respondents express confidence in the efficacy of the existing system, with regards to standards such as medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30, ISO 14971:2019- Medical devices Risk Management, and Regulatory framework- 510K & PMA Approval, a sizable portion, comprising 16% of respondents, voice concerns about its effectiveness. This suggests that there may be perceived inadequacies or shortcomings in the current regulatory framework and standards, prompting doubts about its ability to ensure the safety and quality of orthopaedic knee implant

devices. Additionally, a significant number of respondents, totalling 54%, express uncertainty, indicating a need for further evaluation and potentially, improvements to the existing system.

These findings underscore the importance of ongoing regulatory oversight and continuous improvement efforts to address emerging challenges and enhance patient safety in the orthopaedic knee implant device industry. Further research and stakeholder engagement may be necessary to identify areas for improvement and strengthen the regulatory framework to better align with evolving industry standards and best practices.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

The below Fig-36 shows Chi-square Test value χ 2 = 14.05

Critical Value (χ 2 critical) = 5.99 for Degree of freedom (df) = 3-1 = 2, confidence level = 0.05

2	0.020	0.051	0.103	0.211	4.605	5.991	7.378	9.210

Figure 35: Chi square table.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
Yes	20	0.333333	23.6667	0.56808
No	13	0.333333	23.6667	4.80751
May be	38	0.333333	23.6667	8.68075

Chi-Square Test

N	DF	Chi-Sq	P-Value
71	2	14.0563	0.001

Figure 36: Chi square test result- Minitab.

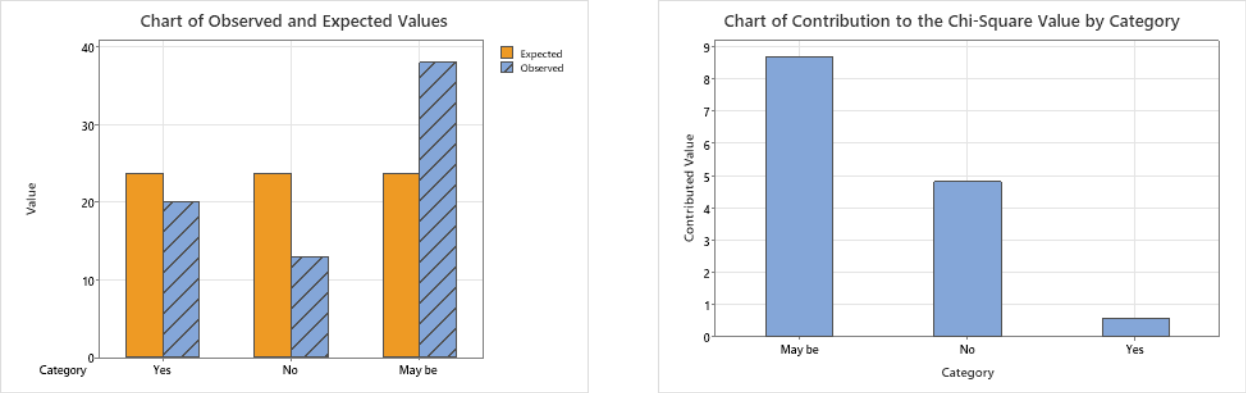


Figure 37:Observed & Expected value graph.

Since the calculated chi-square statistic value (14.05) is much greater than the critical value (5.99), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

4.1.7 Analysis: Identifying gaps on current system on orthopaedic knee implant & see if an improvement required

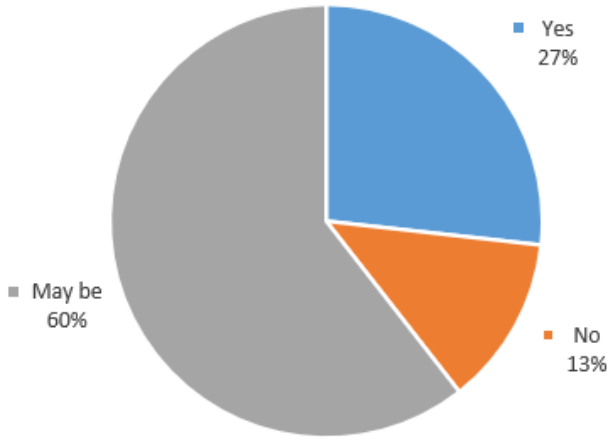


Figure 38: Sentiment about gaps in current system.

The finding reveals a notable level of uncertainty and skepticism regarding the effectiveness of the current regulatory system governing orthopaedic knee implant medical device manufacturing (Fig-38).A significant portion of respondents, totaling 60% individuals, express ambiguity about whether the existing system, including standards such as Medical Device Quality System Regulations (21CFR Part 820), Design Control (FDA 21 CFR 820.30), ISO 14971:2019 for Medical Devices Risk Management, and Regulatory framework for 510K & PMA Approval, has some gaps and requires improvement. This uncertainty underscores the need for further evaluation and potential enhancements to address perceived deficiencies in the regulatory framework.

Moreover, 27% of respondents acknowledge the presence of gaps and the necessity for improvement, indicating concerns about the adequacy of current regulations and standards in ensuring the safety and quality of orthopaedic devices. While a smaller group of 13% respondents express confidence in the sufficiency of the current system, the prevailing sentiment of uncertainty and recognition of potential gaps suggest a critical need for regulatory reform and continuous improvement efforts. These findings underscore the importance of ongoing stakeholder engagement, rigorous oversight, and proactive measures to strengthen the regulatory framework and enhance patient safety in the orthopaedic device industry. Further collaboration between industry stakeholders, regulatory agencies, and policymakers may be necessary to address identified gaps and implement effective reforms that align with evolving industry standards and best practices.

Evaluating whether the responses collected from survey participants conform to a specified distribution by checking if participants' preferences for different options are equally distributed or if they follow a predicted pattern.

The below chart shows Chi-square Test value $\chi 2 = 25.80$

Critical Value (χ 2 critical) = 5.99 for Degree of freedom (df) = 3-1 = 2, confidence level = 0.05

2	0.020	0.051	0.103	0.211	4.605	5.991	7.378	9.210

Figure 39:Chi square table.

Observed and Expected Counts

Category	Observed	Test Proportion	Expected	Contribution to Chi-Square
Yes	19	0.333333	23.6667	0.9202
No	9	0.333333	23.6667	9.0892
May be	43	0.333333	23.6667	15.7934

Chi-Square Test

N	DF	Chi-Sq	P-Value
71	2	25.8028	0.000

Figure 40:Chi square test result- Minitab.

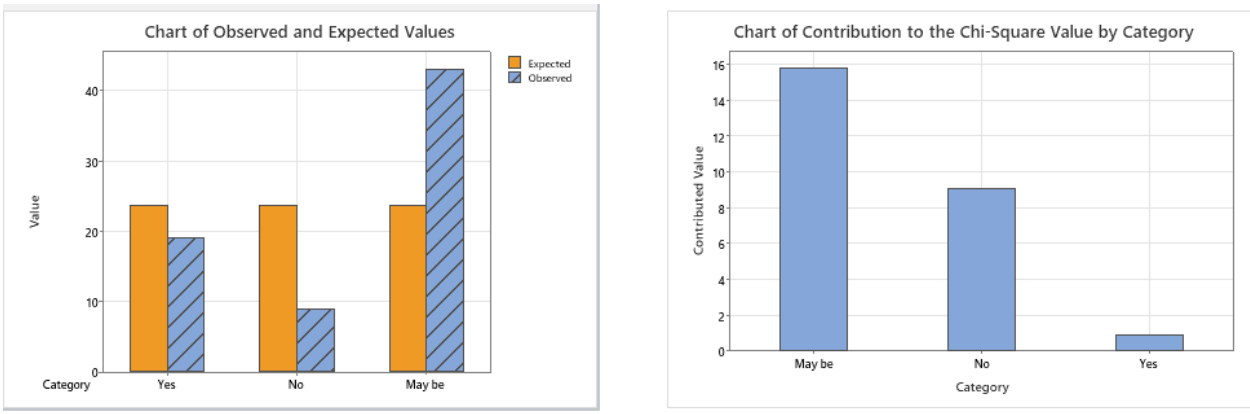


Figure 41:Observed & Expected value graph.

Since the calculated chi-square statistic value (25.08) is much greater than the critical value (5.99), Hence rejecting the null hypothesis. This indicates that the distribution of participants' preference is significantly different from an equal distribution, suggesting that participants do prefer certain modes.

4.1.8 Analysis: Challenges on current system of orthopaedic knee implant

Based on the respondents' feedback, several key themes were emerged regarding the primary challenges and considerations in the field of orthopaedic knee implant device recalls. These themes can be grouped into various categories, each reflecting specific concerns and issues emphasized in the feedback.

The identified main themes are:

Process Design and Control: Emphasizes the need for robust initial controls and attention to detail.

Supplier and Material Issues: Highlights the impact of supplier compliance on product quality.

Regulatory Challenges: Discusses the difficulties of adhering to evolving regulatory requirements and the issues with predicate approval processes.

Innovation and Market Pressures: Points to the risks associated with rapid innovation and the pressure to bring products to market quickly.

Quality Management Systems (QMS): Underlines the importance of comprehensive quality control and alignment with international standards.

Human Factors: Focuses on the human element in maintaining product quality and safety.

Patient Safety and Product Quality: Stresses the importance of meeting patient needs and ensuring product integrity.

Documentation and Compliance: Addresses the challenges of managing extensive documentation and staying compliant with regulations.

The challenges identified within the current system of orthopaedic knee implant medical device regulation and manufacturing are multifaceted and encompass various aspects of process design, regulatory compliance, innovation, and patient safety. Numerous respondents express concerns regarding process design and control, highlighting deficiencies in attention to detail, robust process controls, and supplier-related issues such as material quality and adherence to quality management system standards. Additionally, the pursuit of innovation and speed to market is seen as potentially compromising patient safety, with some companies taking risks to expedite product approval. There are also concerns about the confidence on predictive approval paths and the lack of thorough review leading to recalls. Moreover, the evolving regulatory environment, complex devices, and rapid technological innovation pose significant challenges for manufacturers in ensuring compliance and producing safe, effective products. Other challenges cited include the burden of paperwork, the human element in staff training and operating procedures, and the need to balance cost, quality, and safety in product development.

Overall, these challenges underscore the importance of ongoing regulatory reform, technological innovation, and industry collaboration to address systemic issues and enhance patient outcomes in the orthopaedic medical device sector.

4.1.9 Analysis: Proposing changes on any specific standard – Manufacturing QMS standard, FDA regulatory framework, Clinical study requirement, Hospital use.

Based on the respondents' feedback, several key themes were emerged regarding opinions and suggestions related to the orthopaedic knee implant device recall system.

Here are the identified themes:

Quality Management System (QMS): Emphasis on robust QMS incorporating risk management principles and ensuring compliance.

Regulatory Framework: Need for rigorous and evolving regulatory standards, improvement in FDA processes, and global alignment.

Clinical Study Requirements: Essential role of clinical evidence and post-market surveillance in ensuring product safety and effectiveness.

Risk Management: Importance of effective risk management throughout the product lifecycle.

Approval Process: Necessity for a thorough and systematic approval process for all products.

Regulation and Monitoring: Better monitoring, support from governing bodies, and ensuring strict adherence to standards.

Post-Market Surveillance: Continuous monitoring and data-driven feedback mechanisms.

Industry Dynamics: Addressing the challenges posed by a fast-paced and competitive industry while ensuring compliance and innovation.

The finding reveals regarding specific changes required in the current medical device landscape reflect a diverse range of opinions and perspectives. Some respondents express satisfaction with the current system when followed effectively, suggesting that no changes are necessary. However, others advocate for improvements in various areas, such as enhancing cooperation with small and medium-sized enterprises (SMEs), providing better information, and monitoring from governing bodies, and refining the FDA approval process and manufacturer Quality Management Systems (QMS). Suggestions for incorporating principles from ISO 14971 (Risk Management for Medical Devices) into QMS requirements and addressing risk and lifecycle approaches in QMS are also made. Additionally, there are calls for strengthening post-market surveillance, clinical evidence requirements, and regulation, particularly in highly competitive and dynamic industries. Some respondents emphasize the need for rigorous regulatory reviews and strong risk management systems. Overall, the responses highlight the complexity of the medical device landscape and the importance of continuous improvement to ensure patient safety and product effectiveness.

4.1.10 Analysis: Improvement proposal on current orthopaedic knee implant system to prevent future recalls

Based on the respondents' feedback, several key themes were emerged regarding the suggested improvements and current practices in the orthopaedic knee implant device industry.

Here are the identified themes:

Process Control and Risk Management: Emphasizing better control and risk management throughout the product lifecycle.

Regulatory Framework and Oversight: Need for stricter regulatory standards and oversight, including a separate recall investigation committee.

Quality Management System (QMS): Focus on robust QMS standards, better software systems, and rigorous document reviews.

Regulatory and Clinical Requirements: Strengthening clinical trials, regulatory reviews, and post-market surveillance.

Automation and Technology Integration: Leveraging automation and AI to improve quality, safety, and efficiency.

Organizational and Operational Improvements: Enhancing organizational controls, retaining experienced staff, and adopting a system thinking approach.

Collaboration and Communication: Encouraging collaboration among industry stakeholders and better communication.

Stakeholder Perspectives: Mixed opinions on the need for changes, with some advocating for strict adherence to current standards and others calling for continuous improvements.

The finding reveals that improving the current system to prevent Ortho knee implant device recalls in the future requires a comprehensive approach addressing various aspects of the product lifecycle and regulatory framework. Suggestions from respondents highlight the importance of better control of processes and robust risk management practices to identify and mitigate potential issues early on. Creating a culture of precision among operators, dedicating more time and resources to research and design validation, and retaining experienced staff are also emphasized as critical factors. Some suggest revisiting and refining the current medical device Quality Management System (QMS) standard and FDA regulatory framework to address existing gaps and ensure thorough compliance. Additionally, there are calls for establishing separate teams to handle recalls and implement corrective actions, enhancing regulatory oversight, and promoting collaboration between industry, academia, and regulatory agencies to conduct research and improve risk management practices. Strengthening quality control measures, improving clinical trials and post-market monitoring, and adopting automation where possible are also cited as necessary steps. Overall, the responses underscore the need for a multifaceted approach, encompassing regulatory reforms, enhanced quality control measures, and a culture of continuous improvement to prevent orthopaedic knee implant device recalls in the future.

4.2 Discussion on Findings & Analysis:

Objective#1: Investigate main factors that are contributing to Orthopaedic knee implant device recalls.

Discussion on factors contributing to Orthopaedic knee implant recalls:

The data from the survey provides crucial insights into the factors contributing to orthopaedic knee implant recalls as perceived by respondents, shedding light on various aspects of manufacturing, regulation, and clinical research. Manufacturer defects emerge as the primary concern, with 45% of respondents identifying them as the main contributors to orthopaedic knee implant recalls. This highlights the critical need to address issues within the manufacturing process, such as production errors, design flaws, and quality control lapses, to ensure the reliability and safety of orthopaedic knee implant devices. Strengthening quality control measures and implementing robust design validation protocols are paramount to minimize the risk of defects and subsequent recalls.

Furthermore, the lack of strict FDA regulation is identified by 16% of respondents as a significant factor contributing to orthopaedic knee implant recalls. This underscore concerns regarding

regulatory oversight and enforcement, potentially leading to lapses in product safety and quality standards. Strengthening regulatory measures is imperative to mitigate risks associated with orthopaedic knee implant devices and enhance patient safety. Inadequate clinical study also emerges as a significant contributor to orthopaedic recalls, with 25% of respondents highlighting the importance of robust clinical research in evaluating device efficacy and safety. This suggests that insufficient clinical data may compromise the understanding of device performance, leading to unforeseen complications and recalls.

Hospital-related issues, identified by 7% of respondents, also contribute to orthopaedic knee implant recalls, emphasizing the importance of vigilant monitoring and reporting mechanisms within healthcare institutions to identify and address device-related issues promptly. Additionally, various other factors such as process control, labelling errors, software-related issues, device design, packaging practices, sterility maintenance, and material management are highlighted as contributing to recalls by respondents. Addressing these factors requires comprehensive efforts across the manufacturing process to ensure product quality and safety standards are upheld.

In conclusion, the data underscores the multifaceted nature of contributors to orthopaedic knee implant recalls, emphasizing the need for comprehensive efforts to address manufacturing defects, strengthen regulatory oversight, conduct robust clinical studies, enhance hospital monitoring, and mitigate other contributing factors. By prioritizing these efforts, manufacturers can minimize the risk of recalls and uphold product quality and safety standards in the orthopaedic knee implant device industry, ultimately benefiting patient well-being and fostering public trust.

Discussion on Manufacturer- Orthopaedic knee implant recalls:

The survey findings offer crucial insights into the areas where manufacturer recalls are most prevalent, as perceived by respondents within the orthopaedic knee implant device industry. Process control emerges as a primary concern, with 29% of respondents highlighting its significance. This underscores the critical importance of implementing robust quality control measures throughout the manufacturing process to prevent defects and ensure the safety and reliability of orthopaedic devices. Effective process control mechanisms play a pivotal role in identifying and addressing issues promptly, thereby minimizing the risk of recalls and maintaining product quality standards. Furthermore, labelling errors are identified as a major area where manufacturer recalls occur, with 18% of respondents emphasizing its importance. Ensuring accurate and clear product labelling is crucial to prevent confusion or misinterpretation by healthcare professionals or patients, thereby mitigating the risk of adverse events and recalls. Software-related issues also feature prominently, with 16% of respondents highlighting their significance. This underscores the importance of ensuring the reliability and security of software systems integrated into orthopaedic devices, as software vulnerabilities or malfunctions can compromise device performance and patient safety. Moreover, device design and packaging issues are identified by 9% and 8% of respondents respectively, suggesting the need for thorough design validation and verification activities and robust packaging practices to prevent design flaws and

protect product integrity. Sterility issues and material mix-ups are also highlighted by 3% and 6% of respondents respectively, emphasizing the importance of maintaining sterile conditions throughout the manufacturing process and ensuring proper material management to prevent contamination and associated risks. Lastly, other factors, identified by 8% of respondents, suggest additional complexities within the manufacturing process contributing to recalls. While not explicitly specified, these factors may include various issues such as supplier-related problems, manufacturing process variability, and inadequate quality management systems. Overall, the data underscores the importance of addressing process control, labelling errors, software-related issues, device design, packaging practices, sterility maintenance, and material management to minimize the risk of manufacturer recalls and uphold product quality and safety standards in the orthopaedic knee implant device industry. By prioritizing efforts to address these key areas, manufacturers can enhance patient safety, mitigate risks, and maintain public trust in orthopaedic knee implant devices.

Discussion on FDA Approval pathways leading to Orthopaedic knee implant recalls:

The survey findings provide valuable insights into the FDA approval processes and the frequency of recalls as perceived by respondents within the medical device industry. Significant concerns are highlighted regarding the 510K Premarket Notification Process, with a substantial majority of 39% individuals identifying it as the stage where recalls occur most frequently. This raises questions about the adequacy of safety assessments within this pathway, which relies on demonstrating substantial equivalence rather than extensive clinical data. The potential issue with clearance through this pathway underscores the importance of reevaluating the regulatory approach to ensure robust safety assessments and minimize the occurrence of recalls. Moreover, the identification of mixed approvals as a notable area for recalls by 20% of respondents suggests possible challenges or inconsistencies in the regulatory approach, particularly for devices subject to multiple approval pathways. This finding underscores the need for clearer guidelines and standardized procedures to ensure consistent and robust oversight across all approval pathways. The recognition of general controls as another significant stage for recalls by 17% of respondents raises concerns about systemic issues within the regulatory framework applicable to all medical devices. Addressing these systemic issues is crucial to prevent recurrent recall events and enhance overall patient safety. Conversely, a smaller proportion of respondents, totalling 13%, pinpoint the PMA (Premarket Approval) Process as the stage where recalls occur most frequently. This finding may indicate that the rigorous requirements of the PMA process, which demand comprehensive clinical data for high-risk devices, generally result in fewer recalls compared to the 510K pathway. However, continuous vigilance and improvement within the PMA process are still necessary to uphold safety standards effectively. Furthermore, the acknowledgment by 11% of respondents of other areas where recalls are common underscores the complex and multifaceted challenges inherent in the FDA approval process. This highlights the necessity for a holistic approach to regulatory reforms and interventions aimed at strengthening oversight and safeguarding patient safety across the entire medical device approval lifecycle.

In conclusion, these findings emphasize the urgent need for targeted interventions and regulatory reforms to address the identified concerns and enhance the effectiveness of the FDA approval process. Strengthening oversight and ensuring rigorous safety assessments are essential to minimize the occurrence of recalls and uphold patient safety standards, ultimately benefiting public health and well-being.

Objective#2: Discover if current system is effective or improvement is required.

Discussion on effectiveness of current system:

The survey results reveal a mixed sentiment regarding the effectiveness of the current regulatory framework and standards governing medical device manufacturing within the orthopaedic knee implant device industry. While a portion of respondents, comprising 28% individuals, express confidence in the efficacy of existing standards such as medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30, ISO 14971:2019- Medical devices Risk Management, and Regulatory framework- 510K & PMA Approval, a sizable contingent of 18% individuals voice concerns about its effectiveness. This discrepancy suggests that there may be perceived inadequacies or shortcomings in the current regulatory framework and standards, prompting doubts about their ability to ensure the safety and quality of orthopaedic knee implant devices. Moreover, a significant number of respondents, totalling 54%, express uncertainty, indicating a need for further evaluation and potentially, improvements to the existing system. This uncertainty underscores the complexity and evolving nature of regulatory challenges within the orthopaedic knee implant device industry, necessitating ongoing evaluation and refinement of regulatory practices to address emerging issues effectively. These findings highlight the importance of ongoing regulatory oversight and continuous improvement efforts to address emerging challenges and enhance patient safety in the orthopaedic knee implant device industry. Further research and stakeholder engagement may be necessary to identify areas for improvement and strengthen the regulatory framework to better align with evolving industry standards and best practices.

In conclusion, the mixed sentiment regarding the effectiveness of the current regulatory framework underscores the need for proactive measures to address perceived inadequacies and uncertainties. By prioritizing ongoing regulatory oversight, continuous improvement efforts, and stakeholder engagement, regulatory authorities can work towards enhancing patient safety and ensuring the quality and effectiveness of orthopaedic knee implant devices.

4.3 Critical Analysis: Literature Vs research findings

4.3.1 Common findings: Literature vs research findings

Literature Review: Total orthopaedic device recalls

The literature review categorized the reasons for recalls into two main groups:

- Manufacturer-determined reasoning for recall
- FDA-determined reasoning for recall

Research Findings: Only orthopaedic knee implant device and carried out research on whole orthopaedic knee implant system.

The research categorized the reasons for recalls into five main groups:

- Manufacturer defects are identified as the primary concern (45% of respondents).
- Lack of strict FDA regulation
- Lack of Clinical study
- Hospital
- Other

Literature Review:

- Manufacturer-determined reasoning for recall: The literature review has covered based on different stages of the production cycle: device design, manufacturing, processing, packaging, sterility, software, and marketing.
- FDA-determined reasoning for recall: predominantly 510(k) premarket notification process & PMA process.

Research Findings:

Manufacturer-recall: Research has been covered into Device design, Process design, Process control Labelling, Packaging, Sterility, Software, Material mix up, Others etc.

FDA Approved pathways recall: 510K Premarket notification Process, PMA (Pre- Market Approval Process, General Controls, Mixed Approvals, Others etc.

Effectiveness of the current regulatory system: Mixed sentiments are observed (Confidence & Concerns, uncertainty)

4.3.2 Critical Evaluation: Literature vs research findings

Literature Strengths: Extensive historical data, theoretical grounding.

Research finding Strengths: Current stakeholder feedback, practical recommendations.

Weaknesses: Literature lacks current perspectives, while research has a limited sample size and short period of time, participants perceiving himself or herself as an integral part of the industry.

4.3.3 Comparative Analysis: Literature vs research findings

Overlapping Themes:

Manufacturing and Design Defects:

Both literature and research findings consistently identify manufacturing defects and design flaws as leading causes of recalls. This alignment underscores the critical need for rigorous quality control and design validation.

Regulatory and Approval Processes:

The literature points out the high number of recalls associated with the 510(k) pathway. Research findings echo this concern, with many respondents highlighting inadequate safety assessments within this process. Both sources suggest a need for more stringent regulatory scrutiny.

Software and Labelling Issues:

While software issues were less frequent in the literature, they were more prominent in respondent feedback (16%). Similarly, labelling errors were significant in both sources, emphasizing the necessity for clear and accurate product information.

Manufacturing vs. Regulatory Factors: Both the literature review and research findings emphasize manufacturing defects and regulatory issues as primary recall factors. The literature review focuses on specific stages in the production cycle, while the research highlights broader themes such as process control, regulatory oversight, and clinical research inadequacies.

Statistics vs. Perceptions: The literature review provides detailed statistics on recall reasons, such as packaging errors and manufacturing/design flaws. The research findings, however, reflect respondent perceptions, with highlighting manufacturer defects and pointing out to regulatory lapses.

FDA Approval Pathways: Both sources critique the 510(k) process. The literature shows a higher recall rate among devices approved through 510(k). while the research findings reveal significant concern among respondents about this pathway's adequacy.

Methodological Differences: Literature uses historical data analysis, while research used surveys.

4.3.4 Divergent Insights: Literature vs research findings

Packaging Errors:

The literature emphasizes packaging errors as the leading cause of recalls, a pointing less highlighted in the research findings where process control and manufacturing defects took precedence. This discrepancy suggests that while packaging errors are critical, broader manufacturing controls might address more pervasive issues.

Hospital-Related Issues:

Hospital-related issues were noted by respondents but were not a major focus in the literature review. This highlights the need for better hospital-level vigilance and reporting mechanisms to complement manufacturer controls.

FDA Regulation Perception:

Research findings indicate a significant concern about the lack of strict FDA regulation, a sentiment less emphasized in the literature review. This indicates a potential gap between regulatory expectations and perceived enforcement efficacy.

Recommendations for Improvement:

Enhance Process Control and Quality Management:

Strengthen process control mechanisms and adhere strictly to QMS standards to address manufacturing defects and ensure consistency.

Revise FDA Regulatory Framework:

Reassess the 510(k) process to ensure rigorous safety assessments and consider integrating more stringent clinical data requirements to enhance premarket evaluation.

Strengthen Post-Market Surveillance:

Implement robust post-market surveillance and feedback mechanisms to identify and address issues promptly, leveraging data to inform continuous improvement.

Address Design and Software Reliability:

Prioritize thorough design validation and software reliability to mitigate the risk of recalls related to design flaws and software malfunctions.

Improve Labelling and Packaging Practices:

Ensure accurate and clear product labelling and robust packaging practices to prevent errors and ensure product integrity.

Promote Regulatory and Industry Collaboration:

Foster collaboration between manufacturers, regulatory bodies, and healthcare providers to share best practices, enhance compliance, and improve patient safety.

Improvement Areas Identified:

Process Control and Risk Management

Enhance quality control and process validation.

Implement robust risk management practices throughout the product lifecycle.

Regulatory Framework and Oversight:

Reassess and tighten 510(k) premarket notification criteria.

Strengthen general controls and regulatory oversight.

Introduce a dedicated recall investigation committee.

Quality Management System (QMS):

Adhere to comprehensive QMS standards, incorporating risk management principles.

Conduct thorough design validation and verification.

Clinical Study Requirements:

Emphasize the importance of clinical evidence and post-market surveillance.

Ensure robust clinical trials and ongoing monitoring to evaluate device performance.

Technological Integration:

Leverage automation and AI to enhance quality and efficiency.

Ensure software reliability and security to prevent malfunctions.

Stakeholder Collaboration:

Encourage collaboration among manufacturers, regulatory bodies, healthcare providers, and academic institutions.

Enhance communication and information sharing to address potential issues proactively.

Continuous Improvement and Innovation:

Promote a culture of precision and continuous improvement.

Balance innovation with rigorous safety and quality standards to prevent recalls and ensure patient safety.

4.3.5 Gaps Identified: Literature vs research findings.

- Limited focus on analysing whole system of orthopaedic knee implant products, lack of manufacturer defective area, post-market surveillance, small medium size company involvement and substantial equivalence FDA pathway approval process, clinical study requirements and utilizing automation to enhance efficiency and effectiveness across all stages of the product lifecycle.
- Limited focus on Risk management process.
- Limited focus on analysing effectiveness of current orthopaedic knee Implant device system.

4.3.6 Gaps and Future Research:

Addressed Gaps: The research filled the gap on stakeholder perspectives and practical recommendations.

New Gaps: Future research could explore the effectiveness of proposed changes like a dedicated recall committee, incorporating risk management principles into QMS standards, Stakeholder Collaboration, Technological Integration, utilizing automation to enhance efficiency and effectiveness across all stages of the product lifecycle.

5 CHAPTER

Conclusion & Recommendation:

5.1 Possible limitations in the research methodology

The research data was collected from each individual perceiving himself or herself as an integral part of the industry and therefore it's subjective approach to some extent. To overcome this bias, diversified role in orthopaedic knee implants were chosen to participate in survey to gain a comprehensive overview of the topic.

The study is cross-sectional, capturing data at a single point in time. A longitudinal study tracking professionals over time could offer a more comprehensive understanding of how their perspectives and experiences evolve in response to changes in the industry, regulations, technology, etc.

While the study focused on professionals directly involved in the full life cycle of knee implant products, it did not include perspectives from other stakeholders such as patients, surgeons, or healthcare providers.

With rapid advancements in technology, particularly in Automation manufacturing areas such as artificial intelligence, robotics, and materials science, 3D printing. further research could explore how these emerging technologies are shaping the orthopaedic knee implant industry.

5.2 Recommendations & improvement suggestion for future:

5.2.1 Recommendation For Manufacturer:

Based on the insights gathered from respondent feedback, several key recommendations can be made to manufacturers to prevent recalls and uphold product quality and safety standards (Table-9):

Theme	Percentage of Respondents	Recommendations
Enhance Process Control	27%	Implement rigorous control and monitoring mechanisms, regular quality checks, thorough inspections, and continuous improvement initiatives.
Adhere to Quality Management System (QMS) Standards	24%	Establish comprehensive quality management processes to maintain consistency, compliance, and traceability throughout the manufacturing lifecycle.
Process design & Other factors	Process design: 4%. Others: 2%	Focusing on robust process design to improve efficiency and reduce errors. This

		includes refining design protocols and addressing other minor factors that contribute to overall product quality and safety.
Thoroughly Validate Device Design	8%	Conduct thorough design validation and verification activities to identify and rectify potential design flaws early.
Ensure Software Reliability and Security	12%	Prioritize ensuring the reliability and security of software systems integrated into medical devices to prevent malfunctions or vulnerabilities.
Address Labelling, Packaging, and Material Management Concerns	Labelling:13%, Packaging:4%, Material:3%	Focus on ensuring accurate and clear product labelling, robust packaging practices, and proper material management protocols.
Maintain Sterility Throughout Manufacturing	3%	Implement stringent measures to uphold sterility, including appropriate protocols, equipment, and training.

Table 9: Recommendation for Manufacturer

Enhance Process Control: Given the significant emphasis placed by 27% of respondents on process control, it is imperative for manufacturers to implement rigorous control and monitoring mechanisms throughout the manufacturing process. This includes regular quality checks, thorough inspection procedures, and continuous improvement initiatives to prevent defects and ensure product consistency.

Adhere to Quality Management System (QMS) Standards: The importance of robust QMS implementation, highlighted by 24% of respondents, cannot be overstated. Manufacturers should prioritize establishing comprehensive quality management processes to maintain consistency, compliance, and traceability throughout the manufacturing lifecycle.

Thoroughly Validate Device Design: With 8% of respondents stressing the importance of device design, manufacturers must conduct thorough design validation and verification activities. Identifying and rectifying potential design flaws early on is crucial to prevent issues that could compromise product functionality and safety.

Ensure Software Reliability and Security: Software-related issues, as emphasized by 12% of respondents, need careful attention. Manufacturers should prioritize ensuring the reliability and security of software systems integrated into medical devices to prevent malfunctions or vulnerabilities that could pose risks to patient safety.

Address Labelling, Packaging, and Material Management Concerns: The identification of labelling errors by 13% of respondents, packaging issues by 4% of respondents, and material mix-ups by 3% of respondents underscores the need for meticulous attention to detail in these areas. Manufacturers should focus on ensuring accurate and clear product labelling, robust packaging practices, and proper material management protocols to minimize the risk of errors and ensure product integrity.

Maintain Sterility Throughout Manufacturing: With 3% of respondents highlighting the importance of maintaining sterile conditions, manufacturers must prioritize stringent measures to uphold sterility throughout the manufacturing process. This includes implementing appropriate protocols, equipment, and training to prevent contamination and associated risks.

In conclusion, manufacturers should focus on the key areas identified by respondents: enhancing process control, adhering to QMS standards, validating device design and software, addressing labelling and packaging concerns, maintaining sterility, and mitigating material mix-ups to prevent recalls and ensure product quality and safety. By implementing these recommendations, manufacturers can mitigate risks, enhance patient safety, and uphold public trust in their products.

5.2.2 Recommendation on FDA Approval pathways:

Key Recommendation	Details	Proportion of Respondents (%)
Reassess Criteria for Substantial Equivalence	Enhance scrutiny within the 510K Premarket Notification process to ensure robust safety standards.	41%
Strengthen General Controls	Address systemic issues and improve overall compliance with regulatory standards.	25%
Prioritize Stringent PMA Requirements for High-Risk Devices	Implement stringent requirements within the PMA process to mitigate risks associated with high-risk devices.	11%
Address Mixed Approvals Concerns	Establish a consistent regulatory framework for evaluating devices with multiple approval pathways.	6%
Identify Additional Areas for Regulatory Enhancement	Continuously evaluate and refine the FDA regulatory framework to address emerging concerns and ensure safety.	17%

Table 10: Recommendation for FDA Approval pathways

Based on the insights gathered from respondent feedback, several key recommendations can be made as shown in table-10 to strengthen the FDA regulatory framework and mitigate the risk of future recalls within the orthopaedic knee implant domain. Firstly, there is a pressing need to reassess the criteria for substantial equivalence and enhance scrutiny within the 510K Premarket Notification process, as highlighted by the substantial proportion of 41% respondents. This requires tightening regulations to ensure robust safety standards are met prior to market clearance,

thus reducing the likelihood of recalls stemming from inadequacies in demonstrating device safety and effectiveness. Additionally, strengthening general controls, as advocated by 25% of respondents, is crucial for addressing systemic issues and improving overall compliance with regulatory standards. Prioritizing stringent requirements within the PMA process, particularly for high-risk medical devices, as emphasized by 11% of respondents, is essential to mitigate risks associated with novel or high-risk devices and minimize the occurrence of recalls. Furthermore, addressing concerns related to mixed approvals, identified by a smaller subset of 6% of respondents, is imperative to establish a consistent and robust regulatory framework that effectively evaluates the safety and efficacy of devices subject to multiple approval pathways. Lastly, the identification of additional areas for regulatory enhancement by 17% of respondents underscores the need for ongoing evaluation and refinement of the FDA regulatory framework to address emerging concerns and ensure patient safety. By implementing these recommendations, regulatory authorities can strengthen oversight, mitigate recall risks, and uphold patient safety standards within the orthopaedic knee implant domain.

5.2.3 Improvement suggestions on current orthopaedic knee implant system:

Key Area	Recommendation	Details
Automation	Adopt automation where possible	Utilize automation to enhance efficiency and effectiveness across all stages of the product lifecycle, reducing human error and improving precision.
Quality Control Measures	Strengthen quality control measures	Implement rigorous quality checks and inspections throughout the product lifecycle to ensure product consistency and prevent defects.
Handling Recalls	Establish separate recall management teams	Create dedicated teams to handle recalls and implement corrective actions to prevent recurrence.
Clinical Trials	Improve clinical trials	Ensure comprehensive and thorough clinical testing to validate product safety and effectiveness.
Regulatory Oversight	Enhance regulatory oversight	Strengthen regulations, especially in highly competitive and dynamic industries, to ensure thorough compliance and risk management.

Collaboration	Promote collaboration between industry, academia, and regulatory agencies	Foster a culture of precision, continuous improvement, and risk management through collaboration.
Cooperation with SMEs	Enhance cooperation with small and medium-sized enterprises (SMEs)	Provide better information and monitoring from governing bodies to ensure comprehensive oversight throughout the product lifecycle.
FDA Approval Process	Refine FDA approval process	Incorporate principles from ISO 14971 and address risk and lifecycle approaches effectively.
Manufacturer QMS	Improve Quality Management Systems (QMS)	Strengthen QMS to ensure thorough compliance and effective risk management throughout the product lifecycle.
Post-Market Surveillance	Strengthen post-market surveillance	Enhance monitoring and reporting to identify potential issues early on and ensure ongoing product safety and effectiveness.
Clinical Evidence Requirements	Improve clinical evidence requirements	Ensure robust and comprehensive clinical trials to support product safety and effectiveness.
Post-Market Monitoring	Enhance post-market monitoring	Implement effective monitoring systems to track product performance and safety in the market.

Table 11: Improvement suggestion on current system

Based on the diverse perspectives provided by respondents, several recommendations can be made as shown in table-11 to improve the current medical device landscape and prevent orthopaedic knee implant device recalls in the future. Firstly, there is a need to enhance cooperation with small and medium-sized enterprises (SMEs) and provide better information and monitoring from governing bodies to ensure comprehensive oversight throughout the product lifecycle. This includes refining the FDA approval process and manufacturer Quality Management Systems (QMS) to incorporate principles from ISO 14971 and address risk and lifecycle approaches effectively. Additionally, strengthening post-market surveillance, clinical evidence requirements, and regulation, particularly in highly competitive and dynamic industries, is essential for ensuring thorough compliance and identifying potential issues early on. Establishing separate teams to handle recalls and implement corrective actions, enhancing regulatory oversight, and promoting

collaboration between industry, academia, and regulatory agencies are crucial steps towards fostering a culture of precision, continuous improvement, and risk management within the medical device landscape. Furthermore, strengthening quality control measures, improving clinical trials and post-market monitoring, and adopting automation where possible are necessary to enhance efficiency and effectiveness across all stages of the product lifecycle. By implementing these recommendations, stakeholders can work towards preventing orthopaedic knee implant device recalls and ensuring patient safety and product effectiveness in the future.

5.3 Conclusion:

The survey findings provide comprehensive insights into various aspects of orthopaedic knee implant device manufacturing, regulatory oversight, and clinical requirements, as perceived by respondents within the industry. Manufacturer defects emerge as the primary concern, with a significant majority of respondents identifying them as the main contributors to orthopaedic knee implant recalls. This underscores the critical need to address issues within the manufacturing process, such as production errors, design flaws, and quality control lapses, to ensure the reliability and safety of orthopaedic knee implant devices. Strengthening quality control measures and implementing robust design validation protocols are paramount to minimize the risk of defects and subsequent recalls. Furthermore, concerns are raised regarding the lack of strict FDA regulation, with respondents highlighting potential inadequacies in regulatory oversight and enforcement. Strengthening regulatory measures is imperative to mitigate risks associated with orthopaedic knee implant devices and enhance patient safety. Additionally, insufficient clinical studies are identified as a significant contributor to recalls, emphasizing the importance of robust clinical research in evaluating device efficacy and safety. Hospital-related issues, process control, labelling errors, software-related issues, device design, packaging practices, sterility maintenance, and material management are also highlighted as contributing factors to recalls by respondents. Addressing these multifaceted challenges requires comprehensive efforts across the manufacturing process to ensure product quality and safety standards are upheld. The data also sheds light on the FDA approval processes and the frequency of recalls, indicating concerns about certain stages, particularly the 510K Premarket Notification Process. There is a clear need for targeted interventions and regulatory reforms to strengthen oversight and safeguard patient safety throughout the medical device approval lifecycle. Moreover, the mixed sentiment regarding the effectiveness of the current regulatory framework underscores the necessity for ongoing regulatory oversight, continuous improvement efforts, and stakeholder engagement to address emerging challenges and enhance patient safety within the orthopaedic knee implant device industry.

In conclusion, proactive measures are essential to address perceived inadequacies, uncertainties, and multifaceted challenges within the orthopaedic knee implant device industry. By prioritizing regulatory reforms, continuous improvement efforts, and stakeholder engagement, regulatory authorities and manufacturers can work towards enhancing patient safety, minimizing the risk of recalls, and upholding product quality standards, ultimately benefiting public health and well-being.

6 REFERENCES

Awasthi, D.P. and Stanick, J. (2022) 'The Rise of Global Medical Technology. An Overview of the Market and Trends'. *IQVIA Medtech*.

Commissioner, O. of the. (2021) *Classification of Products as Drugs and Devices and Additional Product Classification Issues*. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/classification-products-drugs-and-devices-and-additional-product-classification-issues (Accessed: 17 December 2023).

Day, C.S. *et al.* (2016) 'Analysis of FDA-Approved Orthopaedic Devices and Their Recalls'. *JBJS*, 98(6), pp. 517–524.

DeRuyter, M.T. *et al.* (2023) 'Risk of Recall for Total Joint Arthroplasty Devices Over 10 Years'. *The Journal of Arthroplasty*, 38(8), pp. 1444–1448. DOI: 10.1016/j.arth.2023.01.068.

Drugwatch (2023) *Knee Replacement Recalls | Stryker, Zimmer & DePuy Knee Recalls*. *Drugwatch.com*. Available at: https://www.drugwatch.com/knee-replacement/recalls/ (Accessed: 19 May 2024).

Fargen, K.M. *et al.* (2013) 'The FDA Approval Process for Medical Devices: An Inherently Flawed System or a Valuable Pathway for Innovation?' *Journal of Neurointerventional Surgery*, 5(4), pp. 269–275.

FDA, C. for D. and R. (2021) 'What Is a Medical Device Recall?' *FDA*. Available at: https://www.fda.gov/medical-devices/medical-device-recalls/what-medical-device-recall (Accessed: 11 October 2023).

Health, C. for D. and R. (2021) 'What Is a Medical Device Recall?' *FDA*. Available at: https://www.fda.gov/medical-devices/medical-device-recalls/what-medical-device-recall (Accessed: 19 May 2024).

Hirschmann, M.T. and Müller, W. (2015) 'Complex Function of the Knee Joint: The Current Understanding of the Knee'. *Knee Surgery, Sports Traumatology, Arthroscopy*, 23, pp. 2780–2788.

HSS (2020) *Knee Revision: When Your Knee Replacement Must Be Replaced*. *Hospital for Special Surgery*. Available at: https://www.hss.edu/condition-list_knee-revision.asp (Accessed: 19 May 2024).

Long, P.H. (2008) 'Medical Devices in Orthopedic Applications'. *Toxicologic Pathology*, 36(1), pp. 85–91.

Munn, J.S. *et al.* (2023) 'Dissatisfaction with Total Knee Arthroplasty at 1 Year Post Surgery Can Be Predicted Using a Short Questionnaire Early in the Recovery Process'. *The Journal of Arthroplasty*, 38(8), pp. 1504–1509.

Ortho Medical Device Recalls. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm (Accessed: 2 April 2024).

Orthoinfo (2024) *Total Knee Replacement - OrthoInfo - AAOS*. Available at: https://www.orthoinfo.org/en/treatment/total-knee-replacement/ (Accessed: 19 May 2024).

Pande, S. and Dhatrak, P. (2021) 'Recent Developments and Advancements in Knee Implants Materials, Manufacturing: A Review'. *Materials Today: Proceedings*, 46, pp. 756–762.

Pellerin, C., Adamson, M. and Janney, C. (2020) *Recall Rates of Total Knee Arthroplasty Devices Are Dependent on the FDA Approval Process. Cureus. 12 (8): E9744*.

Pellerin, C., Panchbhavi, V. and Janney, C.F. (2018) 'An Analysis of Foot and Ankle Device Recalls by the Food and Drug Administration.' *Cureus*, 10(8), p. e3123. DOI: 10.7759/cureus.3123.

Peters, W., Pellerin, C. and Janney, C. (2020) 'Evaluation of Orthopedic Hip Device Recalls by the FDA from 2007 to 2017'. *Biomedical Instrumentation & Technology*, 54(6), pp. 418–426.

Purnama, A. and Drago, D. (2019) *FDA Regulatory Pathways for Medical Devices*. TOPRA.

Ramakrishna, S. *et al.* (2015) *Medical Devices: Regulations, Standards and Practices*. Woodhead Publishing.

Samuel, A.M. *et al.* (2016) 'How Do Orthopaedic Devices Change After Their Initial FDA Premarket Approval?' *Clinical Orthopaedics and Related Research*, 474(4), pp. 1053–1068. DOI: 10.1007/s11999-015-4634-x.

Thirumalai, S. and Sinha, K.K. (2011) 'Product Recalls in the Medical Device Industry: An Empirical Exploration of the Sources and Financial Consequences'. *Management Science*, 57(2), pp. 376–392.

Turney, S. (2022) *Chi-Square Goodness of Fit Test | Formula, Guide & Examples*. *Scribbr*. Available at: https://www.scribbr.com/statistics/chi-square-goodness-of-fit/ (Accessed: 19 May 2024).

Vajapey, S.P. and Li, M. (2020) 'Medical Device Recalls in Orthopedics: Recent Trends and Areas for Improvement'. *The Journal of Arthroplasty*, 35(8), pp. 2259–2266. DOI: 10.1016/j.arth.2020.03.025.

Van Norman, G.A. (2016) 'Drugs, Devices, and the FDA: Part 2: An Overview of Approval Processes: FDA Approval of Medical Devices'. *JACC: Basic to Translational Science*, 1(4), pp. 277–287.

Wang, Yang. *et al.* (2022) 'Investigation and Analysis of Four Countries' Recalls of Osteosynthesis Implants and Joint Replacement Implants from 2011 to 2021'. *Journal of Orthopaedic Surgery and Research*, 17(1), p. 443. DOI: 10.1186/s13018-022-03332-w.

7 APPENDIX

7.1 Survey Questionnaire form:

Evaluation of Orthopedic Knee Implant device FDA recalls (From MFGR to Market release)

The survey will take approximately 5 minutes to complete. The purpose of this research is to evaluate Orthopedic knee implant product recalls which will focus on identifying and analyzing the common factors that contribute to product recalls in the orthopedic industry. This may involve studying orthopedic Knee implant products such as femoral components, tibial components, polyethylene implants, inserts, sleeves, spacers, etc. By examining factors like design flaws, material issues, manufacturing defects, regulatory compliance, regulatory approval pathway and human factors, post market monitoring which will give insights to find out main contributors for orthopedic knee implant recalls in the orthopedic field as well as this study will evaluate existing Ortho medical device industry recall trend, Medical device industry standard, current FDA regulatory frame work for recalls and discover if current system is effective or improvement is required.

I will securely store this data until the end of the year, when the research period is over.

I respect your trust and will protect your privacy and therefore will never sell or share personal data with any third parties. All answers will be strictly confidential.

If you have any questions or change of mind, please feel free to contact me
via thennarasu.selvaganapathi@student.griffith.ie

1. Do you agree to participate in the survey? *

- ◯ Yes
- ◯ No

2. Do you understand the purpose of this reserach? *

- ◯ Yes
- ◯ No

3. What type of organization do you work with? *

Enter your answer

4. What Medical device product do you work with?

Enter your answer

5. What is your experience in Orthopedic knee implants products ?

- ◯ <2 years
- ◯ 2 to 5 years
- ◯ >5 years

6. Which of the below area's do you work in?

- ○ Regulatory Affairs
- ○ Quality Engineering
- ○ Product Development
- ○ Product Compliance
- ○ R&D engineering
- ○ Sustaining engineering
- ○ Manufacturing engineering
- ○ Clinical engineering
- ○ Validation engineering
- ○ Other

7. Are you familiar with Medical device Recalls?

- ○ Yes
- ○ No

8. Based on your experience, what do you think main contributors for Ortho-recalls?

- [ ] Manufacturer defects
- [ ] Lack of strict FDA regulation
- [ ] Lack of Clinical study
- [ ] Hospital
- [ ] Other

9. Do you think the current system (Medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30 , ISO 14971:2019- Medical devices Risk Management and Regulatory framework- 510K & PMA Approval) in place effective?

- ◯ Yes
- ◯ No
- ◯ Maybe

10. Do you think the current system (Medical Device Quality System Regulations)-21CFR Part 820, Design control- FDA 21 CFR 820.30 , ISO 14971:2019- Medical devices Risk Management and Regulatory framework- 510K & PMA Approval)) in place has some gaps and needed improvement?

- ◯ Yes
- ◯ No
- ◯ Maybe

11. What area do you think Manufacturer should focus in order to prevent recalls?

- [ ] Device design
- [ ] Process design
- [ ] Process control
- [ ] Labelling error
- [ ] Packaging
- [ ] Material mix up
- [ ] Software
- [ ] Sterility
- [ ] QMS Standard
- [ ] Other

12. What area do you think Manufacturer recalls happens most?

- [ ] Device design
- [ ] Process design
- [ ] Process control
- [ ] Labelling
- [ ] Packaging
- [ ] Sterility
- [ ] Software
- [ ] Material mix up
- [ ] Other

13. What area do you think FDA regulatory framework should be tighten in order to prevent recalls?

- ( ) 510K Premarket notification Process
- ( ) PMA(Premarket Approval) Process
- ( ) General Controls
- ( ) Mixed Approvals
- ( ) Other

14. In what FDA approval process do you think recalls happens most?

- [ ] 510K Notification Process
- [ ] PMA(Premarket Approval) Process
- [ ] Mixed approvals
- [ ] General controls
- [ ] Other

15. What are the challenges you see in current system?

Enter your answer

16. In your opinion, are there any specific changes required in current Medical device like QMS standard , FDA regulatory frame work, Clinical study requirement, Hospital usage?

Enter your answer

17. In your opinion, what improvement is required in current system (Whole process) in order to prevent Ortho knee implant device recalls in future?

Enter your answer

18. Is there anything else you would like to add regarding Ortho knee implant medical device recalls that was not covered in the survey?

Enter your answer

7.2 Ethic Application & Declaration form

Innopharma education

GRIFFITH COLLEGE

Ethics Application & Declaration Form

DISSERTATION TITLE: Evaluation of Orthopaedic Knee implant device FDA Recalls (From Manufacturing to Market release): 2018-2023.

RESEARCHER'S NAME: Thennarasu Selvaganapathi

PROGRAMME OF STUDY: MSC Medical device technology and Business

SUPERVISOR'S NAME: Aine Behan

DECLARATION:
The information in this application form is accurate to the best of my knowledge. I undertake to abide by the principles outlined by Innopharma/Griffith College ethics policy in my research dissertation. I confirm that I have completed a full ethics assessment for my research dissertation as per the college guidelines. I will not begin my primary research until such approval from my supervisor and/or ethics Committee has been obtained.
I pledge to carry out my research according to the Innopharma/Griffith College academic integrity standards. Any results presented in my dissertation will be from my own, original research, I will reference and/or acknowledge any material or sources used in its preparation and I will not plagiarise the work of anyone else.

For Student:

STUDENT SIGNATURE: S. Thennarasu

DATE: 08 Nov 2023

The research contained within this research dissertation proposal has been approved.

For Supervisor:
Ethics Committee Approval Required: Yes ☑ No ☐

SUPERVISOR SIGNATURE:

DATE: 9/11/23

For Ethics Committee (if required):
Ethics Committee Approval Given: Yes ☐ No ☐

ETHICS COMMITTEE MEMBER SIGNATURE:

DATE:

NOTE: Supervisors are responsible for ensuring their students fill in this form correctly and that all ethical areas have been considered.

SECTION 1: DESCRIPTION OF RESEARCH STUDY

1.1 Purpose and objectives of research *[300 words maximum/ use literature review findings to guide]*

The purpose of this research is to evaluate Orthopaedic knee implant product recalls, which will focus on identifying and analysing the common factors that contribute to product recalls in the orthopaedic industry. This may involve studying orthopaedic Knee implant products such as femoral components, tibial components, polyethylene implants, inserts, sleeves, spacers, etc. By examining factors like design flaws, material issues, manufacturing defects, regulatory compliance, regulatory approval pathway and human factors, post market monitoring which will give insights to find out main contributors for orthopaedic knee implant recalls in the orthopaedic field as well as this study will evaluate existing Ortho medical device industry recall trend, Medical device industry standard, current FDA regulatory frame work for recalls and discover if current system is effective or improvement is required.

Objective#1: Identify current trend of orthopaedic knee implant device recalls.
Objective#2: Investigate factors that are contributing to orthopaedic knee implant device recalls.
Objective#3: Discover if current system* is effective or improvement is required.

*Medical device standard-21CFR Part 820, Design control- FDA 21 CFR 820.30 and Sub-clause 4.4 of ISO 9001, ISO 14971:2019- Medical devices Risk Management and regulatory framework.

1.2 Research methodology: *[300 words maximum/ detail how you will acquire your primary data (focus groups/interviews/online surveys etc). Proposed questions for questionnaires and/or interviews must be included in the appendix].*

A mono-method approach will be used for the research strategy, which will include quantitative data analysis. A survey with qualified participants who have prior experience working in the medical device industries will be part of the core data gathering design. The participant is employed as a 'Quality Engineer, R&D engineer, Sustaining engineer, Regulatory specialist, Clinical Engineer, Manufacturing engineer' in a top ranking multi-national medical device company.

The survey design will consist of both open and closed-ended questions in order to perform quantitative analysis. It will be created on Microsoft Forms and will be distributed online through email, WhatsApp and LinkedIn to professionals who were employed in the medical device industry all over the world. The survey will be structured to gather additional information from individuals specifically with experience in the Orthopaedic sector. The format of the closed-ended questions in the survey will be 'Yes or No' where the participants can provide one answer, or in the form of multiple-choice questions, where all options that apply can be selected. The open-ended questions will allow for the participants to type their opinion or perspectives into the open space provided.

The ideal sample size 61 was calculated by using survey monkey website calculator (Figure-1). The global Orthopaedic knee implant expert population size is not exactly known and estimated roughly 100 globally based on top 10 Orthopaedic companies. The confidence level is maintained at 95% and sampling error is maintained at 8%. Since the study will be conducted globally in a short period of time, the sampling error can be possible in the research study. Thus, it is increased margin of error from 5 to 8%.

Research Methodology	Chosen Action
Philosophy	Positivism, Pragmatism
Research Approach	Abduction
Methodological choice	Mono method - Quantitative
Research Strategy	Online Survey
Time Horizon	Cross sectional
Technique	Questionnaire
Sampling technique	Probability Sampling

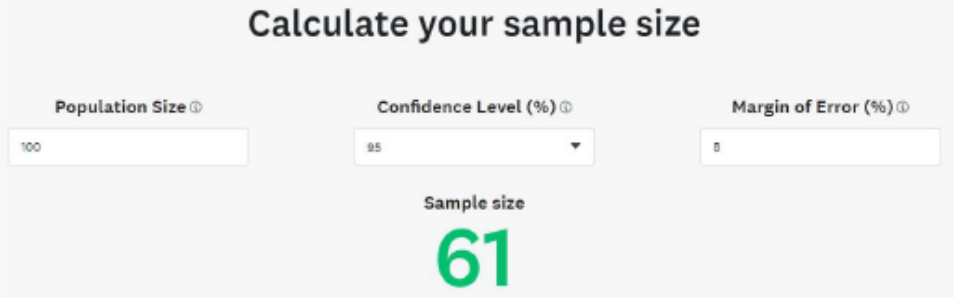


Figure 1: Survey monkey website calculator

SECTION 2: POSSIBLE ETHICAL ISSUES

Answer 'yes' or 'no' to the following questions.

SUBJECT MATTER

Does the research proposal involve:

Research into specific company activities that would be deemed sensitive or confidential	Yes No✓
Research into politically and/or racially/ethnically and/or commercially sensitive areas	Yes No✓
Sensitive, personal, professional or corporate issues	Yes No✓

RESEARCH PROCEDURES

Does the research proposal involve:

Research that might damage the reputation of companies or participants	Yes No✓
Research that may negatively affect the reputation of Griffith College/Innopharma	Yes No✓
Use of personal records without consent	Yes No✓
Use of company data without consent	Yes No✓
The offer of any inducements to participate	Yes No✓
Audio or visual recording without consent	Yes No✓
Using a language other than English	Yes No✓

PARTICIPANTS

Does the research proposal involve:

People who are not competent and/or fluent in English	Yes No✓
Does your research group include any of the following vulnerable groups	Yes No✓

(Adults with psychological impairments; Adults with learning difficulties; Adults under the protection/control /influence of others (e.g. in care/prison); Relatives of ill people (e.g. parents of sick children); Hospital or GP participants recruited in a medical facility; persons under the age of 18)

If you have answered NO to ALL questions, please go straight to Section 4.

If you have answered YES to ANY question in SECTION 2, you must fill in SECTION 3.

SECTION 3: STEPS TAKEN TO AVOID ETHICAL ISSUES

[Only fill in this section if you answered YES to ANY of the questions in Section 3. For example, if you answered yes to including participants who are not fluent in English, you might put forward a plan that offers your survey in two languages to take this into account. Another example could be a study where the researcher wants to include information about the care received by children with a long-term condition but it would not be ethical to approach the children directly but it might be acceptable to instead ask parents questions about their child's care. If these plans are acceptable to your supervisor, you may not need to apply for ethical approval from the Ethics Committee].

3.1. If your ethics relates to ***Subject Matter***, outline your action plan to work around any sensitive issues.
3.2. If your ethics relates to ***Research Procedures***, outline your action plan to deal with possible ethical issues in your research procedures.
3.3. If your ethics relates to ***Participants***, outline how you will protect vulnerable persons or those that do not have English as their first language.

SECTION 4: ABOUT YOUR PARTICIPANTS

4.1. Outline your participant profile and why you have chosen them for this study *[Do not provide names except where it is deemed impossible to conceal identity].*
Participant profile would be Quality engineer, Regulatory engineer, Compliance officer, Research Development engineer, sustaining engineer & Manufacturing engineer having more than 3 years' experience from reputed Orthopaedic companies Stryker, Depuy Synthes, Zimmer Biomet, Smith & Nephew, Arthrex, Globus Medical, Orthofix, Aesculap, ConMed Corporation, DJO Global, Medacta etc.

4.2 How do you plan to gain access to/contact/approach your participant(s).
Plan to approach participants through Email, LinkedIn, WhatsApp's, Instagrams, Regulatory Affairs Professionals Society (RAPS), The Organisation for Professionals in Regulatory Affairs (TOPRA) and other professional networks.

SECTION 5: INFORMATION, CONSENT AND CONFIDENTIALITY

5.1 **Participant Information Letter (PIL) for participants**

[You must submit an information letter for participants with this application, as part of your appendices document. For online surveys, it is sufficient to include a paragraph summarising and explaining the purpose of the research at the beginning of the survey. In all other research e.g. interviews, phonecalls, a PIL should be provided to each participant before they are asked for their consent to take part. A template PIL is available in Moodle].

Please confirm below that your information letter covers:

Description of the research topic and method	Yes No ✓
Details of what participation will involve	Yes No✓
Rights to anonymity	Yes No ✓
Confidentiality	Yes No✓
Rights to withdraw from the research	Yes No ✓
The contact details of the researcher and supervisor (if necessary)	Yes No ✓

5.2 **Informed Consent Form (ICF) for participants**

[Informed consent is required for most research. For online surveys, it is sufficient to get the participant to tick two boxes at the beginning of the survey – one to state they understand the research and one to give consent. In all other research e.g. interviews, phonecalls, a signed consent form is required. If the data is gathered online e.g. zoom, a signed consent form can be scanned and sent to the researcher. A template ICF is available in Moodle. The signed ICFs, along with the surveys, audio files or interview notes etc. must be stored in the primary data folder on moodle and can be accessed by Innopharma staff for the purposes of verifying the authenticity of the research carried out and the data collected].

Please indicate below if your research requires a signed consent form by selecting the relevant option only:

Yes: my research requires signed consent and I have attached an ICF in the appendices of my application.
No: my research study involves an online survey only and/or does not require signed consent ✓

SECTION 6: STORAGE OF DATA

[Please ensure that you are abiding by GDPR and the national Data protection laws https://www.hrb.ie/funding/gdpr-guidance-for-researchers/gdpr-and-health-research/).

The student is responsible for storage of data and this will be handed over to the college in an electronic format as part of the thesis submission i.e. primary data and completed ICFs where applicable will be added to the primary data folder on moodle. The rationale is to keep data as long as it is still useful and there is an intention to use it further for research so if this is not the case then this can be stipulated here and a shorter retention period given.]

6.1. How will you store the research data and for how long? How will you manage data protection issues?

The research data will be stored securely in password protected laptop and it is accessed only by me and no other person has access.it will be kept safely during course of my research and then it will be handed over to Griffith college and data can be destroyed within 2 years of completing my qualification.

SECTION 7: NON-DISCLOSURE AGREEMENT & STUDENT CONSENT

7.1 **Non-Disclosure Agreement (NDA)**
Will the final dissertation contain any information pertaining to any source what would warrant the use of a Non-Disclosure Agreement (NDA) e.g. industry-based research?

Yes No✓

7.2 **Student consent**
If a Non-Disclosure Agreement (NDA) is not required, does the student consent to allow their completed dissertation to be held/published by Innopharma/Griffith College?

Yes✓ No

SECTION 8: RECORDING AND RETENTION OF DISSERTATION VIVA

8.1 **Viva Recording**
The Dissertation viva will be recorded. This recording may be used to facilitate assessment by Innopharma staff, a third reader if necessary and/or if requested by the external examiner for the Programme. The recording will be held in line with current GDPR guidelines and will not be made publicly available.

SECTION 9: DOCUMENT CHECKLIST

NOTE: Applicants must attach the following documents in electronic format to the appendix.

Which documents are added to the appendix? Please tick N/A if not applicable:

9.1 Participant Information Letter (PIL) for participant	Yes N/A✓
9.2 Informed Consent Form (ICF) for participant	Yes N/A✓
9.3 Questions/survey for interviewees/focus groups etc *(can be in draft form)*	Yes✓ N/A
9.4 Any other documents e.g. Non-Disclosure Agreement	Yes N/A✓

I confirm that this application is complete and all required documents are included in the appendix.

For Student:

STUDENT SIGNATURE: 

DATE: 08 Nov 2023