A Comparative Study of the Regulatory Requirements in European Union and United States for Medical Devices.

Research dissertation presented in partial fulfilment of the requirements for the degree of MSc in Pharmaceutical Business and Technology (QQI)

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May 2023

CANDIDATE DECLARATION

Candidate Name: Neenu Suresh

I certify that the dissertation entitled:

"A comparative study of the regulatory requirements in European Union and United States for Medical Devices" submitted for the degree of MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to the work of others, due acknowledgment is given.

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DEDICATION

I dedicate my whole work to my God Almighty for his grace and my family for their relentless support.

ACKNOWLEDGEMENT

I am extremely thankful to my God for his grace and blessings that he has bestowed upon me in completing my Master program.

My sincere gratitude goes to my father Suresh, my mother Sheela and my sister Neethu and my brother Binoy for constantly supporting and encouraging me through the whole journey. I could not have done this Masters without them.

I would like to express my special thanks of gratitude to my supervisor Cecilia Vasquez-Robinet for her support and guidance and my professors at Griffith College Dublin in the entire completion of my project.

I would also thank all the participants who showed their willingness to participate in the survey and provide valuable information.

ABSTRACT

BACKGROUND: There were many debates concerning the regulatory requirements in the United States and European Union for medical device in terms of quality, efficacy and safety. The aim of the study is to compare the regulatory requirements for medical devices in the European Union and United States. This study looks at the differences between these two regulations, post marketing surveillance tools used, reasons for medical device failures after the approval from the regulatory authority and finally the areas of regulations that requires improvement. The purpose of the medical device regulations is to constantly provide safe, effective and efficacious medical devices and taking care of the public health.

METHODS: Research was conducted using scholarly articles, peer-reviewed journals from PubMed and Google Scholar. Most recent articles of less than 10 years were used to conduct literature search. A survey was also conducted using a questionnaire which comprised of 26 questions with 40 responses which consisted of 5 sections with closed and open-ended questions.

FINDINGS: There were not that many differences in the 2 regulations other than differences in the execution of the different processes for example in classification and approval pathway of the regulations. Post marketing surveillance enhancement is another area which requires improvement. Healthcare professionals, manufacturers and patients must be encouraged to report any adverse effects from the devices and upload them to the database. To prevent recalls in the medical device industry the behavior of the medical devices must be observed and studied in different environments and conditions and harmonized collection events must be set up in place that is evidence based.

CONCLUSIONS: The research gives more insight to the regulatory framework of EU and US for the policymakers. Both systems have their own pros and cons. It is difficult to say that one system outweighs the other. Both the system suggested that more clinical data and quality system management are required for the effective and safe approval of devices. There must also be increased participation for adverse events reporting from various stakeholders for effective post marketing surveillance. All these contribute to reduction in medical device failures.

Keywords: Regulations, medical devices, post marketing surveillance, recalls, differences, EU, US.

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ABBREVIATIONS

CAGR- Compound Annual Growth Rate

CDRH- Centre for Devices and Radiological Health

CE- Conformité Européenne

CECP- Clinical Evaluation Consultation Procedure

CFR- Code of Federal Regulations

EMA- European Medicines Agency

EUDAMED- European Union Database on Medical Devices

EU- European Union

FDA- Food and Drug Administration

HDE- Humanitarian Device Exemption

ICRP- International Commission on Radiological Protection

IMDRF- International Medical Device Regulators Forum

IVDR- In Vitro Diagnostic Regulation

MDD- Medical Device Directives

MDR- Medical Device Regulations

PIP- Poly Implant Prothese

PMA- Pre-Market Approval

PMCF- Post-Market Clinical Follow-up

PMN- Pre-Market Notification

PSUR- Periodic Safety Update Reports

SSCP- Summary of Safety and Clinical Performance

UDI- Unique Device Identification

US- United States

WHO- World Health Organisation

CHAPTER 1: INTRODUCTION

1. INTRODUCTION

1.1 MEDICAL DEVICE INDUSTRY

Medical devices are playing a pivotal role in today's healthcare industry. Medical devices must be of excellent quality, easily accessible, affordable, and appropriate for healthier human population. It is used by laypersons to clinicians and other paramedics working in advance medical facilities for diagnosis, treatment, mitigation, and palliative care. According to World Health Organisation (WHO), there are approximately 2 million medical devices in the global market (WHO, 2023).

According to Food and Drug Administration (FDA), a medical device is defined as an instrument, apparatus, machine, implant, in vitro reagent or other similar or related article, including a component part, or accessory which is (i) recognised in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (ii) intended for the 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 (iii) 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 (iii) 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 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 (Health, 2021a).

The statistics provided by the Precedence Research has shown the global market for medical devices in 2021 was valued at US$ 550 billion in 2021 and by 2030 this value is expected to increase US$ 850 billion, with a compound annual growth rate (CAGR) of 5.5 %. The huge demand for the innovations in the medical device industry is to meet the unmet clinical need in the healthcare sector. The advancement in technology has also contributed to the innovation in medical devices (Precedence Research, 2023).

The predominant industries manufacturing medical devices are in US and Europe. The medical device industry is also shifting its development to China, which will gain prominence in the near future. Statistics suggests that the highest revenue in medical

devices is generated in US when compared globally. The largest segment in the global market for medical devices is cardiology devices. Diagnostic imaging devices held the second position in the global market (Statista, 2023).

1.2 HISTORY OF MEDICAL DEVICE REGULATIONS

As medical device ranges from simple devices such as tongue depressors to complex devices like coronary stents, these must be regulated according to their level of risks. Medical devices must be properly regulated for its safety and effectiveness as these are developed for the welfare of humans. They are regulated by the appointed regulatory authority of a country.

There was no or little legislation for medical devices before World War II as the medical devices were not in demand during that period and did not offer considerable risk to the users. During those days the equipment which posed risk was X-ray due to its emission of harmful ionizing radiation. Based on the recommendations of International Commission on Radiological Protection (ICRP 51) to protect the workers from exposure to ionising radiation, several countries adopted and introduced the regulations and took measures to shield the source of radiation. Subsequently, another risk identified was infections due to improper sterilisation of devices used for injections and infusions which imposed legislations to control the marketing of sterile medical devices (Higson, 2001, p. 2-6).

The first medical device legislation in its proper form was put forward by US which is the US Medical device Amendments of 1976. This legislation had to undergo several revisions and changes after criticisms resulting in the development of FDA Modernisation Act of 1997. A new era of medical device legislation was introduced in the European Union (EU) in the years 1993-1998 as European Medical Device Directives. The regulatory approach of EU was adopted and enacted by several other countries such as Canada and Australia.

1.3 REGULATORY AUTHORITIES FOR MEDICAL DEVICES IN DIFFERENT COUNTRIES

Medical devices have been regulated in different countries by its own regulatory authorities. For instance, Food and Drug Administration (FDA) regulates the medical devices in the US. In the EU, the national competent authorities of each EU member states are responsible for regulating the medical devices along with the European Medicines Agency (EMA) who are involved in the regulatory process (EMA, 2018a). Reformations are carried out in the standards and regulations by the regulatory authorities of Asian countries such as India, China, Taiwan, Japan etc (Wu *et al.*, 2016, p. 4).

Countries	**Regulatory Authority**
China	China Food and Drug Administration
Japan	Pharmaceutical Medical Devices Agency
Taiwan	Food and Drug Administration of the Ministry of Health and Welfare
Singapore	Health Sciences Authority
India	Central Drugs Standard Control Organisation
South Korea	Ministry of Food and Drug Safety

Table 1. Regulatory Authorities of Countries

The international harmonization of regulations of medical devices is accelerated by an organisation named International Medical Device Regulators Forum (IMDRF) which was established in 2011.

1.4 PURPOSE OF THE RESEARCH

The purpose of the research is to compare the regulatory requirements of medical devices in the EU and US as medical device is a growing sector of the healthcare industry. This study helps in understanding which system has better regulations for medical devices as these regulatory requirements plays a vital role in ensuring safety and quality of medical devices during its manufacturing and distribution.

This study is aimed:

- To find the differences involved in the regulations for medical devices in EU and US.

- To understand the tools used for post-marketing surveillance for different classes of medical devices in EU and US.
- To evaluate which areas of improvement, need to be focused.
- To analyze the reasons for medical device failures after the approval for marketing in EU and US.

1.5 SMART OBJECTIVES

Specific – This research focuses on regulatory aspects of the medical devices in 2 different key players internationally in the health care industry which are Europe and US.

Measurable- Through secondary research which involves literature review and primary research through questionnaires helps in measuring the differences of both regulations, medical device failures after complying with regulations.

Attainable- Through this research areas of improvements could be identified. All the outcomes for the 4 different objectives could be met.

Relevant- Medical devices sector is a growing industry. Regulatory requirements are essential for safeguarding public health. This research identifies the setbacks in both the regulations and determines the domain to be focused for improvement.

Time - This research takes approximately 3 months to complete.

1.6 STRUCTURE OF THE RESEARCH

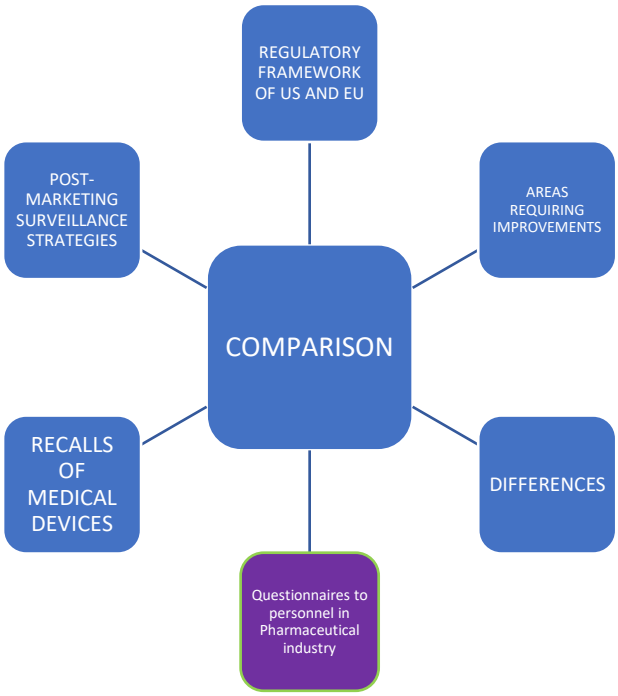

Figure 1. Conceptual Framework

CHAPTER 2: LITERATURE REVIEW

2. LITERATURE REVIEW

2.1 INTRODUCTION

Literature review is the collection, modifying and finding gaps in the previous research. The objectives in this research can be addressed with the help of performing literature review. When carrying out a research, literature search is imperative in all the research disciplines. This chapter deals with information obtained from different peer reviewed journals and discuss about the overview of regulatory framework, classification of medical devices, regulatory approval pathway used, post marketing surveillance tools, medical device recalls and areas of improvement in the EU and US. It also discusses about the new Medical Device Regulations (MDR) and In Vitro Diagnostic Regulations (IVDR).

2.2 OVERVIEW OF REGULATORY FRAMEWORK IN THE EU

The EU is currently witnessing major changes in its regulatory framework after the implementation of new regulations in the year 2017. Until 2017, there were 3 Medical Device Directives (MDD) for medical devices which were:

- General medical devices- 93/42/EEC
- Active implantable devices- 90/385/EEC
- *In vitro* diagnostic medical devices- 98/79/EEC

The MDD underwent multiple revisions between the year 1998 and 2007 to keep in pace with the novel technologies and improved surveillance after the marketing of the devices. These directives did not require stringent testing and therefore medical devices introduced led to many catastrophic failures for some of the devices (Melvin and Torre, 2019, p. 352). This motivated the regulatory authorities to replace the directives with regulations in May 2017. Regulations are applicable to all member states and must be strictly followed by all the member states in the EU. Directives are set of treaties which has certain outcomes to be achieved and it is the discretion of each member states to convert the directives into a state law. The new regulations include:

- Regulation (EU) 2017/745 Medical Device Regulation with effect from 26 May 2021.
- Regulation (EU) 2017/746 In vitro diagnostic medical devices with effect from 26 May 2022 (European Commission, 2023).

These new regulations allow more transparency and public safety. It also reinforces innovation and equip to face upcoming challenges in the medical device industry (Rastegayeva, 2023).

2.2.1 JOURNEY TO THE INTRODUCTION OF MEDICAL DEVICE REGULATIONS

In 2012, the European Commission proposed the revision of medical devices and in 2014, a set of amendments were put forward by the European Parliament. Subsequent discussions by all the ministers of each EU states agreed on a general approach to the regulations of medical devices. In June 2016, the MDR and IVDR was published by the European Commission, Council, and the Parliament. It was adopted in April 2017 by the European Parliament and legalised on 26 May 2017. With effect from 26 May 2021 and 26 May 2022, the MDR and IVDR are applicable respectively. The transition period is until 26 May 2024 (Vasiljeva *et al.*, 2020, p. 124).

2.3 OVERVIEW OF REGULATORY FRAMEWORK IN THE US

FDA and Centre for Devices and Radiological Health (CDRH) (a body that functions under FDA) are responsible for the regulation of medical devices in US. CDRH oversees the companies that manufacture, packs, label and imports the medical devices and also regulates the electronic products that emit radiation such as X-rays etc. According to 21 Code of Federal regulations (CFR), the manufacturers and distributors of medical devices should register with FDA where the document submission is done electronically, and this is termed as establishment registration. Every year between October 1st and December 31st the information pertaining to the registration is verified by the FDA. A registration fee is collected annually for the establishments (Health, 2022a). There are about 6000 medical devices regulated by the CDRH of FDA which are listed in the Medical Device Product Classification Database (Health, 2021b).

2.4 CLASSIFICATION OF MEDICAL DEVICES IN EU

In the EU, medical devices are classified based on the risk associated with it to the human population. There are certain factors which determine the classification of medical devices such as the duration of time of use, degree of invasiveness, and toxicity. Class I medical devices are non-invasive in general. Class IIa are non-invasive medical devices

used for channelling or storing of cells, tissues, body liquids for the introduction into the body. Class IIb medical devices changes the composition of the blood, tissues, cells or body liquids to administer into the body. Invasive devices which are used in direct contact *in vitro* with human cells or human embryos are classified under Class III which are "high risk" devices. Cardiovascular medical devices comprise 40% of the high-risk devices. There are about 22 rules to be followed for the classification of medical devices based on its intended medical purpose. A manufacturer must use these rules to determine which class their medical device falls under. It is important to classify the medical device appropriately otherwise it might lead the patient to danger (MDCG, 2021).

System	**Classification**	**Description**	**Examples**
EUROPEAN UNION	CLASS I	Simple and safe to use	Glasses, thermometers, stethoscopes
	CLASS IIa	For short term or long-term use. Low risk relatively	Catheters, infusion pumps
	CLASS IIb	Medium risk	Respirators, dialyzers
	CLASS III	High risk, surgical devices cause potential harm to patients	Cochlear implants, pacemaker

Table 2. Classification of Medical devices in EU

2.5 CLASSIFICATION OF MEDICAL DEVICES IN US

About 1700 generic medical devices have been classified by the FDA based on the level of risk each of them possesses to the patient and assigned to either of three regulatory classes. These medical devices are further grouped into 16 medical specialities known as panels. They can be found in the CFR parts 862 to 892. The regulatory market approval depends on the class under which the medical devices fall. The device classification depends on indicated and intended use for the particular device. Classification database of the FDA helps in determining the classification of the medical device. (Health, 2020).

Class I medical devices do not lead to any injury or hazard to the patients. These devices do not require scrutiny by the FDA, hence general control is adequate, and a separate evaluation is not performed by the FDA. Evaluation of safety and effectiveness is not required before its marketing. Class II devices pose greater risk than Class I and requires

special control for its regulation and requires formal scrutiny by the FDA. Class III devices can be hazardous to the patients and have the potential to impair human health. Before the launch of Class III medical devices there must be a thorough evaluation for its safety and effectiveness (Kumar Gupta, 2015 p. 6-7). Pre-clinical and clinical studies are often not required for Class I and Class II medical devices but they have to undergo the registration, manufacturing and labelling process. Certain Class III devices that have similarities to devices that are previously approved, the so-called predicate devices can be classified under Class I or Class II. Such devices do not require to undergo strict regulations for approval. Around 75% of class I devices and a minor proportion of class II devices do not require to demonstrate efficacy, safety and clinical profiles and are considered to be "exempt". They are also excluded from the standard pre-market notification (PMN) process or 510 [k] clearance. Major proportion of class II devices has to undergo PMN process, but it does not need to undergo clinical testing. As class III medical devices have potential risk, it must undergo stringent regulations prior to approval. It requires pre-market approval (PMA) process which necessitates clinical evaluation of the medical device along with the submission of the application (Van Norman, 2016, p. 278).

SYSTEM	**Classification**	**Description**	**Examples**
UNITED STATES	CLASS I (General control)	Simple and safe to use.	Tongue depressors, crutches
	CLASS II (General control and Special Control)	Complicated and have high level of risk than Class I.	Endoscopes, infusion pumps
	CLASS III (General Control and Premarket Approval)	To support and sustain the life of patients. Has potential risk than Class II.	Coronary stents, defibrillators

Table 3. Classification of Medical devices in US

2.6 REGULATORY APPROVAL IN EU

Before placing the medical devices on the market, it should undergo conformity assessment procedures to ensure its safety and performance. After the medical devices passes the conformity assessment procedure a Conformité Européenne (CE) is placed on it by the manufacturer (EMA, 2018b). After obtaining the CE mark, the medical device can be marketed. The CE mark indicates that the medical device is manufactured complying to the applicable regulatory requirements, or it has complied with the essential requirements and can be marketed anywhere across the EU without any further control. The CE mark has a validity of five years and has to be renewed afterwards (Daigle and Torsekar, 2019, p. 6-7). The conformity is assessed by the notified body. The notified body is assigned by the competent authority of each member state of the EU. The competent authority of each member state designates the notified bodies to evaluate the conformity to the type of medical device and the manufacturer can pick any notified body designated to them according to the respective medical device. The manufacturer must submit certain documents to the notified bodies (Behan *et al.*, 2017, p. 21). Class I medical devices obtain the CE mark through self-assessment procedure. Class II and Class III (higher risk devices) obtain CE from notified bodies (Ben-Menahem *et al.*, 2020, p. 1). The manufacturers of higher risk devices must submit documents pertaining to technical aspects of the devices, quality management system, inspection of the product and all aspects related to the device design and its manufacturing (Behan *et al.*, 2017, p. 21).

2.6.1 CONFORMITY ASSESSMENT BODY

Notified bodies are otherwise called conformity assessment bodies which are responsible to carry out conformity assessment procedures. They must have personnel who have expertise in clinical, administrative, scientific and technical sections and must be employed by the notified bodies. They must submit all the required documentation to the competent authority upon request including the tasks fulfilled by them, how they conducted the assessment and monitoring. They must function independently and must not be influenced by the manufacturer who has particular interest in the device or its

competitors. They must maintain confidentiality of information during its assessment activities (EUR-Lex, 2017). Most of the functions performed by the CDRH and FDA in the US is done by the notified bodies in EU.

2.6.2 CLINICAL EVALUATION CONSULTATION PROCEDURE

According to MDR Article 106, published on 11 September 2019 the EU established an independent body to evaluate the high-risk medical devices clinically with the help of expert panels in Clinical Evaluation Consultation Procedure (CECP). They provide expert opinion to the manufacturers and notified bodies. Some of the responsibilities of CECP are:

- To begin with, a manufacturer can approach the CECP for consultation and advice regarding the development of the medical device.
- In addition, CECP reviews the clinical evidence submitted by the manufacturers and the notified bodies regarding Class III implantable and Class IIb active medical devices. The clinical evidence submitted by the notified body is Clinical Evaluation Assessment Report. The manufacturer submits Clinical Evaluation Report, Summary of Safety and Clinical Performance (SSCP) and the Post-Market Clinical Follow-up (PMCF). The panel reviews the documents forwarded by the European Commission which was send to them by the notified bodies and responds within 60 days. The report will be published in the EU database on medical devices (EUDAMED).
- Thirdly, the expert panel provides advise to the regulators related to the safety and performance of the devices (Fraser *et al.*, 2020, p. 2590-2591).

2.7 REGULATORY APPROVAL IN US

The legislations for medical devices in US are controlled by Medical Device Amendments of May 28, 1976 to the Federal Food Drug and Cosmetic Act and is implemented by 21 CFR Parts 800-1299. The market authorization procedures for FDA are based on its classification are:

- PMN or 510 (k) pathway
- PMA

PMA requires the comprehensive submission of documents to the FDA. In case of PMN, manufacturers must prove that their device is substantially equivalent to the devices already placed in the market.

2.7.1 PRE-MARKET APPROVAL

Most class III devices are approved by PMA as it includes the assessment of safety and effectiveness apart from the special controls. Manufacturers must verify the application before submission to the FDA. The documents for submission include both administrative and clinical evidence sections. If any of the section is lacking, the application would be rejected and the device is considered to be adulterated. The scientific evidence section is from clinical and non-clinical research. Non-clinical research includes microbiology, immunology, toxicology and clinical research must have information on safety, effectiveness, adverse reactions, subject information and results.

2.7.2 PRE-MARKET NOTIFICATION

Mostly, class II devices are getting approval through PMN or 510[k] pathway. The device is compared with a device already on the market termed as predicate and the medical device is substantially equivalent to the predicate if the intended use and technological characteristics are the same. The device can be considered substantially equivalent even if the device has same intended use, but different technological characteristics and the FDA doesn't raise any concern about its safety or effectiveness. The manufacturer must submit the following documents while submitting application for the PMN:

- Description of the device
- Description of the predicate
- Intended use of the device. If the device has a different use from the predicate, an explanation must be provided claiming that it does not affect its safety and effectiveness.
- A comparison must be provided if the device and predicate has same technological characteristics. A summary of how both the devices are similar must be provided if they differ in technological characteristics.

Class I devices are termed as exempt devices as it does not require PMN but should undergo device listing and establishment registration (Van Drongelen *et al.*, 2015, p. 16-19).

2.7.3 DE NOVO DEVICES

Certain new devices get classified under Class III medical devices and undergo the full PMA process as they do not have a predicate to go through 510 [k] pathway. Such devices can be petitioned by the sponsor to reclassify as low or moderate risk devices which are termed de novo devices. De novo devices undergo the PMN process rather than the rigorous PMA process. These de novo devices can be a predicate for other new devices developed (Van Norman, 2016, p. 281).

2.7.4 PRE-MARKET NOTIFICATION REVIEW PROCESS

In the PMN process the sponsor has to submit the application along with the user fees to the document control centre of the CDRH. The application must consist of 2 copies, one of which should be an electronic copy of the application. If any of the 2 items (user fees or 2 copies) are not submitted by the sponsor, the CDRH holds the application and notifies the sponsor within 7 days of the application by sending a hold letter. The sponsor has to respond and submit both the requirements within 180 days after the receipt of the hold letter. If the sponsor resolves the issue, the CDRH acknowledges them with the receipt containing date of the application received and a unique control number is assigned to the application. The unique control number is called the 510K number or K number. This number indicates the review process of the application has started. After assigning the K number, the application is transferred to the CDRH department depending on the type and medical speciality of the device. An acceptance review is then conducted be a lead reviewer to confirm all the elements required are present in the application followed by a substantive review. The FDA reviewers must address some of the basic questions put forward by the lead reviewers about the product or device within 15 days of the notification of substantive review. All the inquiries made can be found in the FDA website under Refuse to Accept Policy for 510 [k]s. FDA must either approve or deny the PMN process within 60 days of addressing the basic questions (Van Norman, 2016, p. 281).

2.7.5 THE HUMANITARIAN DEVICE EXEMPTION PATHWAY (HDE)

This is for lesser than 4000 individuals who are affected with a certain rare conditions or diagnosis in US and its submission does not require any scientific evidence as the number of subjects for participation for the trials would be inadequate and might take longer years. These devices are humanitarian use device. In addition to the FDA, these devices require approval from the local institutional review board (Van Norman, 2016, p. 281).

2.8 POST MARKETING SURVEILLANCE TOOLS IN EU

Post marketing surveillance can be proactive and reactive. It is mainly monitoring of medical devices. In proactive post marketing surveillance, data s gathered prior to any potential issues whereas in reactive post marketing surveillance otherwise termed vigilance where data is gathered after an incident has been reported by the manufacturers. Since 1992, the EU has described the lifecycle of the medical device before its approval and the post marketing surveillance in the MDD. It has been updated by the MDR (Badnjević *et al.*, 2022, p. 1316).

In the EU, post-marketing surveillance is done independently of the manufacturers. As per MDR Article 86, every year from the clinical evidence obtained from post-market surveillance and PMCF, periodic safety update reports (PSUR) must be provided by the manufacturer for class III and class IIb devices. Through, the EUDAMED database, the PSUR is circulated to the notified bodies and competent authorities which would be summarised in the SSCP. An increase in the severity and frequency of incidents must be reported by the manufacturer and monitored by the commission. Physicians also play a responsible role in reporting of adverse events after careful follow up of patients in the medical device registries. The Unique Device Identification (UDI) system practiced in the US is now adopted by the EU with the new regulations of the MDR where the patients with any unexpected events could be traced. The manufacturer can now submit any information available in the independent medical registries to notified bodies. (Fraser *et al.*, 2020, p-2591-2593). The MDR requires the manufacturers to conduct post marketing surveillance studies to all devices irrespective of the level of risk. Additional surveillance is required for those devices which cause serious health issues, implantation of device for more than a year, devices used in paediatric population and devices intended for supporting life (Daigle and Torsekar, 2019, p. 12).

In case of serious consequence with the usage of a device such as death or deterioration of a condition, manufacturers take steps to correct it termed as Field Safety Corrective Actions. Corrective actions may vary from labelling of the product to recall of the product (Kramer *et al.*, 2013, p. 2).

2.9 POST MARKETING SURVEILLANCE TOOLS IN US

Any serious issues such as death or injury related to a device irrespective of the class or risk must be reported to the FDA, once the device is in market. If the incidents are not serious manufacturer must file that can be inspected as per the Good Manufacturing Practices regulation. Devices approved by PMA should submit annual report and which requires post approval studies should submit results of its progression. (Ciarkowski, 2000, p. 3500).

A system used in US to report the adverse events by manufacturers, user facilities or importers is through medical device reporting. More information on the use of devices can be obtained from device user facility reporting a mechanism proposed by Congress. For example, the post marketing experiences of deep brain stimulation devices was better understood by these 2 mechanisms (Peña *et al.*, 2007, p. 423).

For post marketing surveillance, epidemiological methods are required which can be enhanced by data networks. They are Medical Device Epidemiology Network Initiative, Medical Device Surveillance Network and MedWatch (Sorenson and Drummond, 2014, pp 117-120)

Quality manufacturing control systems must be maintained by the manufacturers after getting approval. As it is not mandatory for the health care providers to report adverse events, most of it is reported by the company representatives. UDI is also used for device tracking. It also assists in timely collection of adverse event reports, coordination of recalls, speed up the reporting of its usage and effectiveness. Post-marketing surveillance in US includes post approval studies for devices approved by PMA or HDE and 522 studies for lower risk devices approved via 510 [K] pathway. The data gathered through post-market surveillance is made publicly available (Kramer *et al.*, 2013, p. 2).

2.10 MEDICAL DEVICE RECALLS IN EU

A non-peer review was conducted by Advamed to compare the recalls in US and EU, which stated that the device recalls in both the system had no difference between 2005 and 2009. Before the introduction of EUDAMED the EU did not have a proper channel to report the device recalls and events affecting safety. The devices that obtained a CE mark in EU were unable to obtain approval from FDA. For example, radial head fractures were treated with an elbow implant. A safety issue of implant fracture was observed by the FDA for the device and the FDA application was withdrawn. Still, the device was marketed in the EU and finally various reports of fractures led to the recall of the device which questioned the safety of regulations (Maak and Wylie, 2016, p-539-540).

Another major failure in this sector was the use of low graded silicone unfit for medical use in breast implants. This was manufactured by Poly Implant Prothese (PIP) which paved the way to development of five immediate actions in 2012 by the EU commission. One of the plans were to develop implant registers (Melvin and Torre, 2019, p-351). The PIP breast implant scandal gave the impression of a fraud case more than a failure in the medical device regulatory approval process. However, notified bodies who performed the conformity assessment procedure were held responsible as their negligence in assessing the manufacturer (Byrne, 2019, p. 647).

2.11 MEDICAL DEVICE RECALLS IN US

A major medical device failure which resulted in 700 deaths and 10,000 injuries from intrauterine device manufactured by Dalkon Shield resulted in the 1976 US FDA medical device amendments. Between 2003-2007, many high-risk devices were approved through PMN process which has to be originally approved through PMA as per the 2009 report by Government Accountability Office. The orthopaedic industry has suffered major recalls. For instance, the hip implant device (Articular surface replacement) was implanted in 93000 patients until it was recalled and categorised as the most flawed implant (Day *et al.*, 2016, p-518).

According to a study conducted on class I medical device failures after its approval was due to 3 main issues.

- Packaging
- Component
- Design

The industry growth is now overtaken by serious adverse events of medical devices by 8%. The FDA has the authority to command the manufacturer to recall the device if the manufacturer does not withdraw the device from the market. The medical device recall classification follows the reverse order of classification of medical devices in terms of risk. Class I recalls – due to death or other serious health consequences.
Class II recalls- due to reversible and temporary health conditions.
Class III recalls- due to violation of rules without any harm or minimal risk.
The FDA maintains a publicly transparent database to store the medical device recalls. It mentions the cause and reason for recall by the FDA and the manufacturer, respectively. The root cause for recalls is essential to determine the preventive and corrective actions. The main causes determined by the FDA errors by employee, device design and some are under investigation. Some of the recall reasons are wrong instructions for use, battery depletion, faulty relay, interruption of electrical connection. The largest recall events have occurred for class III medical devices such as defibrillator, automatic implantable cardioverter, with cardiac resynchronisation produced by St Jude Medical, Inc. due to its inappropriate design. Another top recall was for a glucose test strip which is a class II device due to inappropriate labelling (Sarkissian, 2018, p-2-7).

2.12 NEW MDR AND IVDR REGULATIONS

The MDR and IVDR regulations has replaced the directives of the EU. These regulations mainly aim at patient safety and effectiveness along with increase in competition and innovation in the field of medical device sector. The novel regulations integrate advancement in the scientific and technological areas and establish a new high standard worldwide for medical devices. The updated rules help EU to be a leader globally in the long run in this sector. The products which are included in these regulations are medical devices, in vitro diagnostic medical devices, contact lenses, liposuction equipment. Notified bodies are assigned to oversee the process of medium or high-risk devices. Conformity assessment procedures also differ based on the device risk. This agreement took so long to reach as all the aspects of the regulation had to be carefully scrutinized

since it must be beneficial and effective to the patients. The new regulations have few important revisions which are capable of addressing challenges in the future, improve the security, harmonise the device regulations and mainly focus on incorporating innovations in the industry. The new regulations are framed in a way that the medical devices supply is not hampered and is accessible to the patients which is ensured by the EU commission, competent authorities, notified bodies and stakeholders. The new regulation has enabled manufacturers to register at EU level where previously manufacturers have to register in each member state to market the devices. In Europe, the medical device industry is a major leading sector which employs more than 500,000 in 25,000 companies. These regulations will make EU a competitor to others globally. These regulations will now resolve the ambiguity by clarifying the exemption regimes in case of single use devices reprocessing and in house devices. The positive sides of the regulations outweigh the additional costs that the companies incur (Directorate-General for Internal Market, 2018, pp. 1-4).

2.13 HOW IS MDR 2017/745 BETTER THAN PREVIOUS EU REGULATIONS

First and foremost, it safeguards the health and safety of the patients. More strict regulations for high-risk devices are put forward before its marketing including coloured contact lenses and other aesthetic devices. Rules on clinical evaluation and investigation are made more stricter and there are new requirements for the use of hazardous materials.

Additionally, the EU database known as EUDAMED is made publicly transparent and available for the knowledge of the public. It shows the real picture of the products available in the market and the summary of safety and performance for high risk and implantable devices will made available to the public. It is the responsibility of the EU Commission to maintain it.

Thirdly, the use UDI to increase the device traceability when used in patients which is placed on the packaging or label. As per Article 87, field safety corrective actions and serious incidents must use UDI for reporting. The EU commission is authorised to set up and manage a UDI database. The database is designed in such a way that it is accessible to multiple users to download and upload the data supported by the EU commission in technical and administrative sections.

In addition, a new system was introduced by attaching an implant card in all implantable devices. This is also to disseminate the information to the patients regarding the device and its use and safety.

Furthermore, if patients received any damage or defective medical devices compensation is provided by the development of a strong financial system. Countermeasures such as financial support must be provided to the patients financially according to their potential and capacity by the manufacturers. The financial coverage also depends on certain factors such as risk classification of the device, device type and size of the manufacturing company (Directorate-General for Internal Market, 2018, p. 1-4).

2.14 AREAS OF IMPROVEMENT REQUIRED IN EU AND US

Both the EU and US faces same challenges and require improvement in protecting the patient safety and health with more requirement in clinical evidence while using the medical devices. The main concern of the US is approval of high-risk devices through less stringent procedures without proper evaluation. The percent of medical devices that has undergone evaluation through PMA is just 2% when analysed over a decade. Another area to be considered is the approval of drugs through substantial equivalence for previously cleared devices without any safety or effectiveness data or if the predicate was recalled for any reason. The quality of the device has to be taken into account. FDA analysed internally to understand the quality issues where the device lacked the basic quality elements such as indication for use and device description. Another improvement required is to improve the adverse event reporting to enhance the post marketing surveillance of the devices. One of the problems associated is if a manufacturer decides that there is no causal relationship between the event and the device it is not mandatory to report from their end. Voluntary reporting of healthcare professionals and patients must be encouraged. According to the previous directives before the introduction of MDR EUDAMED it was not made available to the public. Exchange of data was only between the competent authorities and the EU commission., But according to the new regulations, there is increased transparency, and most data has been made publicly available. An organised and systematic collection of adverse events is required in case of post market surveillance to analyse the exact results of a particular device to continue its use safely (Sorenson and Drummond, 2014, pp. 125-130).

However, after analysing the MDR regulations by the experts, it is observed that it can hinder innovations. There must be a balance between the current and new evidence assessment. As per the new regulation, recertification of devices is a requirement, and it has to be done by 27 May 2024. There are approximately 500,000 medical devices which should undergo recertification which is a considerable number therefore, the transition period may not be enough. During MDR implementation, recertification took nearly 6 months. Costs for certification would be increased in MDR and it might lead to shortage in the availability of medical devices which has to appropriately monitored. Another requirement under MDR is that the notified bodies will also require recertification. Due to these new requirements by May 2021 about five notified bodies withdrew the market as they couldn't meet the requirements specified which is also a contributing factor to impede the recertification of medical devices. There were 56 notified bodies previously and the number has declined to 26. This is a big challenge for the enterprises. There are certain terms which has to be described in the new regulations which are not elaborated in Article 2. These terms have to be described otherwise would lead to various interpretations (Shatrov and Blankart, 2022, p. 1236-1237).

CHAPTER 3: RESEARCH METHODOLOGY

3. RESEARCH METHODOLOGY

3.1 AN OVERVIEW

In a general sense, research is nothing but quest for knowledge. It is a systematic and well organised way of investigating or searching data and information regarding a particular topic. This is conducted as an academic activity. It is the curiosity to understand the known to the unknown. In a project research, objectives are framed. The solutions to these objectives are attained through a systematic way of data collection. There is a pattern to be followed for research which includes formulating hypothesis or objectives, collecting and analysing the data, finally reaching conclusions and recommendations to the objectives proposed in the beginning.

3.2 WHY IS RESEARCH CONDUCTED

According to (Kothari, 2004), the purpose of the research is to

- To obtain new insights
- To depict the characteristics of a particular population, group or scenario
- To test hypothesis in a research study

3.3 RESEARCH TYPES

- Descriptive Research: In these type of research surveys is normally used. The researcher can only assess the present situation or the past situation and has no control over variables.
- Analytical Research: The researcher conducts research with the material already present and critically evaluate the available information
- Applied Research: The aim of the applied research is to solve a problem which is causing a need of urgency in the society, industry or business organisation.
- Fundamental Research: The research carried out by forming generalisations with the aid of theories already formulated.
- Quantitative Research: The name itself suggests that the research is based upon measuring the quantity.

- Qualitative Research: As the name suggests, it involves quality in these types of research. These types of research are conducted by performing interviews to understand the reasons for an underlying issue and motives. The other techniques used are story and sentence completion tests. This is done to find the opinions and suggestions people have on a particular topic.

3.4 CONCEPTUAL FRAMEWORK

Approach	Quantitative Approach
Philosophy	Inductive Reasoning
Source	Survey
Method	Questionnaire
Structure	26 questions
Participants	Personnel working in the regulatory affairs sector

Table 4. Overview of Research Methodology

3.5 RESEARCH STRATEGY

The research strategy is to compare the regulatory requirements of medical devices in European Union and United States. The identical features and differences of both the regulations would be identified by studying the regulatory requirements in detail. Various approaches taken for post marketing surveillance and the reasons for failure of the medical devices after its approval would be identified along with further areas of improvement in both regulations.

3.6 RESEARCH APPROACH

A quantitative research method is used in this study. The data is gathered through secondary and primary research. Secondary research involves literature review and peer reviewed journals. PubMed and Google Scholar were used as search databases. The search terms used were comparison, regulatory affairs, EU, US, medical devices, post marketing surveillance, medical device recalls, failures, differences, similarities, EU

MDR regulations and challenges. Most of the data for the research could be obtained through the secondary literature search. Most recent articles of less than 10 years old were used for the literature review. The articles which were inaccessible through either PubMed and Google Scholar were obtained through research gate by searching with the aid of digital object identifier and PubMed unique identifier.

3.7 RESEARCH PHILOSOPHY

3.7.1 RESEARCH REASONING

Two types of reasoning in research methodology are inductive and deductive reasoning.

Inductive reasoning starts with observations, analyzing the pattern, experimenting and finally reaching a conclusion by developing a theory based on these observations. For example, the common symptoms of urinary tract infection are hematuria, cloudy urine, pelvic pain, pyuria etc. with these symptoms a nurse can make an assumption that those patients with similar symptoms have urinary tract infection.

Deductive reasoning is just opposite to the inductive reasoning. Firstly, a theory is found, hypothesis and predictions based on the theory are made and then experiments are carried out to test the theory developed (Ryan, 2018, p. 3).

Inductive reasoning is used in this research where questions are framed and then the information is gathered to finally reach to a conclusion.

There are 3 types of research philosophies

- Positivism
- Interpretivism
- Critical theory

Positivism and interpretivism are the philosophies that are being used here. The questionnaire was asked with minimum interaction through social media rather than asking the questionnaire face to face to the professionals. Only facts are considered in the research and the reality that is being followed for regulations.

Interpretivism is also called anti-positivism as it is opposite to positivism. Certain questions in the questionnaire are subjective which is aimed at an answer based on the knowledge and experience gained by the professionals. It helps in analyzing, understanding, and interpreting the data as per the perspectives of regulatory professionals.

3.8 PRIMARY DATA COLLECTION

Primary research includes data gathering by quantitative methods. The quantitative approach used here is through a questionnaire. The questionnaire was divided into 5 sections. It consisted of 26 questions. 21 questions were closed ended questions and 5 were open ended questions. The first section described the aim of the study and general information to give a brief idea about the research study to the participants. The second section is to collect general details of the participants. The third section contains common questions to be answered by EU and US working professionals. The fourth and fifth sections are to be filled by the US and EU working professionals respectively. The survey helped in getting more information than could be obtained through published sources.

3.9 RESEARCH PARTICIPANTS

The participants in the survey were professionals working in the regulatory affairs sector for medical devices in the EU and US. These personnel are chosen as they are more appropriate because of the experience and the knowledge they possess by working in the regulatory affair sector. They would be more updated regarding the different updates in the regulatory framework of medical devices.

The questionnaires were sent to members working in the regulatory affairs sector of the medical device industry. It was sent through LinkedIn, WhatsApp and some of them were mailed. The questionnaire was created using google forms and the link was circulated among the professionals. The rate of participation was increased by sending personal messages through LinkedIn and sending reminders to the participants. 40 people participated in the survey.

3.10 ETHICAL CONCERNS

Consent was obtained from the participants before starting the survey. Participation was completely voluntary, and it enabled the participants to withdraw from taking part in the survey at any point during the survey. It was solely the interest of the participants to take part in the survey. No personal information was collected during the survey. All the questions were framed in such a way that it is relevant to the study research. No confidential or company sensitive information was collected during the survey. Before commencing the survey, a brief introductory description of the study was provided. All the data was stored according to the Global Data Protection Regulations.

3.11 INCLUSION AND EXCLUSION CRITERIA

The professionals working in the US and EU in the regulatory affairs for medical devices sector were considered and included in the study. The surveys which, were completely filled were included in the study. Those who were disinclined to participate in the study were excluded. The people who withdrew the participation in the middle of the survey were also excluded.

3.12 CHALLENGES FACED DURING SURVEY

Difficulties with this approach of survey included limited participation of the participants as it requires voluntary participation in the survey to answer all the questions in the questionnaire. Consent to participate in the survey is more important and it was complicated. The identity of the participants was kept confidential.

Data will be analyzed using the information obtained from secondary research such as through literature review and the responses gathered through survey. Both the information and the results from the survey will be compared to obtain the answers to the research questions.

3.13 CONCLUSION

This chapter dealt with the research methodology used for conducting the project research for the comparative study of the regulatory requirements in EU and US for medical

devices. It described the research strategy, approach, design and the participants. It also gave an overall idea of the primary data collection of the research.

The next chapter deals with the findings obtained through the primary data collection which is survey and analyze those findings to reach a conclusion.

CHAPTER 4: FINDINGS AND DISCUSSION

4. FINDINGS AND DISCUSSION

4.1 INTRODUCTION

This chapter deals with the data from primary data collection through questionnaire. It will also include the analysis of the information collected. Graphs are used to represent the data. It helps in understanding and interpreting the objectives of the research. Comparison of the results are done with already published sources and conclusions are drawn accordingly. It also represents the study significance.

4.2 DEMOGRAPHIC INFORMATION

All the respondents willingly participated in the survey after proper understanding. A total of 40 regulatory professionals participated in the survey who provided an adequate response. Out of which 18 were US working professionals and 22 were EU working professionals.

	Number of Participants
EU	22
US	18

Table 5. Demographic Data

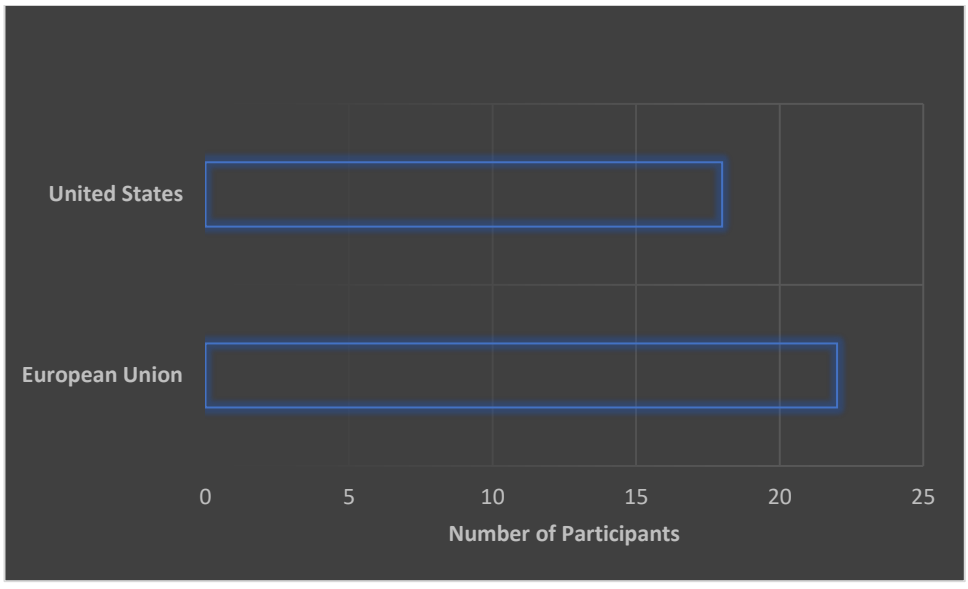

Figure 2. Bar Chart Showing Demographic Data

4.3 LEVEL OF EXPERIENCE

Experience Level	Participants
0-1 year	25%
1-5 years	35%
Greater than 5 years	40%

Table 6. Level of Experience

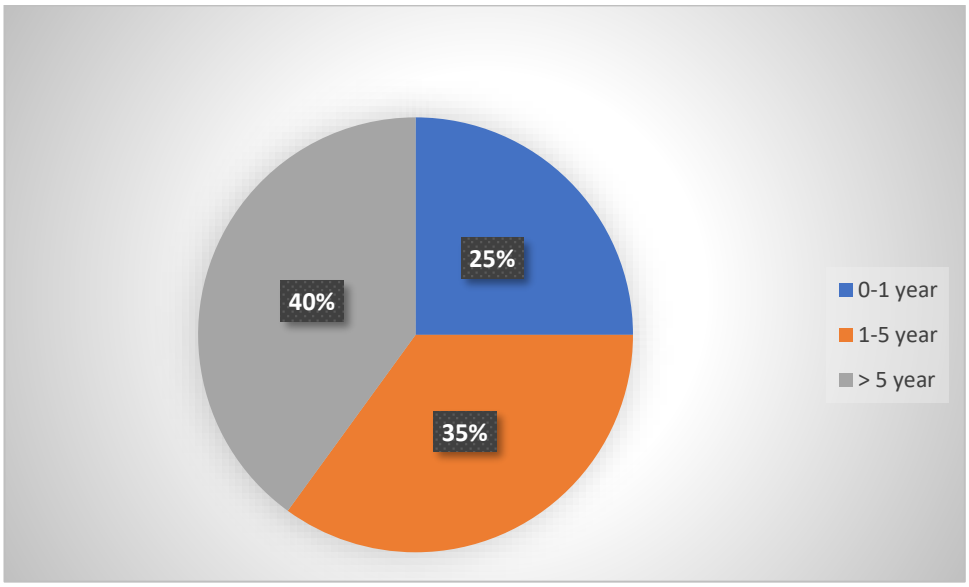

Figure 3. Pie Chart Representing Level of Experience

40% of the responses were obtained from professionals who had work experience greater than 5 years. 35% were obtained from professionals with 1 to 5 years of working in the regulatory sector and 25% were freshers with experience of 0 to 1 year.

4.4 ANALYSIS OF OBJECTIVE 1: TO FIND THE DIFFERENCES INVOLVED IN THE REGULATIONS FOR MEDICAL DEVICES IN EU AND US.

From the literature review by analyzing the differences between the regulatory system for medical devices for both the EU and US they both aimed at providing safe and effective medical devices. From the past history and the recalls that happened had made both the regulations more stringent. The implementation of MDR regulations in 2017 has made

the requirements for regulatory approval in EU stricter. The regulatory marketing authorizations of both these systems are similar in one aspect as the rules get stricter with an increase in the risk associated with the devices. When considering both the systems marketing authorization becomes easier through equivalence of the medical devices already on the market. There are certain differences as well during comparison. The marketing approval for a medical device is granted by a single body FDA, which is a government organization. The marketing authorization in EU is done through the notified bodies supervised by competent authorities by performing a conformity assessment procedure.

According to (Van Drongelen *et al.*, 2015, p. 45), there is no detail when considering the technical requirements of both the systems. In EU, manufacturers demonstrate the conformity with the essential requirements by the standards which detail technical requirements and specifications. In EU, certain states such as Netherlands and Sweden exercise the power to develop standards. Whereas in US, there are either national standards or international standards which are developed by the FDA. It is the discretion of the FDA to decide to which extent the standard has to be recognized and they have the power to influence the standard of the content.

4.4.1 SAFE AND EFFECTIVE MEDICINES

According to (Van Drongelen *et al.*, 2015, p. 45), it has been reported by the FDA that the US system is better than the European Union from its 2012 report. There were 12 devices which were approved in EU and remained unapproved in US and the same devices were also marketed in EU. The clinical investigations conducted during PMA clearance also showed adverse effects from the devices so the FDA prevented the devices from marketing. One such device was the elbow implant which resulted in fractures. These examples justify that USA has a better system by evaluating the safety and efficacy of medical devices. This in turn results in the longer time for a device to get approval. It can even take 2 years.

4.4.2 EASIER PATH OF APPROVAL

According to (Maak and Wylie, 2016, p. 540), the approval of medical devices in EU was faster than US when comparing the procedure to obtain CE mark is far easier than to obtain PMA approval of US FDA. The requirement to obtain CE mark is to provide evidence of the performance of the device whereas the PMA approval is purely based on the device efficacy and safety. The performance of the device is studied through single arm studies whereas the device efficacy and safety are accomplished through large studies involving comparison of the patients with the control group. An example can be provided to explain this scenario where an orthopedic device named GuardWire (Medtronic) device which is a temporary occlusion and aspiration system received approval from US FDA and EU CE mark through different pathways. To obtain CE mark, 22 patients were used in a single arm study whereas for the US FDA approval 800 subjects were randomized for the clinical trial which demonstrated that the device could decrease the complications of angioplasty.

4.4.3 TIME FOR APPROVAL

According to (Maak and Wylie, 2016, p. 540), as the clinical trial studies in US is more intense and it requires large number of population it is considered to be expensive and take longer time for approval from the FDA. On an average it took almost 2.5 years for the approval of devices through 510 [k] pathway and 4.5 years for the approval of devices through PMA pathway according to a survey published in 2010. As per the EU system, the duration for approval was 7 and 11 months for similar devices. Even though the time taken for granting approval in the US is longer than EU, there are no studies proving that FDA process is safer.

4.4.4 QUALITY MANAGEMENT SYSTEM

Both the regulations, FDA and EU MDR enforces the requirement of quality management system and the implementation of its software by the medical device manufacturers.

4.4.5 PUBLIC TRANSPARENCY

Each system ensures public transparency where FDA has the FDA medical device database and EU has the EUDAMED for all information related to the medical device.

4.4.6 UDI

UDI is a system adopted by both FDA and EU. EU MDR expanded UDI by adding additional features by categorizing medical devices based on the purpose, risk class, design and characteristics of manufacturing. The UDI differs only in placing the labels on medical devices in both these systems.

The EU MDR requires Clinical Evaluation Report is required to be prepared by the manufacturers for class III and IIb medical devices, whereas it is not a prerequisite by the FDA for devices approved through 510 [k] pathway.

Another requirement posed by both the system is technical documentation. the FDA and EU technical files contains similarities but could not be exchanged or considered equal as it differs in classification and management of risk (Gosia, 2022).

4.4.7 QUESTION 1: WHICH SYSTEM IN YOUR OPINION HAS THE BEST REGULATORY FRAMEWORK FOR MEDICAL DEVICES?

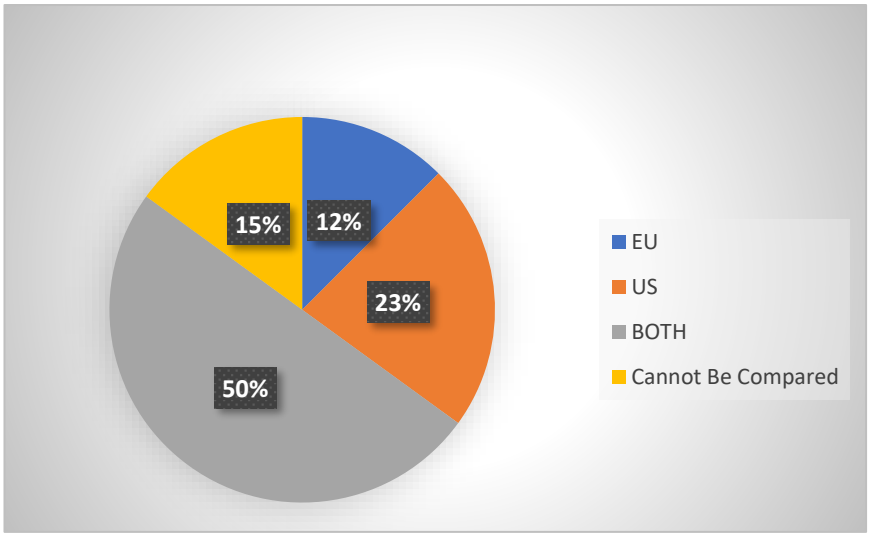

Figure 4. Best Regulatory Framework of Medical Devices

By looking at the pie chart, it can be observed that most of the participants has supported that both the EU and US system has better regulatory framework for medical devices.

23% and respondents has responded that US have better regulatory framework for medical devices. 12% chose EU has better framework of regulations and 15% are on the stand that both the regulations are not comparable.

As both of the systems are looking forward for the safety of patients rather than viewing it in a business perspective and with the history of many recalls it is difficult to point out one outweighs the other.

4.4.8 QUESTION 2: DO YOU AGREE TO THE STATEMENT THAT EU HAS FASTER ACCESSIBILITY TO NEW MEDICAL DEVICES TREATMENT COMPARED TO USA?

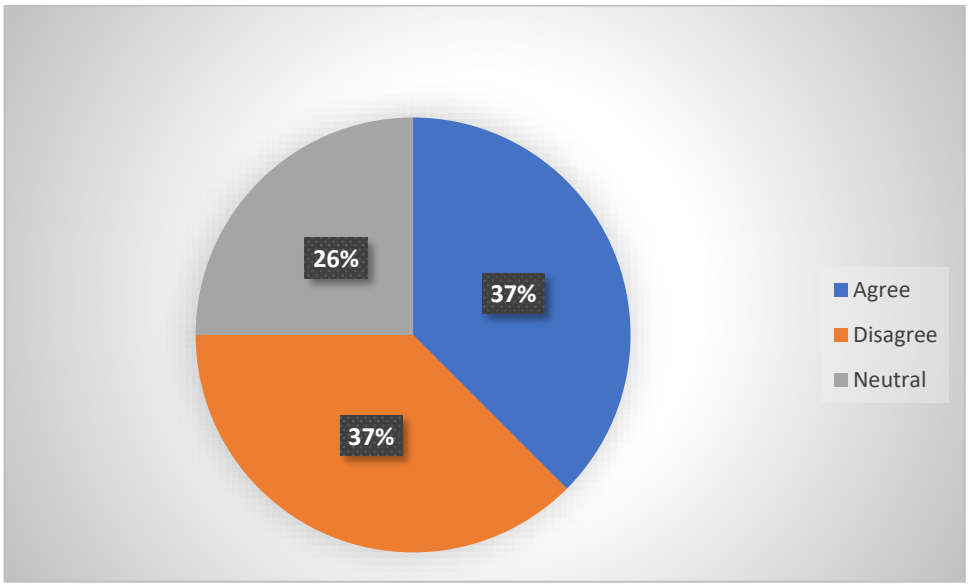

Figure 5. Faster Accessibility to Medical Devices

According to the survey, 37% of the participants has disagreed and agreed that EU has faster accessibility to medical devices. 26% chose to stay neutral on the opinion. This might be due to the previous directives of EU regulations i.e., MDD where the procedure allowed easy accessibility to medical devices for patients due to less stricter regulations whereas the new EU MDR 2017/745 is more concerned about the safety and efficacy of the devices which has led to evaluating the devices clinically and takes more time for the device approval than the previous directives.

4.4.9 QUESTION 3: COMPARISON OF COMMON WAY OF GRANTING MARKETING AUTHORIZATION IN EU AND US.

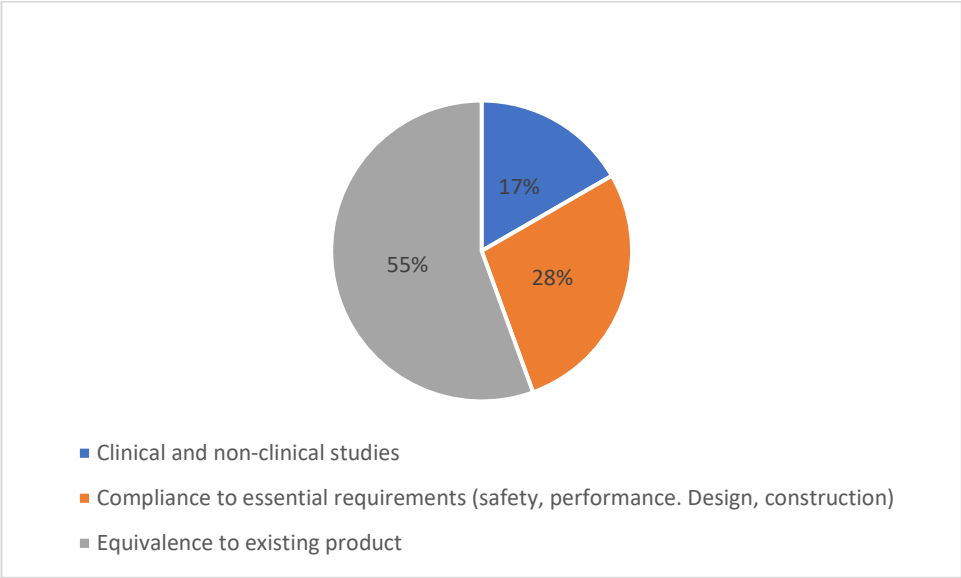

Figure 6. Marketing Authorisation in US

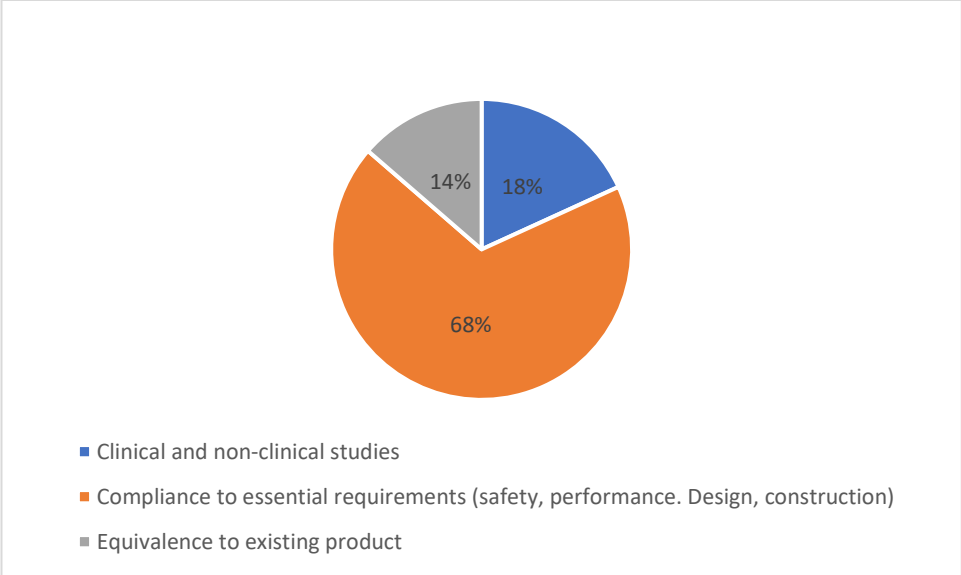

Figure 7. Marketing Authorization in EU

From the 2 charts, it could be observed that the most common way of granting marketing authorisation in US is through equivalence to existing product or the 510 [K] pathway which contributes to 55% of the response. Compliance to essential requirements and clinical and non-clinical studies account for only 28% and 17% respectively. While considering EU, 68% has responded that the most common way of marketing authorisation is through compliance to essential requirements (safety, performance,

design and construction) and the other 2 ways accounts for a very less percentage which is 18% for clinical and non-clinical studies and 14% for equivalence to existing product.

Most of the medical devices in US were approved through 510 [K] pathway. 4000 applications were received by the FDA in a year for approval via 510 [K] pathway whereas only less than 100 applications were received to be approved through PMA pathway (Maak and Wylie, 2016, p. 538).

The medical devices must comply with essential requirements as per the MDD and general safety and performance requirements according to MDR for its approval. The CE certification is only obtained after it is complied with these essential requirements. There are 16 essential requirements in the MDD and 23 safety and performance requirements (Macomber and Schroeder, 2018, p. 1).

4.4.10 QUESTION 4: COMPARISON OF DURATION OF GRANTING THE MARKETING APPROVAL OF A MEDICAL DEVICE IN THE US AND EU.

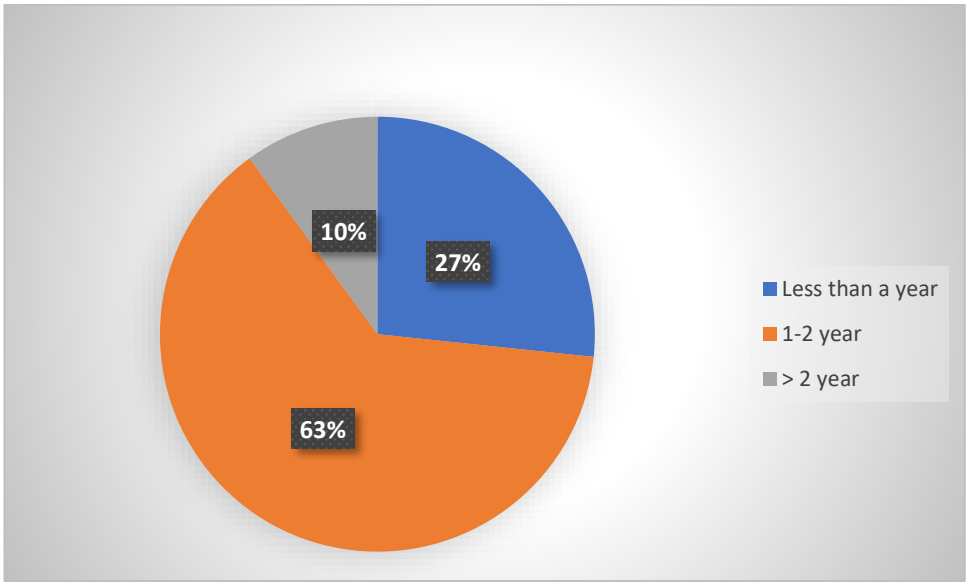

Figure 8. Time Taken for Approval of Medical Devices In US

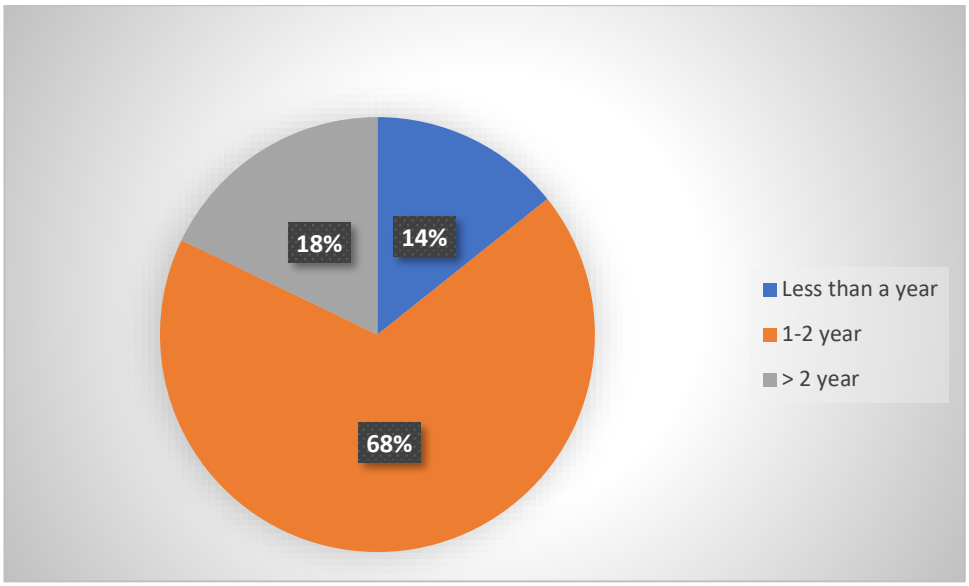

Figure 9. Time Taken for Approval of Medical Devices In EU

When analysing both the charts 8 and 9 it is observed that on an average the time taken for granting market access for medical devices are 1-2 year in US and EU with a percentage of 63 and 68 which is almost the same with a slight increase in the accessibility of medical devices in EU. 27% says that it takes 1-2 year for market approval and 10% for more than 2 years in US. When looking at the chart for EU, 14% chose less than a year and 18% chose greater than 2 years for market approval for medical devices.

4.4.11 QUESTION 5: REQUIREMENT OF REVISION OF REGULATORY FRAMEWORK FOR US AND EU

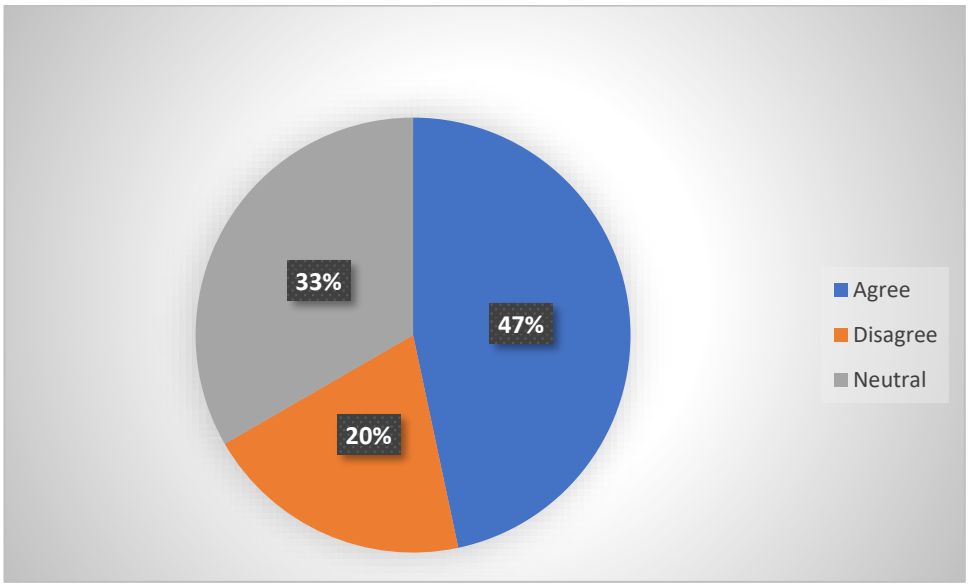

Figure 10. Requirement of Revision in the Regulatory Framework in US

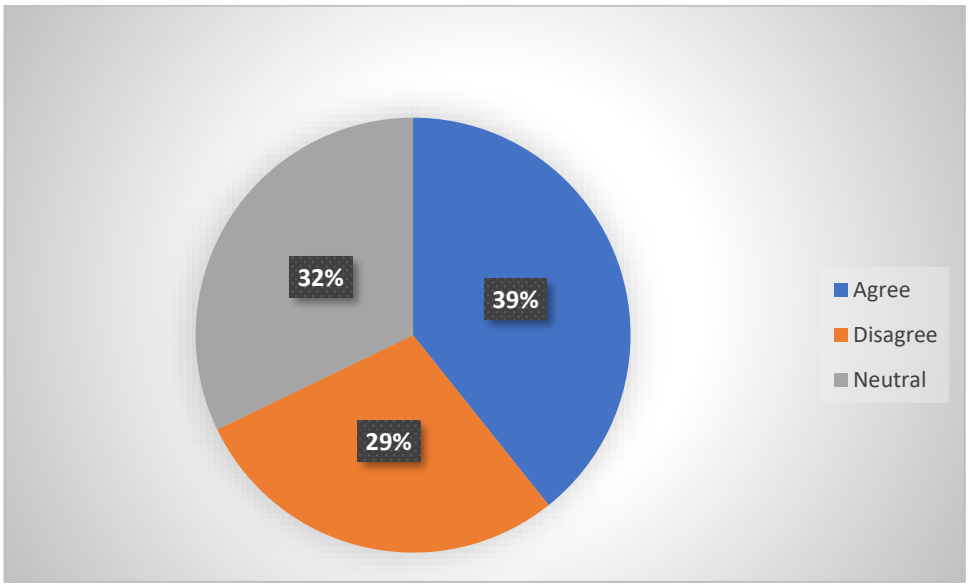

Figure 11. Requirement of Revision in the Regulatory Framework in EU

From the figures 10 and 11 it can be observed that 47% of the total participants supports revision to the existing regulatory framework in US, 20% does not support for the revision and 33% of the professionals neither agree nor disagree for the amendments. When looking at figure 11 it is observed that 39% agrees for the revision of the current regulatory framework for medical devices in EU, 29% disagrees for the revision and 32% stays neutral in regard to the revision.

4.4.12 QUESTION 6: SAFETY OF NEW MEDICAL DEVICES APPROVED THROUGH EQUIVALENCE TO DEVICES ALREADY ON THE MARKET IN US AND EU.

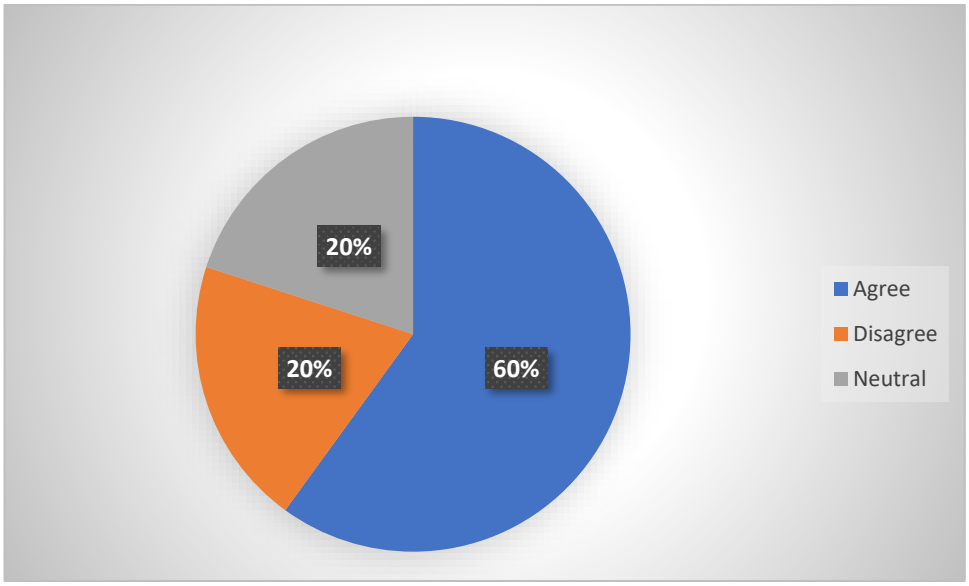

Figure 12. New Medical Devices Safety Approved through Equivalence in US

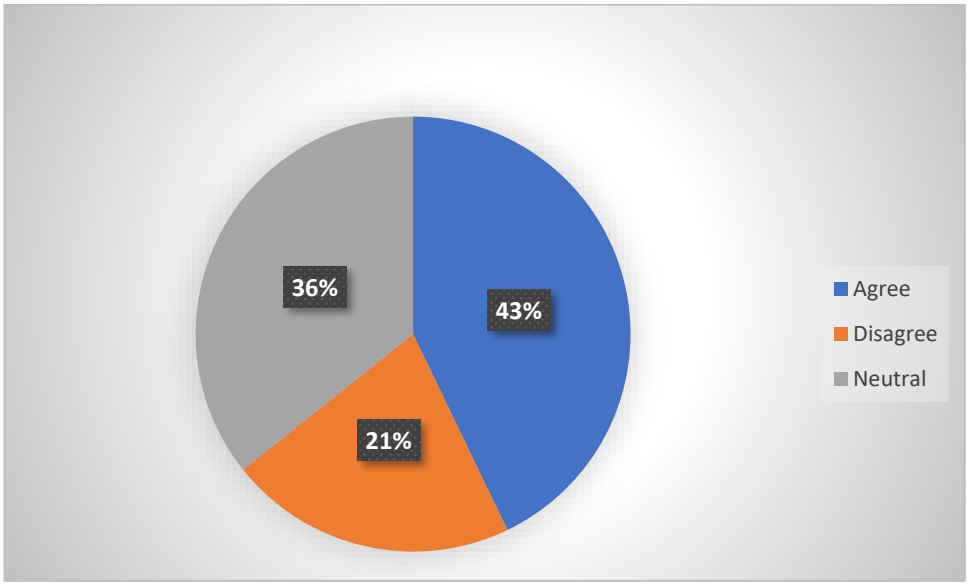

Figure 13. New Medical Devices Safety Approved through Equivalence in EU

The figures 12 and 13 compares the safety of medical devices which are approved through equivalence to devices already on the market which is its predicate in US and EU. As the data suggests, 60% of the participants has agreed that the devices are safer when approved by substantial equivalence in US and 43% in EU.

From the survey, US respondents have commented that the substantial equivalence pathway for approval has enabled the pharmaceutical companies to launch medical

devices by selecting its predicate products. One of the respondents supported the method to be safer as it requires evidence that the device is substantially the same for the indication of use, evidence of efficacy and safety. Second respondent has suggested that as long there was accountability to make sure the comparison is accurate it should be sufficient to ensure the measure of patient safety. Third respondent says a direct comparison to an effective device is an effective measure by meeting the standards and regulations. Another respondent has compared this with a biosimilar device and noted that establishing equivalence with existing comparator is acceptable which includes safety which may otherwise leads to increase in the cost of the device. Another professional commented that FDA has tightened the requirements on claiming substantial equivalence and it has a very beneficial, free and interactive feedback process called the Q submission. This system can be utilised by the manufacturer and is entirely voluntary.

Q submission helps in interacting with FDA on clinical and non-clinical studies to receive comments can enhance the subsequent submission quality and improves the development process by reducing the total review time for a device (Health, 2021c).

The fourth participant responded that more strict parameters are required for substantial equivalence and all aspects not limiting to indications for use, clinical data and technology must be compared. Substantial equivalence is acceptable for class II devices and not for devices which pose a higher risk. Another response was that if a medical device approved with a small potential risk and has given breakthrough alarm in terms of sales, the new device which is approved through equivalence would also raise the same issue.

According to the opinions of professionals working in the EU, with the implementation of new EU MDR regulations, device approval through equivalence would not be possible as the rules have become more stringent. An EU participant has opposed the statement by pointing out that equivalence cannot demonstrate the safety and effectiveness or clinical performance of a medical device.

4.5 ANALYSIS OF OBJECTIVE 2: TO UNDERSTAND THE TOOLS USED FOR POST-MARKETING SURVEILLANCE FOR DIFFERENT CLASSES OF MEDICAL DEVICES IN EUROPE AND USA

4.5.1 QUESTION 7: ACCORDING TO YOUR OPINION WHICH IS THE BEST METHOD FOR POST MARKETING SURVEILLANCE OF MEDICAL DEVICES?

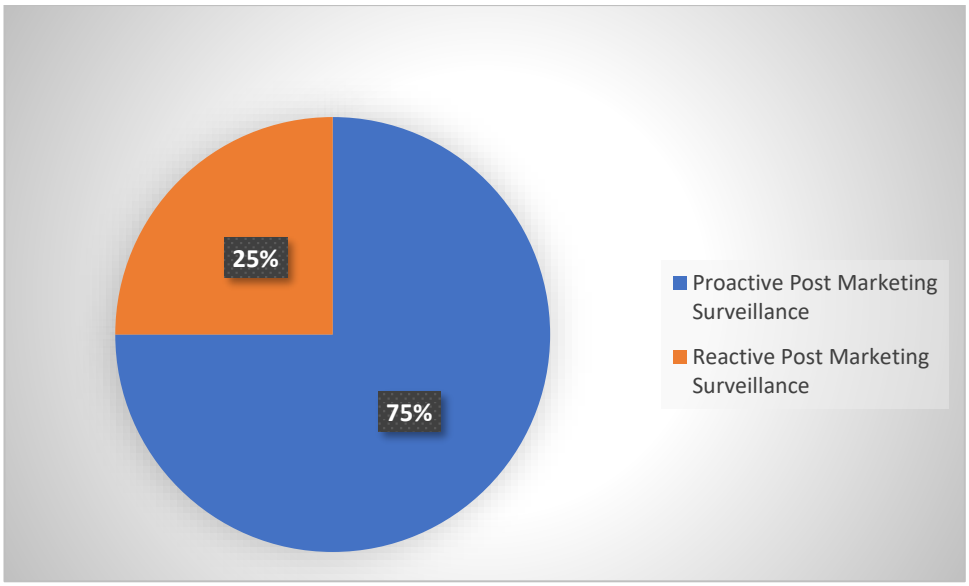

Figure 14. Best Method for Post Marketing Surveillance

75% of the participants have an opinion of conducting the post marketing surveillance proactively and 25% of them have responded reactive post marketing surveillance as the best method. The participants have elaborated the answer for choosing their option. One of the respondents suggested that potential issues on the post market must be mapped on a regular and on-going basis and any adverse effects must be anticipated and prevented before they occur. The problems must be identified before it leads to any significant issue and hazard to the health of the people in the post marketing phase. Another respondent suggested that potential risk assessment has to be done by the researchers proactively for the devices which has some known or minor risk which would have an impact on the service user than afterwards.

One of the respondents has commented on the difference in approach of post marketing surveillance of EU and US systems. FDA has a better grasp in determining the product safety and effectiveness whereas EU has more developed post market approach.

Previously EU was a better market to launch innovative medical devices due to poor scrutiny whereas with the implementation of EU MDR the scenario has changed. According to another respondent, proactive post marketing surveillance gives an alarm to avoid non conformities, and prevent a potential device issue before it leads to an event or worser than an adverse event. It plays a vital role in identifying the hazards in the field with respect to safety and performance. Continuous monitoring of the market performance is the real evidence opinionated by another participant. The time taken to resolve an issue proactively is less rather than reacting to an issue which is more tedious and time consuming. Some of the professionals have supported for the combination of reactive and proactive methods where reactive method helps in close monitoring of the device and tends to gather more information about a particular device through survey, customer complaints and feedback. Another participant explained that the method depends on the device type. If the device is completely a new innovative product such as comprehensive genomic profiling tissue test, the adverse events could not be predicted whereas the risk of the devices can be predicted for the devices whose post marketing studies conducted for equivalence devices. Similarly, for novel medical devices proactive measures could be useful whereas for devices with well-known risk reactive measures are sufficient according to a respondent. Another professional has disagreed to the practice of post market clinical follow up suggesting to be a waste of time for clinicians and manufacturers as there are historic data to show adverse issues are isolated events.

4.5.2 QUESTION 8: DO YOU THINK THAT THE EXISTING POST MARKETING SURVEILLANCE TOOLS FOR MEDICAL DEVICES IN EU AND US ARE BENEFICIAL TO THE PUBLIC?

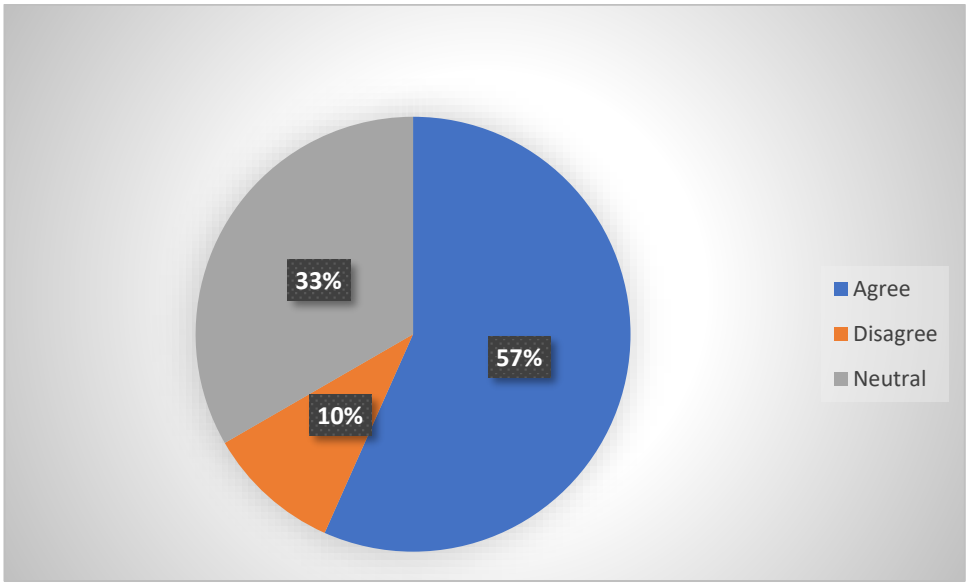

Figure 15. Post Marketing Methods in US Being Beneficial to the Public

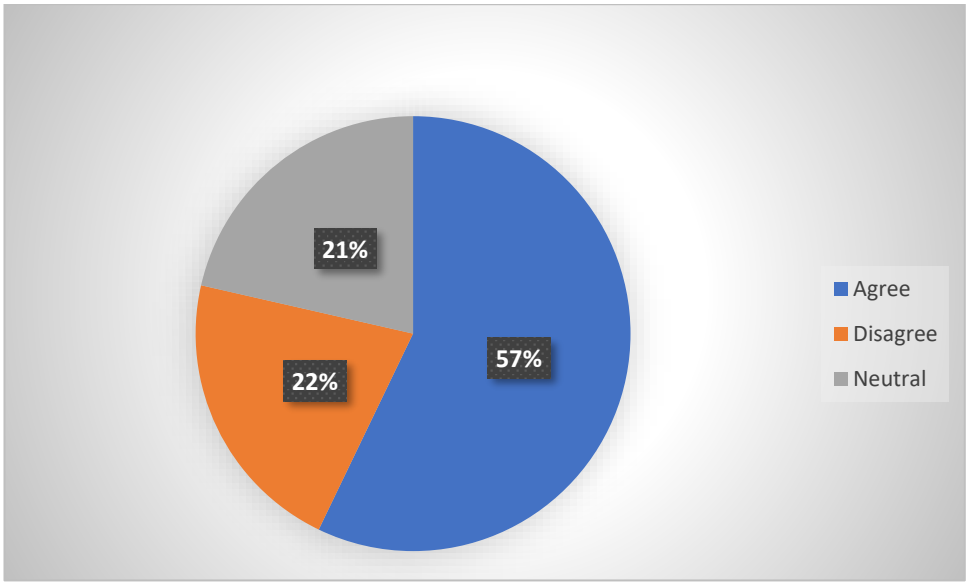

Figure 16. Post Marketing Methods in EU Being Beneficial to the Public

As shown in figures 15 and 16, it can be concluded that most of the participants have supported that existing post marketing surveillance methods followed by both the systems by FDA and EU are beneficial to the public. From figure 10 it can be interpreted that 57% agreed to the statement, 10% disagreed that the existing systems of post marketing

surveillance does not serve to be beneficial to the public and 33% were neutral on their opinion.

The US FDA uses a system termed as Manufacturer and User Facility Device Experience Database (MAUDE) for collection of adverse events for post marketing surveillance (Sorenson and Drummond, 2014, p. 118).

According to Badnjevic and collaborators (Badnjević *et al.*, 2022, p. 1321-1322), majority of the adverse events (96.6%) are reported by the manufacturers, then comes the patients and their relatives and lastly comes the physicians who should take the initiative to report as a healthcare professional responsible for guarding the safety of patients. Post marketing survey results conducted in 2012 by US noted that most of the recalls are due to issues in the software system. There were many devices which were not operating according to the standards, specifications, and electrical safety requirements such as ventilators, incubators, anaesthesia machines. Further improvements are required in the post marketing surveillance by evaluating the performance and utilisation of device, even reporting of the stakeholders.

4.6 ANALYSIS OF OBJECTIVE 3: TO EVALUATE WHICH AREAS OF IMPROVEMENT, NEED TO BE FOCUSED.

4.6.1 QUESTION 9: IMPROVEMENTS TO BE MADE IN THE PROCESS OF REGULATORY AFFAIRS FOR MEDICAL DEVICES IN THE US AND EU?

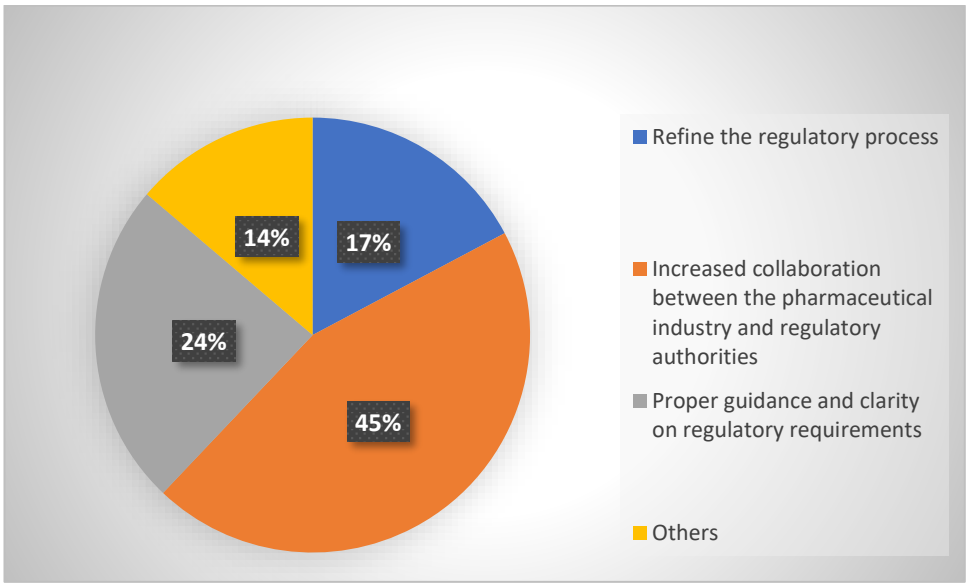

Figure 17. Improvements to be made in the process of regulatory affairs for medical devices in the US

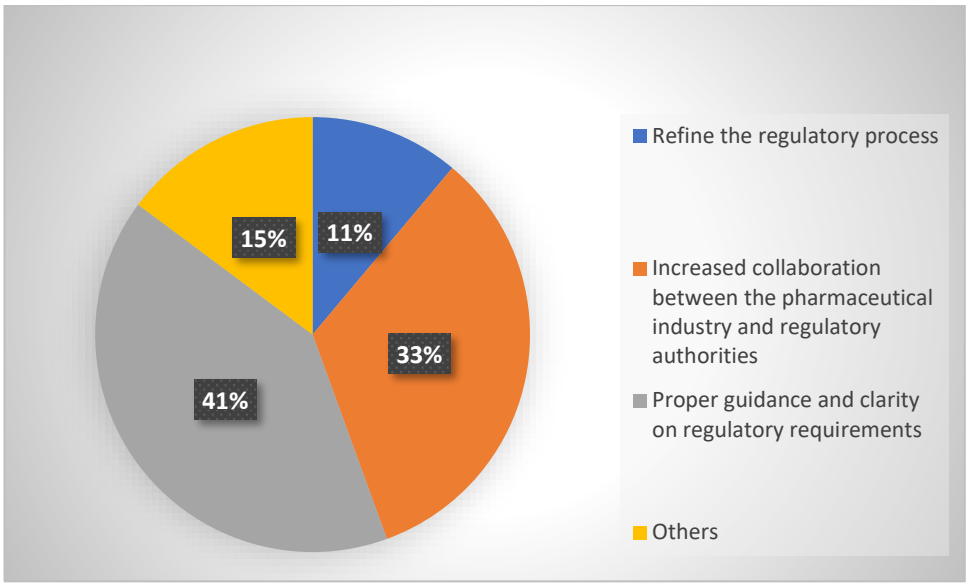

Figure 18. Improvements to be made in the process of regulatory affairs for medical devices in the EU

The pie charts 17 and 18 illustrates the improvements to be made in the process of regulatory affairs in the US and EU. Major proportion of the US professionals (45%) agree that there must be increased collaboration between the pharmaceutical industry and regulatory authorities and the EU professionals chose proper guidance and clarity on regulatory requirements which accounts for 41%. 11% and 17% of the EU and US are in the opinion to refine the regulatory process. 14% chose improvements to be made in other aspects of the regulations in US such as clinical evaluation and device equivalency when going down the path of predicates. One of the participants stated that quality management system regulation (QMSR) should come into place and must be fully harmonized with IMDRF.

In 2022 FDA proposed a new rule for amending the quality system regulations so that the regulations would go hand in hand with the other international regulatory standards for medical devices. When the QSMR comes into effect it harmonizes with other regulations and aim at continually improving the patient needs. This requires training to be provided by the FDA to the staff for checking compliance, propose a new inspection procedure, update systems used for information technology (Health, 2022b).

15% of the regulatory professionals in the EU chose other areas of improvement required which included more training to educate regarding the existing regulatory affairs and quality assurance individuals in the following methodologies such as complete intelligence surveillance, risk management, post marketing surveillance and design

controls. One of them stated that more notified bodies and sub notified bodies are required for the pre review approval process to be performed faster.

4.6.2 QUESTION 10: DO YOU THINK THE AMENDMENT MADE FOR THE MEDICAL DEVICE REGULATION (EU) 2017/745 AND IN VITRO MEDICAL DEVICE REGULATION (EU) 2017/746 IN EU IN 2017 WILL IMPROVE THE CONFIDENCE IN PATIENTS AND HEALTHCARE PROFESSIONALS CONCERNING THE SAFETY OF MEDICAL DEVICES?

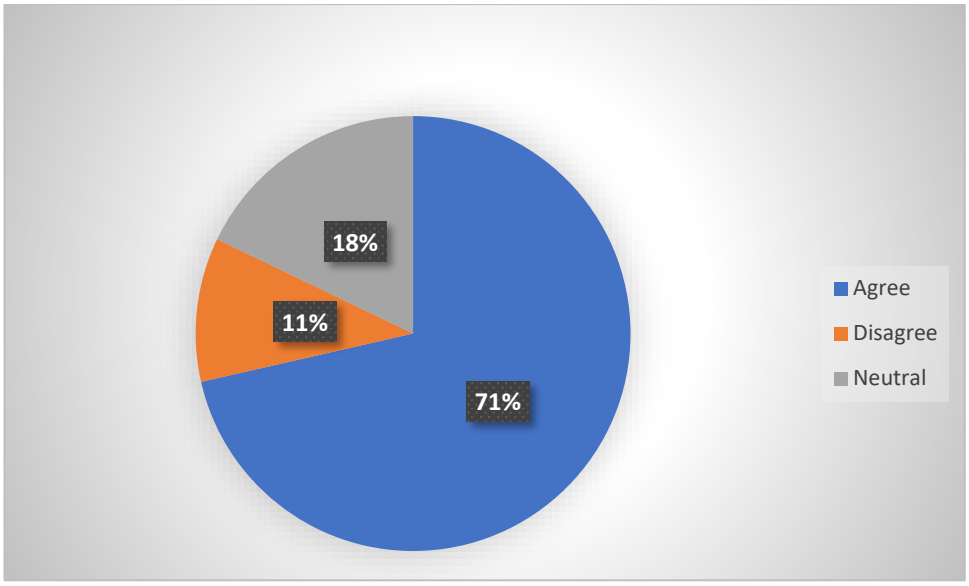

Figure 19. New EU Regulations and its Impact on Improving the Safety and Confidence of Patients

From the above pie chart 71% agreed to the statement that new EU regulations (MDR and IVDR) would improve the safety and confidence of patients whereas, a minor proportion (11%) disagreed to the statement and 18% were neutral on their opinion.

According to (Migliore, 2017, P. 921-922), the new regulations address all the problems and issues with the past regulations. With the advent of MDR, easier approval of medical devices would be used less frequently. Proper documentation is required. The responsibility and duties of the notified bodies are increased to have a balance which otherwise consider profit other than safety of patients. Access to clinical investigation data is the new aspect introduced in this regulation that improves traceability which was an obstacle in the previous directives.

The driving factor for the introduction of EU MDR was series of scandals in various specialities urogynaecology, orthopaedics and breast implants. Experts analysed many drawbacks of the previous regulation such as errors from the manufacturers and operators' side and recurring adverse issues related to the medical device. The new regulation will improve innovation and patient safety. These regulations enforce the establishment of a quality management system as per the risk classification. A person is entrusted with the responsibility to ensure compliance of medical devices by the manufacturer who has the expertise and acquired training in the area. (Shatrov and Blankart, 2022, p. 1233-1234).

4.6.3 QUESTION 11: WOULD IT BE CHALLENGING FOR PATIENTS WHEN THE MANUFACTURERS WITHDRAW THE EXISTING MEDICAL DEVICES FROM THE MARKET AFTER THE IMPLEMENTATION OF NEW MEDICAL DEVICE REGULATION (EU)2017/745 AND IN VITRO MEDICAL DEVICE REGULATION (EU) 2017/746 IN EU?

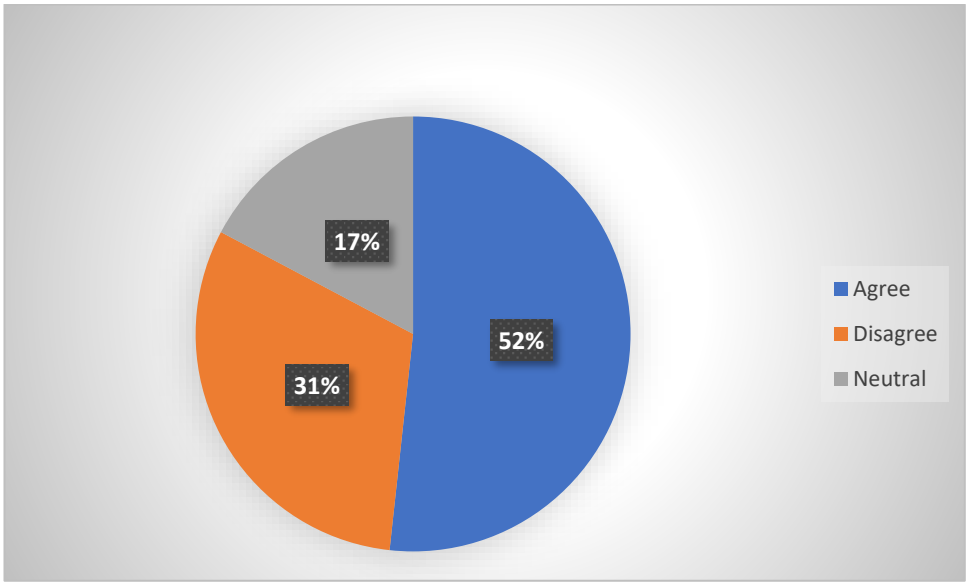

Figure 20. Impact on the Availability of Medical Devices after the Implementation of EU MDR

52% of the respondents agreed that it would be challenging for the patients for the accessibility of medical devices with the implementation of MDR, 31% opposed the statement and 17% was neutral on the matter.

According to Migliore (Migliore, 2017, p. 922), with the introduction of the revision the accessibility of medical devices could be reduced and market access delayed due to the

lack of resources for the small and medium enterprises to keep in pace with the requirements specified by the new regulations.

Moreover, small and medium sized enterprises are forced to release their products in other markets as the time and cost for under MDR are not known. The priority of the manufacturers would be recertification of medical devices under MDR which can be challenging as it would take more time (Vasiljeva *et al.*, 2020, p. 128).

4.6.4 QUESTION 12: ACCORDING TO YOUR VIEWPOINT DOES THE EXISTING NOTIFIED BODIES IN THE EU HAVE THE CAPACITY AND POTENTIAL FOR APPROVING THE MEDICAL DEVICES AS PER THE NEW REGULATORY FRAMEWORK OF THE EU?

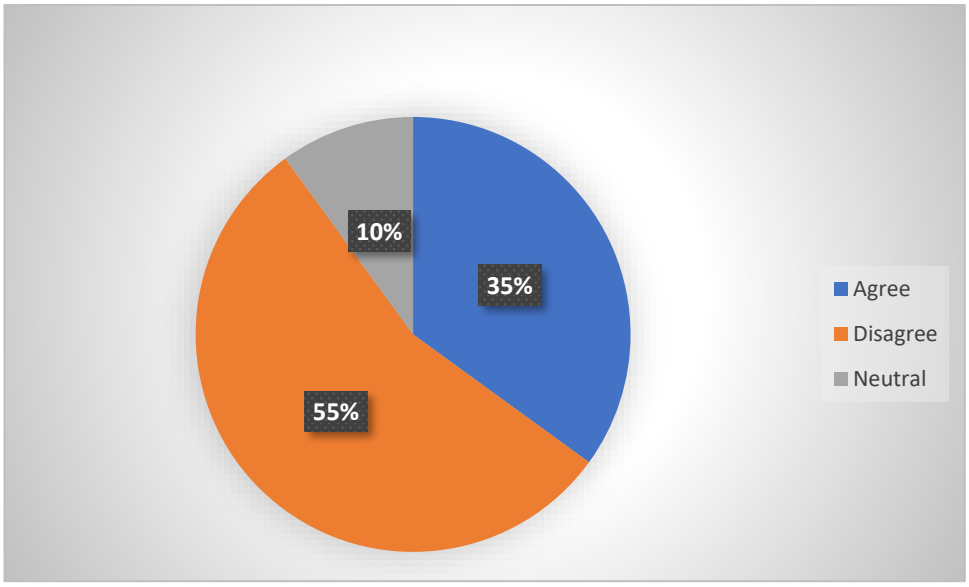

Figure 21. The Potential and Capacity of the Existing Notified Bodies in Approving Medical Devices as Per New EU Regulations

From the above pie chart, it can be inferred that 55% responded that the notified bodies in the EU does not have the capacity and potential for approving the medical devices as per the new regulatory framework, 35% agreed to the question and 10% stayed neutral.

According to a recent article (Fraser *et al.*, 2020, p. 2595), there are only 12 notified bodies which are given authority to function under MDR. Hence the reviewing process by the notified bodies has become slower. This strongly supports the delay in approval of the medical devices as number of notified bodies are less.

There are certain criteria to be fulfilled by the notified bodies under MDR. Many notified bodies have been withdrawn from the market as of 2021. Out of the 56 notified bodies only 20 have been assigned responsibility under MDR. This has created a great hurdle for

the manufacturers thus had slowed down the certification of medical devices (Shatrov and Blankart, 2022, p. 1237).

One of the main difficulties is the severe shortage of notified bodies for conformity assessment. With the change in the regulations the notified bodies already present has to get approval from the Competent Authority of the state to freely function (Vasiljeva *et al.*, 2020, p. 128).

The notified bodies have to align with the stricter regulations. This can be done with improving the resources and clinical expertise along with cross functional team to meet the stringent regulations. (Tarricone *et al.*, 2020, p. 3).

According to (Daigle and Torsekar, 2019, p. 15), the workload of the notified bodies would be laborious. All the formal procedures of regulatory, clinical evaluation, assessment and certification will take more time. Notified bodies and contract development and manufacturing organisations have observed this. The reduction in the number of notified bodies can cause issues in the internal market and strain on the other notified bodies. This further leads to decrease in the entry of new medical devices to the European market.

4.7 ANALYSIS OF OBJECTIVE 4: TO ANALYZE THE REASONS FOR MEDICAL DEVICE FAILURES AFTER THE APPROVAL FOR MARKETING IN US AND EUROPE.

4.7.1 QUESTION 13: REASONS FOR MEDICAL DEVICE FAILURES AFTER ITS APPROVAL IN US

The professionals working in the US have given a number of reasons for the medical device recalls and failures after the approval from the regulatory authority based on their working experience. One of the participants pointed out that pharmaceutical companies are unwilling to accept new technologies for the development of medical devices. The second participant commented that the non-conformities are caused by the patient's failure to adhere to the instructions for use provided by the manufacturer on the safety, efficacy and storage of the medical devices. Another reason is the potential to cause failure depends on the device, an issue in the software being used, insufficient separation in the product verification and validation. One of the major issues are with the insufficient application of design controls and risk management methodologies. A participant has

commented that approval of devices through 510 [k] pathway, lack of clinical effectiveness studies, lack of backup documentation has contributed to the failure. Inadequate supplier evaluations are also another reason.

4.7.2 QUESTION 14: REASONS FOR MEDICAL DEVICE FAILURES AFTER ITS APPROVAL IN EU

The participants working in the EU have also mentioned similar reasons as mentioned for the failure in US. People are reluctant to accept new technology in the pharmaceutical sector. The other major issues mentioned are insufficient verification, validation, quality assurance, risk management and poor post marketing surveillance. When considering the MDD, ineffective post marketing surveillance has an impact on the failure of the medical device. As mentioned by another respondent, there is a lack of device specific performance evaluation according to the standards and inadequate feedback from the clinician to make sure they have sufficient knowledge about a particular device technology. Wrong instructions for use and rushing to market the device is another explanation provided by a participant. Another professional clarified by addressing the implementation of risk control measures (inherent safety by design, protective measures in the medical device or in the manufacturing process and information for safety which are not in accordance with the intended use or intended purpose of the medical device as claimed by the manufacturer. An EU participant observed the mismatch between the documentation and manufacturing process which includes control on incoming goods. Any changes that occur for the devices after marketing are considered as standalone changes. However, if there are several changes to a device the overall impact of the changes has to be assessed.

CHAPTER 5: RESEARCH CONCLUSION

5. RESEARCH CONCLUSIONS

5.1 BASED ON THE FOUR MAIN RESEARCH OBJECTIVES

Objective 1: To find the differences involved in the regulations for medical devices in EU and US.

From the responses of the survey and review of the literature, there are not many notable differences in the regulatory framework. Both aim at improving the patient's safety. Under MDD, EU was lagging behind the safety and effectiveness of medical devices, it rather looked for providing easier access to medical devices. When considering the new EU regulations of MDR, the time taken for conformity assessment by the notified bodies is causing delay in the approval of marketing of medical devices. Both the US and EU had faced recalls which resulted in the amendments leading to stringent rules and regulation. From the survey it can be concluded that EU and US, both the regulatory framework is good. It cannot be said one is better than the other.

Even though there are positive aspects for both the regulations, some of the challenges faced by the EU MDR are more requirements for clinical evaluation of the device, more data on the research of the device representing safety and efficacy, lack of notified bodies and costs that has to be incurred by the firms to initiate and conduct all these formal procedures. US FDA also faces challenges in the requirements of labeling, maintaining quality management system and the database management containing information pertaining to the safety of the devices.

Another difference noted by comparison of both frameworks is the approval pathway of the devices where in FDA the government is directly involved in marketing authorization whereas in EU this is done by the notified bodies and competent authorities.

The most common way of granting marketing authorization in EU is compliance to essential requirements (safety, performance. Design and construction) and in US, it is the substantial equivalence or 510 [K] pathway by the comparison with its predicate.

It can be observed that the approval of medical devices through equivalence has its own merits and demerits. The marketing authorization through equivalence saves a lot of time of the manufacturers and regulatory authorities and increases the accessibility to the patients thereby compensating the shortage of medical devices.

When considering the revision of regulatory framework of medical devices in US there are conflicting views where when the regulations of US are eased there are high chances

of ineffective devices being placed on the market and when the regulations are made stringent the time taken by the medical devices to reach the market takes ages. The FDA is not ready to compromise on the safety of the patients. So, a revision must be made by balancing the accessibility and safety of medical devices.

Th EU has made a revision very recently where it underwent a transformation from MDD to MDR which has its own positive side and there are merits compared to the previous directives which include better transparency to the public regarding the data, device traceability, compensation is provided to the patients in case of any damage or adverse issues to name a few.

Objective 2: To understand the tools used for post-marketing surveillance for different classes of medical devices in EU and US.

The tools used in the post marketing surveillance tools are beneficial to the public as per the survey conducted. Proactive post marketing surveillance are considered better compared to reactive post marketing surveillance as prevention is better than the occurrence of a serious consequence which requires the regulators and manufacturers to devote more time from their regular schedule to resolve the issue.

Proper establishment of operations are required for effective post marketing surveillance. Both the medical device registries and patient registries help in achieving that thereby ensuring safety and quality of medical devices.

Legislation to increase the adverse event reporting by clinicians must be encouraged and enforced. Another key aspect is to collect information regarding the utilization of medical devices in the market.

To prevent recalls in the medical device industry the behaviour of the medical devices must be observed and studied in different environments and conditions and harmonized collection events must be set up in place that is evidence based.

From the literature review certain gaps were found in the post marketing surveillance which included inappropriate functioning and maintenance of the medical device registries, different response, and reporting rates of adverse events by various stakeholders.

Objective 3: To evaluate which areas of improvement need to be focused.

The main area to be improved in the US according to the opinions from survey in US is increased collaboration between the pharmaceutical industry and regulatory authorities and in EU was the proper guidance and clarity on regulatory requirements. The major challenge faced by both the regulations is to conduct clinical trials for devices with higher risk. QSMR must be completely implemented and harmonized with IMDRF.

Another area of improvement is the reduction of workload for the notified bodies by increasing the number of notified bodies which have the capability to scrutinize and maintain the compliance of manufacturers with the regulations.

Post marketing surveillance enhancement is another area which requires improvement. Healthcare professionals, manufacturers and patients must be encouraged to report any adverse effects from the devices and upload them to the database.

Proper quality management system must be in place with adequately trained staff and professional experience in the field.

Objective 4: To analyze the reasons for medical device failures after the approval for marketing in EU and US

Different responses were obtained for the reasons of medical device failures after its approval by the regulatory authorities. As medical devices have become an indispensable component of the healthcare sector, the quality related issues have resulted in major concern in the field of medical devices. It has a large impact on the people involved in the supply chain. It can range from minor to major undesirable outcomes.

It has been observed that the disinclination of the manufacturing companies to accept new technologies and innovations are one of the reasons for medical device failure. Those firms with higher research and development focus have higher risk of medical device recalls and it is decreased with those firms having previous experiences.

The initiative of FDA to publish weekly enforcement report is commendable as it provides all the relevant information about product recalls.

From different reasons of the failure, it is well understood that attention to detail is important, patient adherence to the instructions provided by the manufacturers is necessary

The financial consequences of these product recalls are beyond the scope of the study.

5.2 FINAL CONCLUSION

The research gave more insight to the regulatory framework of EU and US for the policymakers. Both the system has its own pros and cons. It cannot be concluded that one system is better than the other. The way the system executes their operations are different. More research is required after the complete transition of the EU MDR regulations to understand the benefits of the changes and other complications associated with its introduction. A comparison with EU MDR is also required with US FDA regulatory framework after its complete implementation. There must be more research in this area to understand the better outcomes of both these systems and adopting and harmonizing the regulations to maintain uniformity and standard. Both the system suggested that more clinical data and quality system management are required for the effective and safe approval of devices. There must also be increased participation for adverse events reporting for effective post marketing surveillance. All these can contribute to reduction in medical device failures.

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APPENDIX

QUESTIONNAIRE

SECTION 1

Dear Respondent,

I am Neenu Suresh, a post-graduate student at Griffith College Dublin, Ireland. I am conducting this survey for my dissertation on a comparative study of the regulatory requirements in European Union and United States for medical devices as part of the course of my study in Masters in Pharmaceutical Business and Technology.

The purpose of this study is to compare the differences on the regulatory framework of medical devices in the United States (US) and European Union (EU). It also assesses the post marketing surveillance methods used, reasons for medical device recalls after regulatory approval and areas of improvement to be considered in the regulatory sector of medical devices in the EU and US.

This survey is divided into Four sections, where the first section includes the general information of the participants. The second section is requested to be completed by both US and EU professionals in the regulatory sector. The third section is for professionals working in the US and the final section is for professionals working in the EU. The participation is completely voluntary, and you have the right to refuse participation, refuse any question and withdraw at any time without any consequences. Confidentiality and anonymity for all participants will be maintained and the data obtained from this survey will be solely used for the research and handled in compliance with current General Data Protection Regulation.

This survey takes about 10 minutes to complete. Thank you for your participation

SECTION 2

1. Do you understand the purpose of this survey?
    - Yes
    - No

2. Are you willing to participate in this survey?
    - Yes
    - No

3. How long have you been working in the regulatory sector?
    - 0-1 year
    - 1-5 year
    - >5years

SECTION 3

4. Which system in your opinion has the best regulatory framework for medical devices?
    - United States
    - European Union
    - Both
    - Cannot be compared

5. Do you agree to the statement that EU has faster accessibility to new medical devices treatment compared to US?
    - Agree
    - Disagree
    - Neutral

6. According to your opinion which is the best method for post marketing surveillance of medical devices?
    - Proactive Post market surveillance (Planned approach of gathering information in advance before a potential issue).
    - Reactive Post market surveillance (passive form of data collection activities when manufacturers respond after an event has occurred).

    Could you please elaborate your above answer?

    _____

SECTION 4

7. Which is the most common way of granting marketing authorization in the US for high-risk devices?
    - Clinical and non-clinical studies
    - Equivalence to existing product
    - Compliance to essential requirements (safety, performance. Design, construction)

8. How long will it take to grant the marketing approval of a medical device in the US?
    - Less than a year
    - 1-2 year
    - >2 years

9. Do you think a revision is required in the current US regulatory framework for medical devices?
    - Agree
    - Disagree
    - Neutral

10. Do you think that the existing post marketing surveillance tools in the US for medical devices are beneficial to the public?
    - Agree
    - Disagree
    - Neutral

11. In your opinion do you think it is safe for patients to use new medical devices approved through substantial equivalence to devices already on the market in US?
    - Agree
    - Disagree
    - Neutral

    Could you please elaborate the above answer?

    _____

12. According to your experience, what improvement must be made in the process of regulatory affairs for medical devices in the US?
    - Refine the regulatory process
    - Increased collaboration between the pharmaceutical industry and regulatory authorities
    - Proper guidance and clarity on regulatory requirements
    - Others (please specify)

    _____

13. From your experience, what are the reasons for medical device failures after its approval in the US?

SECTION 5

14. Which is the most common way of granting marketing authorization in EU for high-risk devices?
    - Clinical and non-clinical studies
    - Equivalence to existing product
    - Compliance to essential requirements (safety, performance. Design, construction)

15. How long will it take to grant the marketing approval of a medical device in EU?
    - Less than a year
    - 1-2 year
    - >2 year

16. Do you think a revision is required in the current EU regulatory framework for medical devices?
    - Agree
    - Disagree
    - Neutral

17. In your opinion do you think it is safe for the patients to use new medical devices approved through substantial equivalence to devices already on the market in EU?
    - Agree
    - Disagree
    - Neutral

    Could you please elaborate the above answer?

18. Do you think the amendment made for the medical device regulation (EU) 2017/745 and in vitro medical device regulation (EU) 2017/746 in European Union in 2017 will improve the confidence in patients and healthcare professionals concerning the safety of medical devices?
    - Agree
    - Disagree
    - Neutral

19. Would it be challenging for patients when the manufacturers withdraw the existing medical devices from the market after the implementation of new medical device regulation (EU)2017/745 and in vitro medical device regulation (EU) 2017/746 in European Union?
    - Agree
    - Disagree
    - Neutral

20. According to your viewpoint does the existing notified bodies in the EU have the capacity and potential for approving the medical devices as per the new regulatory framework of the European Union?
    - Agree
    - Disagree
    - Neutral

21. Do you think that the existing post marketing surveillance tools in the European Union for medical devices are beneficial to the public?
    - Agree
    - Disagree
    - Neutral

22. According to your experience, what improvement must be made in the process of regulatory affairs for medical devices in the EU?
    - Refine the regulatory process
    - Increased collaboration between the pharmaceutical industry and regulatory authorities
    - Proper guidance and clarity on regulatory requirements
    - Others (please specify)

23. From your experience, what are the reasons for medical device failures after its approval in EU?