Regulatory Landscape and comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in Pharmaceutical manufacturing facilities in India.

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

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CANDIDATE DECLARATION

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I certify that the dissertation entitled: “Regulatory Landscape and comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in Pharmaceutical manufacturing facilities in India” submitted for MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to work of others, due acknowledgment is given.

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ABSTRACT

Pharmaceutical manufacturing facilities constantly works on providing the people lifesaving drugs. Documentation is a vital process in the lifecycle of a drug. Batch records reflects the quality of specific lots of drugs manufactured. All industries are currently undergoing Digital Transformation and pharmaceutical manufacturing facilities are no exception. The main purpose of these research is to comparatively analyse Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in Pharmaceutical manufacturing facilities with different regulatory landscape in India and to evaluate whether the proposed technological platforms are effective in reducing the data integrity issues. The health regulatory system of India, The Central Drugs Standard Control Organization (CDSCO) provides only limited information regarding the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process. In conclusion, majority of the pharmaceutical manufacturing facilities operating in India follows strict regulatory systems like U.S. Food and Drug Administration (US FDA), Medical and Healthcare Products Regulatory Agency (MHRA), The European Medicines Agency (EMA), The National Health Surveillance Agency (ANVISA), Therapeutic Goods Administration (TGA), and Health Canada. At the same time, India has several small-scale pharmaceutical manufacturing facilities for supplying drug products to domestic markets and third countries like Africa, Nigeria, Zimbabwe, Uganda, Philippines, Sudan, Tanzania, Kenya, Ghana, Namibia, and Sri Lanka which are not highly regulated as the former regulatory systems. Strict and accepted regulatory systems have advanced technologies and are continuously promoting digitalization. In addition, the study also helps other researchers to understand about the regulatory landscape of India and supportive measures the Government should initiate for the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process.

Keywords: Manufacturing Execution System (MES) Software, Computer System Validation (CSV) Process, The Central Drugs Standard Control Organization (CDSCO) India, Data integrity, Patient safety.

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LIST OF ABBREVIATIONS

MES: Manufacturing Execution System

CSV: Computer System Validation

AR: Augmented Reality

VR: Virtual Reality

IoT: Internet if Things

US FDA: The United States Food and Drug Administration

CFR: The Code of Federal Regulations

CDSCO: The Central Drugs Standard Control Organization

ICH: The International Council for Harmonization of Technical Requirements of Pharmaceuticals for Human use.

GAMP: Good Automated Manufacturing Practices

ISPE: International Society for Pharmaceutical Engineering

ISO: International Organization for Standardization

PMDA: Pharmaceutical and Medical Devices Agency

EMA: The European Medicines Agency

GMP: Good Manufacturing Practices

IT: Information Technology

eBMR: Electronic Batch Manufacturing Records

KPI: Key Performance Indicators

PC: Personal computer

PLC: Programmable Logic Controllers

COTS: Commercial Off the Shelf

PMA: Pharmaceutical Manufacturers Association

SCADA: Supervisory Control and Data Acquisition

EU: The European Union

QA: Quality Assurance

QC: Quality Control

UK: United Kingdom

MHRA: Medical and Healthcare Products Regulatory Agency

EMI: Electro Magnetic Interference

RFI: Radio Frequency Interference

ESD: Electro Static Discharge

FS: Functional Specification

URS: User Requirement Specification

IQ: Installation Qualification

OQ: Operational Qualification

PQ: Performance Qualification

GDPR: General Data Protection Regulation

CSA: Computer System Assurance

ANVISA: The National Health Surveillance Agency

TGA: Therapeutic Goods Administration

WHO: World Health Organization

SAHPRA: South African Health Products Regulatory Authority

NAFDAC: The National Agency for Food and Drug Administration and Control

NMPB: National Medicines and Poisons Board

NDA: National Drug Authority

TMDA: Tanzania Medicines and Medical Device Authority

MCAZ: Medicines Control Authority of Zimbabwe

MOH, Yemen: Ministry of Public Health and Population, Yemen

PPB: Pharmacy and Poisons Board

FDA, Ghana: Food and Drug Authority, Ghana

MHSS: Ministry of Health and Amp; Social Services

FDA, Philippines: Food and Drug Administration, Philippines

MOH, Sri Lanka: Ministry of Health, Sri Lanka

GM: Gioia Methodology

ID: Identification

PIC/S: The Pharmaceutical Inspection Co-operation Scheme

QMS: Quality Management System

CHAPTER 1 - INTRODUCTION

Pharmaceutical manufacturing facilities constantly works on providing the people lifesaving drugs. Documentation is a vital process in the lifecycle of a drug. Batch records reflects the quality of specific lots of drugs manufactured.

The credibility of the manufacturing facility, the quality of the drug and the current good documentation practises will be under question if there is a breach in the data integrity. Innovative computerization technologies like Manufacturing Execution System (MES) Software(Saenz De Ugarte *et al.*, 2009) and Computer System Validation (CSV) Process are explored and researched in this study. Proposed technologies will not help and improve the data retention, retrieval but also it increases the traceability and security of the stored data(Johner, 2018).

All industries are currently undergoing Digital Transformation and pharmaceutical manufacturing facilities are no exception. The main advantage of digitalization is that all data and the information can be kept at single place which will produce medicinal products of superior quality to the public. Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process are two key elements in the digital transformation. The main role of the Manufacturing Execution System (MES) Software is to collect and provide information in real time and it will enable a paperless manufacturing process(NNIT, 2024b).

All the data in the pharmaceutical manufacturing facilities are generated and processes by computerized systems. Hence, it is mandatory to validate those computer systems in periodic intervals so that the data generated and processed will meet the quality criteria set by the different regulatory bodies(Carlos *et al.*, 2022).

1.1 Purpose of the Research Study

The main purpose of these research is to comparatively analyse Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities with different regulatory landscape and to evaluate whether the proposed technological platforms are effective in reducing the data integrity issues(eCFR, 2024). Manufacturing Execution System (MES) Software helps in increasing the efficiency of the overall manufacturing processes and quality of the production. Computer

System Validation (CSV) Process assures that all the computerized systems exactly perform the way it is designed to perform(Johner, 2018).

Figure 1.1 MES: Transformation from manual paper work to MES Software(Kynection, 2021)

MES Software is a key element in the digitalization of the Pharmaceutical manufacturing facilities and industry 4.0. MES Software helps to achieve paperless documentation and thereby preventing human data errors and data integrity issues.

The level of compliance enforced by the various regulatory bodies are divergent in different pharmaceutical manufacturing facilities. Therefore, a comparative analysis is highly beneficial to analyse Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process implementation in different pharmaceutical manufacturing facilities with different regulatory systems(eCFR, 2024).

Life cycle phases of CSV Process

Figure 1.1 CSV: Life cycle phases of CSV Process (Levi, 2023)

In the concept phase, the system will be defined and the risks will be identified. In the project phase overall system will be implemented and tested based on preapproved documents. Validation plans, software documentation and testing plans, traceability matrix are performed during this phase. Operation phase involves the day-to-day activities associated with the system which includes reliable data backup testing, business continuity and disaster recovery servers, and periodic reviews. The computer system will be no longer functional in this phase. Retirement is the final life cycle phase of the CSV Process(Levi, 2023).

The five objectives of the research study include comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process implementation in different pharmaceutical manufacturing facilities with different regulatory systems and the information provided by different regulatory systems on the need for digitalisation in pharmaceutical industries, to evaluate the advantages and disadvantages of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process implementation in oral solid dosage manufacturing process, to explore the types of Manufacturing Execution Systems (MES) software mostly used in different manufacturing facilities across the globe, to understand the challenges and barriers in the process of implementation of the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical companies with different regulatory systems, and to clarify the safety concerns associated with Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process implementation in different manufacturing facilities.

1.2 Hypothesis:

Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process are vital for maintaining the integrity of data and complying with the discrete regulatory landscape in different pharmaceutical manufacturing facilities. Stringent regulatory authorities have a profound impact on the implementation of these innovative technologies in pharmaceutical manufacturing facilities. Furthermore, if the regulatory systems are very stringent, it will be difficult to amend changes or revision to existing guidelines. Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process are really effective but expensive too, which makes it difficult for the small and medium size pharmaceutical manufacturing facilities to incorporate such innovative technologies.

1.3 Research Questions:

The main aim of this research was to collect information by mixed research methodology so that the following research questions can be answered.

- Do you agree or disagree that regulatory authorities have a crucial role in the implementation of MES Software in pharmaceutical manufacturing facilities through their regulatory guidelines?
- Do you agree or disagree that regulatory authorities have a crucial role in the implementation of CSV Process in pharmaceutical manufacturing facilities through their regulatory guidelines?
- Under what regulatory system does your company operates?
- Is your company using MES Software?
- In your opinion what are the advantages and disadvantages in implementation of MES Software in different pharmaceutical manufacturing facilities?
- In your opinion what are the advantages and disadvantages in implementation of CSV Process in different pharmaceutical manufacturing facilities?
- What are the types of MES Software operating in your workplace?
- In your opinion what are the challenges influencing adaptation of MES Software in different pharmaceutical manufacturing facilities?
- In your opinion what are the challenges influencing adaptation of CSV Process in different pharmaceutical manufacturing facilities?
- In your opinion what type of support Government authorities should initiate for the implementation of innovative computerization technologies?
- In your opinion what are the common safety attributes of MES Software in different pharmaceutical manufacturing facilities?
- In your opinion what are the common safety attributes of CSV Process in different pharmaceutical manufacturing facilities?

1.4 Research Objectives:

Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.

The level of compliance enforced by different regulatory bodies are not the same in different pharmaceutical manufacturing facilities. Therefore, a comparative analysis is highly beneficial to analyse Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process implementation in different pharmaceutical manufacturing facilities with different regulatory systems.

Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.

Evaluation the advantages and disadvantages Manufacturing Execution Systems (MES) Software is essential to understand the exact need for using such modern technologies over conventional paper documentation. Likewise, analysing the advantages and disadvantages of the Computer System Validation (CSV) Process, will be useful in understanding whether the proposed technological platform adds value in producing quality products.

Objective III: To examine the different types of Manufacturing Execution Systems (MES) software available across the industry.

By the evaluation of various types of Manufacturing Execution Systems (MES) Software used in Indian manufacturing facilities to other countries, it is highly advantageous for the pharmaceutical manufacturing companies to pick the most efficient Manufacturing Execution Systems (MES) Software available for implementation.

Objective IV: To analyse the challenges in the implementation of the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities in India.

The implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process may face various hurdles including financial, technological, resource, and regulatory hurdles. This dissertation helps to understand the various hurdles that need to manage for the effective implementation of Manufacturing Execution System (MES)

Software and Computer System Validation (CSV) Process in different pharmaceutical companies with different regulatory systems.

Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process.

All the safety concerns associated with Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process can be easily clarified or addressed by understanding the advanced safety features offered by the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process.

CHAPTER 2 - LITERATURE REVIEW

2.1 Digital Transformation in Pharmaceutical manufacturing facilities

Pharmaceutical manufacturing facilities must be willing to adapt and evolve by implementing newer technological platforms. Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process are the best examples of such innovative technological platforms(NNIT, 2024b). Information is one of the most important production assets and digitalization is a key factor in the management of the information in the pharmaceutical sector. Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process are two key elements in the digital architecture. Manufacturing Execution System (MES) Software helps in the real time capturing and processing of data and it removes the huge paper consumption in the production process(NNIT, 2024b). According to recent surveys by NNIT life sciences, 30 % of the pharmaceutical companies has not implemented Manufacturing Execution System (MES) Software. The main challenges are the complexity of Manufacturing Execution System (MES) Software, expensive nature of the projects, generation of a huge organizational change, and time consumption in the implementation of Manufacturing Execution System (MES) Software(NNIT, 2024a).

Manufacturing Execution System (MES) Software implementation is very complex. It involves careful selection of vendor and the type of the software required. The Manufacturing Execution System (MES) Software implementation may cause excess time consumption along with huge organizational change(NNIT, 2024a). Due to the expensive nature of the Manufacturing Execution System (MES) Software, the operation managers are often interested in buying newer equipment's or machineries instead of going for such systems. The huge organizational change produced by the Manufacturing Execution System (MES) Software implementation may cause unexpected delays in the manufacturing operations and may affect the overall output and profit of the firm(NNIT, 2024a). The Manufacturing Execution System (MES) Software should be developed, implemented, configured, installed, tested, and validated. This makes the whole process time consuming in nature. Usually, the standard implementation of Manufacturing Execution System (MES) Software will take 18-24 months(NNIT, 2024a).

Figure 2.1. Key benefits of Manufacturing Execution System (MES) Software (andreas, 2020)

Among all of the key benefits of the Manufacturing Execution System (MES) Software, traceability is a promising functionality. Any batch records of interest, details about the time stamped audit trails can be easily traced with help of MES. With the Key Performance Indicator, weakness of the manufacturing process can be easily identified and resolved. Scheduling can be achieved by timely planning and sequencing of activities. Another important feature is the real time data capturing facility offered by the MES Software. Various documents like standard operating procedures, logbooks, batch records can be easily managed and tracked using MES Software. Equipment in the pharmaceutical manufacturing facilities can be conveniently integrated to the MES Software thereby reducing the human errors while documenting processes(andreas, 2020).

In addition, MES Software helps in resource, machine, materials, labor allocations. Another advantage is the maintenance management that can be achieved by the implementation of Manufacturing Execution System (MES) Software. The underlying issues of the equipment used in the pharmaceutical manufacturing facilities can be easily foreseen and identified by the effective monitoring offered by the Manufacturing Execution System (MES) Software(SAP, 2024).

2.2 Steps in Computer System Validation (CSV) Process

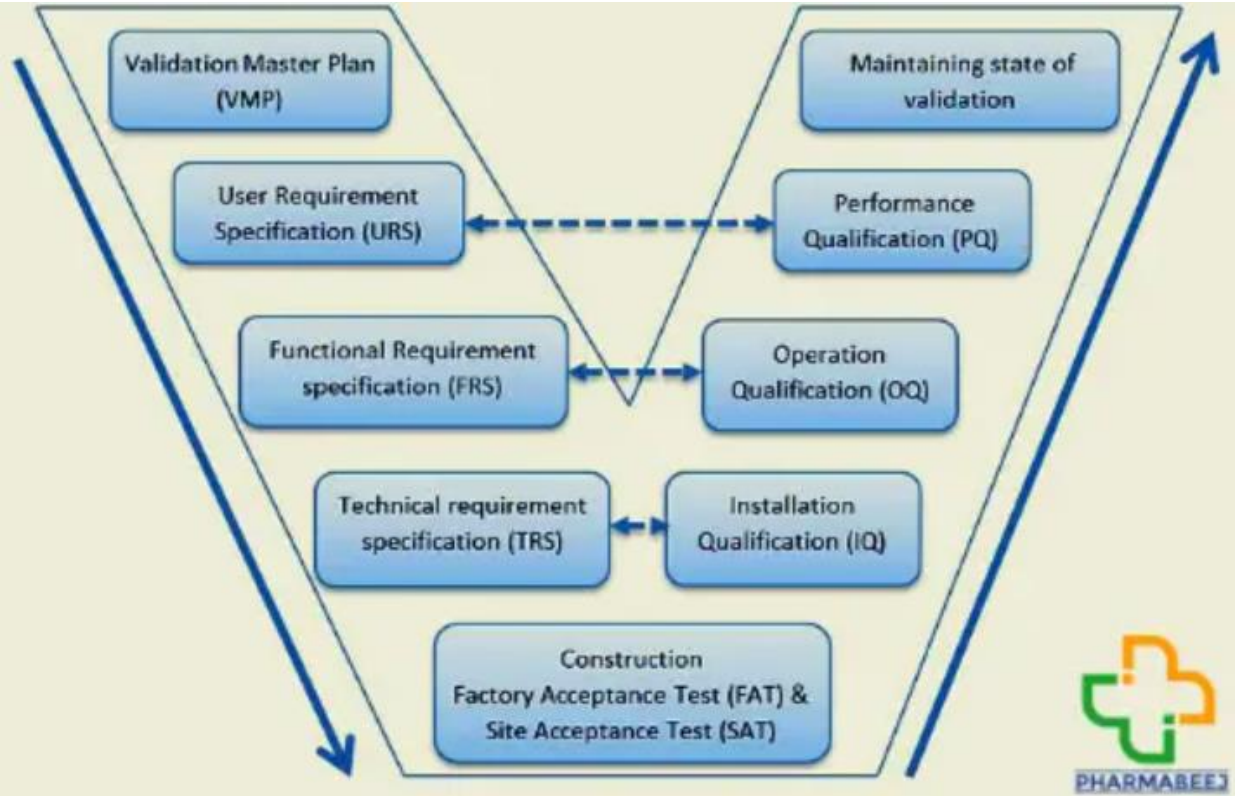

Figure 2.2. Steps in the Computer System Validation (Pharma Beej, 2024)

Site Preparations

The computer system's operating environment must be checked against its specification, including compliance with vendor recommendations, alignment with Engineering Line Diagrams, and accessibility of instrumentation. To assure overall quality of the process, manufacture, production facilities and quality control systems must be strictly commissioned and qualified in compliance with the GMP requirements(Gübitz, 2023).

Commissioning

Commissioning is the physical installation of a computer system, involving interface card addressing, field wiring checks, input/output continuity testing, and calibration and tuning of instrumentation(Wingate, 2004). It involves snagging to address unforeseen issues and errors, and verification is documented through Installation Qualification. Automation and digitalization are vital elements in the area of Commissioning(Gübitz, 2023).

Calibration

The ICH Good Manufacturing Guide for Active Pharmaceutical Ingredients recommends calibration of critical equipment and instrumentation according to established procedures and schedules. Calibrations should use traceable standards and be documented. Equipment that doesn't meet calibration criteria should be avoided. Deviations from calibration standards should be investigated to determine if they affect product quality since the last calibration(ICH, 2024).

The Good Automated Manufacturing Practices (GAMP) Good Practice Guide for Calibration Management recommends establishing a calibration master list, assigning unique numbers to all instruments, defining calibration methods in approved procedures, using more accurate measuring standards, tracing standards to recognized standards, using electronic systems, and ensuring competent personnel(Wingate, 2004).

Data Load

Data load is a crucial element in computer systems validation, and is determined by the integrity of data it processes. It involves five steps: data sourcing, mapping, collection, entry, and verification. Proper management of data load is essential in meeting both business and regulatory requirements. The receiver must get the same data that is forwarded from the receiver without any modifications(Rani *et al.*, 2023).

Installation Qualification

Installation Qualification is a process that verifies the installation of a computer system according to preapproved specifications. It involves confirming the integration of hardware, software, and instrumentation for the subsequent Operational Qualification activity(Wingate, 2004). Installation Qualification ensures that all the critical activities are in compliance with the installation(Amol Amrutkar *et al.*, 2022).

Operational Qualification

Operational Qualification (OQ) is a process that ensures a computer system operates according to preapproved specifications throughout its specified operating ranges. It begins after the successful completion of the Installation Qualification (IQ), which involves user acceptance testing to demonstrate the system's functionality under normal operating conditions and

realistic stress conditions(Wingate, 2004). It ensures the equipment works as it is intended to perform(Amol Amrutkar *et al.*, 2022).

Performance Qualification

Performance Qualification (PQ) is a crucial process in drug product manufacturing, ensuring a computer system is capable of controlling processes according to preapproved specifications and operating in its specified environment(Wingate, 2004). Performance Qualification (PQ) should be initiated after the successful completion of the Operational Qualification (OQ) stage, which includes product and process performance qualification (Amol Amrutkar *et al.*, 2022).

Validation Reports

Validation Reports are crucial documents that provide management with a review of the success of a validation exercise and any concessions made during it. They aim to seek approval for the completion and acceptance of the validation. When large documents need to be incorporated onto papers, the need for digitalization emerges(Carlos *et al.*, 2022).

Validation Certificate

Validation Certificate is a one-page summary statement defining constraints on a computer system(Wingate, 2004). These certificates are displayed alongside the system. Validation Certificates should be approved by Quality Assurance (QA) inspectors, as they are the highest level of evidence of validation(N and Kamaraj, 2020).

Periodic Review

After completion of data assessment, computer systems should be periodically reviewed to confirm their validated status(Amol Amrutkar *et al.*, 2022). Companies typically conduct these reviews every 12 months for their most critical systems. Intervals should not exceed 3 years to reduce undetected deviations. Less critical systems can be reviewed by product or physical area. Periodic reviews can combine process validation and computer validation. Criteria for selecting intervals and scope of review include the nature of use, system character, design changes, system performance, and changes to regulations(Wingate, 2004).

Effective collaboration with Quality Assurance department

Computer systems are complex and require constant evaluation and monitoring of processes. Clear and accurate documentation is crucial for these tasks. Staff often struggle with CSVs, collaboration with Quality Assurance department is found beneficial to solve the hurdles. The

department communicates with process managers, assesses the validity of CSVs, and assists with validation or re-validation. This ensures that both departments are well-informed about the processes and current Computer System Validation (CSV) Process requirements, ensuring efficient and effective management(Carlos *et al.*, 2022).

The Good Automated Manufacturing Practices (GAMP) 5 document emphasizes the importance of a risk-based approach in computer system validation. Identifying risks helps minimize the likelihood of risks occurring, strengthen opportunities, and improve overall performance(Carlos *et al.*, 2022).

Computer system validation had been made compulsory for medicinal product and medical device production processes by the regulatory authorities. This ensures companies can prove their systems function as expected, enhancing the process's effectiveness. A Computer System Validation (CSV) helps define processes, minimize risks, and increase opportunities, making the high investment in validation resources a long-term investment(Carlos *et al.*, 2022).

2.3 Manufacturing Execution System (MES) Software and Industry 4.0

Industry 4.0 is a transformation that uses data to inform intelligent actions in the physical world, improving efficiency and minimizing manual paper work. Manufacturing Execution System (MES) Software is crucial for real-time visibility of operations, reducing manual work and identifying areas of competitive advantage. Industry 4.0 focuses on reduced costs, improved quality, and higher throughput through smart products and equipment. Technologies required include IoT, mobile computing, cloud storage, big data, advanced analytics, machine learning, robotics, and VR/AR. A new Manufacturing Execution System (MES) Software must be Industry 4.0-ready, service-oriented, and adaptable, allowing for IoT data analysis, AR interaction, and running on mobile and cloud platforms(Shojaeinasab *et al.*, 2022).

This paper(Shojaeinasab *et al.*, 2022), provides a systematic literature review on smart manufacturing and industry 4.0, highlighting trends in MESs and manufacturing systems. It analyzes existing surveys, identifying technologies and research challenges. The paper presents main MES functionalities and five intelligence levels, evaluating novel industrial software systems. Based on findings, a conceptual model is proposed for Manufacturing Execution System (MES) Software tasks with prediction capabilities and high adaptability, suitable for the Fourth Industrial Revolution(Shojaeinasab *et al.*, 2022).

2.4 Economic efficiency of Manufacturing Execution System (MES) Software

A Manufacturing Execution System (MES) is an information system that monitors and tracks the production process on the factory floor, aiming to improve production output by tracking real-time data about the entire production lifecycle. It controls all activities, from customer orders to building layouts, ensuring efficient, low-cost, and high-quality production of pharmaceutical products(Aptean Staff Writer, 2020).

Companies often recognize process quality as a potential for increased operational efficiency in production. To assess economic efficiency, companies should define process-oriented objectives like reducing lead time, increasing machine utilization, improving delivery reliability, reducing work in progress inventories, and reducing defect costs. Reduced lead times are crucial for economic efficiency in production, impacting delivery time, customer satisfaction, inventory, and throughput(Aptean Staff Writer, 2020).

2.5 Regulatory Guidelines on Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process

Validation of computer systems is a mandatory and vital requirement as per U.S. FDA 21 CFR 11.10(a)(CFR - Code of Federal Regulations, 2023) and EudraLex (EU) annex 11(Steinborn, 2004). Along with this systems, guidelines of other regulatory systems including ICH(ICH, 2024), PMDA Japan(Yakushoku-kanma, 2010), CDSCO India(Central Drugs Standard Control Organization, 2024) will also be carefully evaluated All the Regulatory systems emphasize the importance of integrating the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process into the pharmaceutical manufacturing processes and documentation. By properly implementing Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process, we can improve the ICH Q7(Abraham, 2010) Quality regulatory requirements. Section 5.4 of the ICH Q7 module, explains the computerized systems, and section 6 explains the criteria for electronic documentation.

The webpage by Prof. Dr. Christian Johner “Computerized System Validation CSV” explains the need for computer system validation in all production and quality systems. According to (Johner, 2018).,in Europe, the Computer System Validation (CSV) Process is mandatory for all computers and automated data processing systems used in production and quality systems.

As per GAMP 5(ISPE, 2022), ISO 13485:2016, 21 CFR part 820.70, 21 CFR part 11 CSV Process is inevitable in production and quality systems(Johner, 2018).

Section 1.2 “Computerized Systems under regulation” of Pharmaceuticals and Medical Devices Agency (PMDA) Japan (Yakushoku-kanma, 2010) guidelines also describes the need for the implementation of the proposed systems. 21 CFR part 11 ELECTRONIC RECORDS; ELECTRONIC SIGNATURES, also explains in detail the need for a validated computer system and the strict regulations to be followed while performing such electronic batch documentation(eCFR, 2024).

2.6 History of Manufacturing Execution System (MES) Software

Manufacturing Execution System (MES) Software have evolved from simple data collection applications in the late 1980s to modern software in today's age. Manufacturing Execution System (MES) Software, first coined by AMR Research in 1992, is a dynamic information system that drives effective execution of manufacturing operations. It includes inventory management, material planning, control, and production definition(Aptean Staff Writer, 2020).

Manufacturing execution systems, which include data collection, scheduling, staff management, process management, performance analysis, and document management, can significantly improve profitability, on-time delivery, and product quality. Benefits include reduced manufacturing cycle time, data entry, work-in-process, lead times, and improved planning(Aptean Staff Writer, 2020).

In recent years, the pharmaceutical manufacturing space has been shaped by three key business drivers: quality and speed to market, sustainability, and lean manufacturing principles. Data-driven decision-making is crucial for these drivers, enabling faster optimizations through a unified platform approach and a "connected by intent" mindset. Manufacturing execution systems (MES) are at the heart of many companies' strategies to achieve this interconnectivity and improve decision-making(Cognizant, 2023).

2.7 Types of Manufacturing Execution System (MES) Software

Various types of Manufacturing Execution System (MES) Software are used in the pharmaceutical industries in India. Some of them includes Hitachi Manufacturing Execution System (MES) Software (HITACHI, 2024). Hitachi Manufacturing Execution System (MES) Software offers various tasks like inventory control, control over manufacturing operations,

quality and system control. The Hitachi manufacturing execution system is a software package that streamlines all pharmaceutical manufacturing processes, from stock production to production. It ensures high-quality, reliable pharmaceuticals by controlling manufacturing instructions and result records. The system reinforces manufacture control and quality control by controlling standard operation procedures, confirming tasks, and executing approvals. It also links a manufacturing plan with the key system, enabling data collection and sorting of production plans among processes, thereby achieving efficient production operation(HITACHI, 2024). The system promotes task accuracy by automatically collecting online data and preventing omissions in manufacturing records. It facilitates online and paperless operations, allowing for continuous flow of preparation, approval, and issuance of manufacturing instructions. It allows end-users to register SOPs and define forms, offering a wide range of systems to suit site scale. It also allows flexibility with system environment changes(HITACHI, 2024).

Another MES Software used in India is Laurel Manufacturing Execution System (MES) Software. This software is exclusively developed for the pharmaceutical manufacturing companies. Both batch manufacturing and batch packing records are developed by using this Manufacturing Execution System (MES) Software (Laurel MES, 2020). Laurel Manufacturing Execution System (MES) Software develops electronic batch manufacturing records (eBMR) which ensures that the products manufactured are of good quality and meets the regulatory standards. The Laurel MES (eBMR) Electronic Batch Manufacturing Record Management System is a low-code application developed in collaboration with the FDA's Good Manufacturing Practice. It ensures that drug production procedures are satisfactory and no procedures are overlooked. The Pharma Manufacturing Execution System package provides complete control over high-quality pharmaceutical production, standard operation procedures, task confirmation, and approval by control delegates. The pharmaceuticals and life science industry is expected to hold the largest market size for Manufacturing Execution System (MES) Software, seeking solutions to standardize manufacturing processes across multiple sites(Laurel MES, 2020).

2.8 Global MES Program Initiative

Another globally used Manufacturing Execution System (MES) Software is the POMS aquila Manufacturing Execution System (MES) Software company. They are providing Manufacturing Execution System (MES) Software services over 20 countries with over 25,000

clients. The main attraction is the “global MES program” initiative by the company. By using the integration of internal resources, the Manufacturing Execution System (MES) Software interface of companies with multi-site and multi-geography can be inter connected(POMS, 2024).

PAS-X developed by the Koerber in Germany. This software is used by more than 50 % of world’s top 30 pharmaceutical companies. The software complies with strict and stringent regulatory guidelines like 21 CFR part 211 and part 11, EudraLex and GAMP 5(Koerber Pharma Software, 2024). The main advantage of PAS-X is that it can be useful in both pharmaceutical and biopharmaceutical industries. The Manufacturing Execution System (MES) Software uses the advantage of Artificial Intelligence along with the PAS-X savvy suite platform and delivers promising results. Weighing and dispensing activities, electronic batch documentation, track and trace facilities, equipment management, KPI evaluation are some of the promising features offered by the PAS-X MES Software(Körber, 2024). Werum PAS-X Manufacturing Execution System (MES) from Körber is a market-leading software for pharma digitalization, production process transformation, and data integration. It offers more than just a manufacturing execution system; it also provides data management and analysis products, such as the Werum PAS-X Savvy Suite, which ensures problem-free production, quick problem resolution, and optimal process utilization. PAS-X's versatility extends to various industry segments and enterprise scales, making it a reliable foundation for AI in pharmaceutical and biotechnology production(Körber, 2024).

A scientific journal article, “Manufacturing execution system – a literature review” by B. Saenz de Ugarte et al., emphasizes the limitations and challenges that may arise in the Manufacturing Execution System (MES) Software implementation. This includes architectural, connectivity, and integration challenges. Connectivity is an essential factor that is required for the proper functioning of the Manufacturing Execution System (MES) Software system and should operate in real time basis(Aptean Staff Writer, 2020). Implementation of Manufacturing Execution System (MES) Software and the Computer System Validation (CSV) Process is not a big hurdle for highly regulated multinational companies; however, for small-sized or medium-scale companies, it is very difficult to implement this type of innovative technology. The journal article proposes limited insights on the economic implications of implementing Manufacturing Execution System (MES) Software in medium- or small-sized pharmaceutical companies(Saenz De Ugarte *et al.*, 2009).

The journal article published by (Shojaeinasab *et al.*, 2022), evaluates the different functionalities of the Manufacturing Execution System (MES) Software. It is evident from the findings of the journal that India is lagging behind other countries like the United States of America, Australia, China, England, and Singapore in providing research articles related to Manufacturing Execution System (MES) Software. This dissertation will not only benefit pharmaceutical manufacturing companies in India but also other countries. The journal provides information on Manufacturing Execution System (MES) Software; however, it fails to communicate the importance of validating such automated manufacturing systems.

Despite the global implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different countries, there is still a gap in the literature review regarding the Drug and Cosmetics Act 1940 guidelines followed by the CDSCO Indian regulatory system. Limited information is only available about the Computerized Systems in the Drug and Cosmetics Act 1940 guidelines followed by the CDSCO Indian regulatory system(ICH, 2024). This research will be beneficial for further researchers and pharmaceutical manufacturing facilities who would be interested in understanding the benefits of Manufacturing Execution System (MES) Software and the Computer System Validation (CSV) Process. In addition, the research will serve as a reference document for the future revisions of the guidelines (Drug and Cosmetics Act 1940: CDSCO) followed by the Indian regulatory systems.

2.9 History of Computer System Validation (CSV) Process

In the 1970s, computer systems were introduced in the pharmaceutical industry for real-time process control and monitoring. Later, they became information management systems, based on database engines. Initially based on dedicated hardware like personal computers (PCs), programmable logic controllers (PLCs), and mainframe computers, applications later utilized Commercial Off-The-Shelf (COTS) software. The need to validate computer systems emerged in 1979 with the introduction of GMP regulatory legislation in the United States. The first FDA citation for noncompliance was issued in 1985, followed by regulatory guidance for various practices in 1982. In 1983, the FDA issued the Blue Book, introducing a documented life-cycle approach to computer system validation. This aimed to build quality into software from the earliest stages of the life cycle, rather than testing it at the end. The Pharmaceutical Manufacturers Association (PMA) formed a Computer Systems Validation Committee to represent industry views. A Position Paper presented prospective and retrospective validation

approaches, with GxP legislation requiring compliance in both new and existing facilities. Debates on computer systems validation primarily focused in the United States.(Wingate, 2004)

2.10 Importance of Computer System Validation (CSV) Process

Computer system validation (CSV) is a crucial process to ensure a computer system performs its intended purpose. It involves checking system requirements and stakeholder requirements. High demands are placed on computer-assisted systems, particularly in the pharmaceutical industry. Once validated, a computer-assisted system must comply with regulations and avoid mistakes, as outlined in FDA warning letters(Carlos *et al.*, 2022).

Computers and automated equipment are used in various pharmaceutical company operations, including research, development, and production. Embedded systems like programmable logic, Supervisory Control and Data Acquisition (SCADA), and robotics are increasingly used. Software tools are used to design and test computer systems, and commercial software applications are used for system implementation. All computerized equipment, systems, and applications are subject to GxP regulations and computer software validation(Bendale *et al.*, 2011).

The FDA regularly audits companies under FDA regulations, making the observations public. Warning letters provide valuable information on mistakes made by companies, including Computer System Validation. These letters contain information on observations and corrective actions. If not met, a report is published, instructing companies to correct mistakes. This is crucial as it may affect the company's reputation, economic consequences, and prevents continued production of sub-standard products(Carlos *et al.*, 2022).

The FDA warns against common mistakes in computer system validation, such as lack of backups, access restrictions, neglecting software's data storage capabilities, incomplete documentation, data protection, lack of user accounts, and using unvalidated spreadsheets. These errors can lead to data breaches and misuse of computer systems(Johner, 2018).

Today, two-thirds of the inspections include some aspect of computer systems validation, and this trend is expected to continue(Wingate, 2004). Many regulatory authorities have sent inspectors on training programs for computer systems validation in countries like France, Germany, Norway, Poland, Singapore, and Sweden. In the future, up to one-fifth of FDA/MHRA inspection time could be devoted to assessing computer system usage and

validation steps. The complexity of data systems and data integrity challenges are significant(Carlos *et al.*, 2022).

Computerized systems require documented authorization for usage and recording of any restrictions resulting from their validated status at the time of authorization. Before implementing changes that affect a computer system's validated status, they must be approved. The FDA and U.K. MHRA have been increasing their scrutiny of computer systems in the pharmaceutical and healthcare industries since 2000. Before 2000, less than half of inspections included computer systems validation(Carlos *et al.*, 2022).

System Owners/Users and Developer/Operational Support organizations are responsible for ensuring computer systems used in pharmaceutical regulatory areas comply with agency regulations, validated, and used in compliance. System access must be restricted to authorized individuals, with authority checks in place to ensure only authorized users can access the system, sign records, and perform operations. Operational system checks enforce permitted sequencing of steps and events. Device checks verify data input or instruction validity. Signings must verify identity and password, and electronic signatures unique to individual users should be used for approval and authorization. Electronic records signed must include the signer's name, execution date and time, and the meaning associated with the signature, which must be included in any human-readable form(Wingate, 2004). Validation should follow predefined procedures to enhance quality throughout the computer system life cycle, with their effectiveness assessed periodically and improvements made as needed. System requirements must be traceable throughout validation records, and suppliers must be managed to ensure software, hardware, and services are fit for purpose(Carlos *et al.*, 2022).

CHAPTER 3 - RESEARCH METHODOLOGY

Research study can be defined as an investigation for acquiring new knowledge using systematic, scientific, and analytical approach(Verma *et al.*, 2024). The purpose of the research study is to find answers for the research questions(Verma *et al.*, 2024).

According to (Kothari, 2004)., research methodology is the systematic way to solve the research problem. Qualitative methodology will not be having a clear starting and finishing point. Depth interviews are example for qualitative methodology. The researcher or interviewer must plan his interview schedule and choose a suitable place and time so that the interviewee

will be in a relaxed state. The interviewer's approach to the interviewee should be polite and informal. The interviewer should possess the ability to listen with curiosity, understanding, and respect.

In this research, all the specific research questions mentioned with the research objectives are planned to be solved by the survey questionnaire development methodology and by conducting interviews with experts. The participants required for answering the questionnaire will be selected randomly having/ not having work experience and exposure in the fields of manufacturing execution systems and the computer system validation field associated with the pharmaceutical sector which makes the comparison of data easier. However, participants who do not have any practical pharmaceutical industry knowledge will be excluded from the study.

The primary research mainly aims in exploring the benefits of MES Software integration with batch documents. The data involving installation, validation and the usability of the MES Software will be analysed. Various benefits of MES Software including audit trail batch reports and alarms, online batch record review process, recipe creation and management, sample collection, electronic signature integration into the batch records will be investigated through the research. The prepared questionnaires will be having provisions to answer about the future concepts of MES Software and CSV Process. Their role in developing a pharma 4.0 centred pharmaceutical manufacturing facilities will be investigated.

Research is a systematic and scientific search for knowledge on a specific topic. It involves defining problems, formulating hypotheses, collecting and evaluating data, making deductions, reaching conclusions, and evaluating them to determine if they meet the formulated hypothesis(Kothari, 2004).

A good research must be logical, empirical, systematic, and replicable(Verma *et al.*, 2024).

3.1 Research Philosophy

According to (Saunders *et al.*, 2023).,research methodology contains structured plan of the research project. The research design employed in research can be of 3 types: Qualitative analysis, Quantitative analysis, and mixed research method.

This research will be performed by mixed research methodology which is a combination of both qualitative and quantitative methodologies(Saunders *et al.*, 2023).

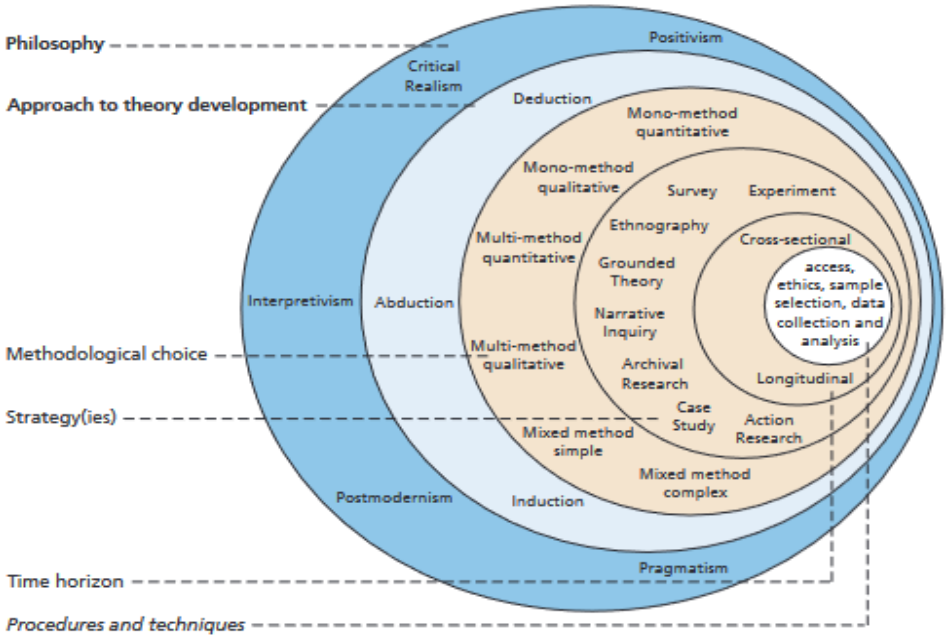

Figure 3.1 Research Onion (Saunders et al., 2023)

According to the Research Onion, the five research philosophies are Positivism, Interpretivism, Pragmatism, and Realism. Positivism is based on deductive research approach which is normally hypothesis testing. Interpretivism is based on inductive approach which is hypothesis building. Pragmatism is a combination of positivism and interpretivism(Mitchell, 2018).

This research study falls under Pragmatism research philosophy since it is a mixed method research and is a combination of deductive and inductive approach. In Pragmatism, two paradigms are combined together.

3.2 Research Approach

Research Approach can be either deductive or inductive(Saunders *et al.*, 2023). Deductive approach is theory testing and inductive approach is theory building(Mitchell, 2018).

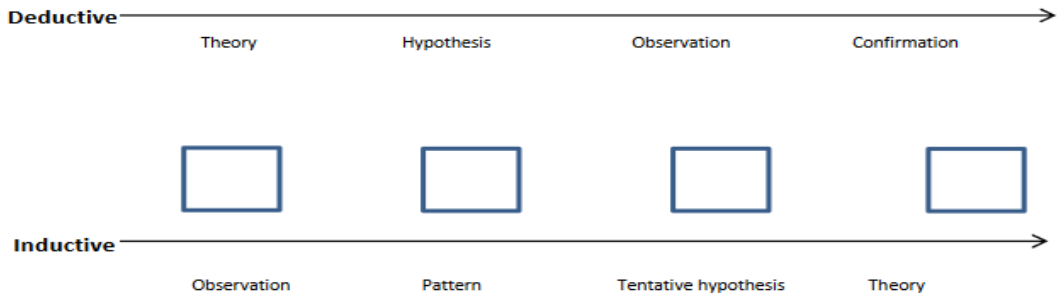

Figure 3.2 Research Approach (Mitchell, 2018)

This dissertation is a combination of deductive and inductive approach. It involves qualitative data collection methods like interviews, open-ended survey questionnaires, and critical analysis of academic books, journals, company websites, official government websites of different regulatory authorities which is an inductive approach. In addition, this research study also consists of closed-ended survey questionnaire which is a quantitative data collection method and belongs to deductive research approach(Mitchell, 2018).

3.3 Research design

Research design provides the structure for the research(Verma *et al.*, 2024). The commonly employed research designs are Exploratory and Conclusive designs. Exploratory design is a combination of Primary research methods and secondary research methods whereas Conclusive design is heavily dependent on quantitative data(Voxco, 2021). The Primary research of this dissertation consists of data collection by interviews and surveys and the Secondary research consists of the evaluation of academic books, published scientific journals, articles, company websites, and official government websites of different regulatory authorities(Voxco, 2021). Therefore, this research study is more of an exploratory study than the conclusive one.

3.4 Primary Research Strategy

Quantitative methodology usually deals with numerical values(Verma *et al.*, 2024). It has a clear starting and finishing point. The interpretation of the quantitative results is generally dependant to the interpretation made by the researcher. In this methodology, the researcher tests the theory by means of a conceptual model(Jonker and Pennink, 2009). Questionnaire preparation is an example for quantitative analysis. Questionnaire is form of interview on paper. The title of the questionnaire should be precise and clear(Verma *et al.*, 2024). It can be of two types; open form and close form questionnaires. Open form questionnaires are selected when comprehensive responses are required. Close form questionnaire are generally “Yes or No” questions(Singh, 2006).

3.5 Secondary Research Strategy

The secondary research methodology includes the evaluation of academic books, published scientific journals, articles, and company websites related to the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process technologies, ICH

official website(ICH, 2024) which provides all the ICH regulatory guidelines, webpages that explain the advanced technologies, and peer-reviewed journals for assessing the benefits of proposed methods and their challenges. Secondary sources like academic books, published scientific journals, articles, and company websites related to Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process were carefully analysed for the relevance of these modern technologies(ICH, 2024).

3.6 Research Choice

The different Research choices includes Mono choice, multi choice, and mixed choice. Mono choice is the technique in which the researcher typically employs only one strategy. But in the mixed choice, the researcher uses both qualitative and quantitative methods in the research study(Saunders *et al.*, 2023). In Multi choice, more than one mainly qualitative or more than one mainly quantitative methods will be used in the research study(Vizcarguenaga-Aguirre, 2020).

This research study is a mixed choice research since, it employs both qualitative as well as quantitative data collection methods.

3.7 Time horizon

Time horizon gives an idea about the time period required for the completion of the research study(Saunders *et al.*, 2023). Cross sectional study will be completed in a short span of time and longitudinal study which will be completed gradually over a longer period of time. longitudinal study is really helpful in understanding the variations or changes that happen gradually over time.(Iovino and Tsitsianis, 2020).

The total time horizon of this research study is only 3 months which makes it a Cross sectional study.

3.8 Study Population and Sample Size

Quantitative methodology in this research consists of developing survey questionnaires of approximately 80-120 participants. Qualitative methodology involves conducting interviews in approximately 8-10 participants through telephone or zoom meetings. Participants of this research mainly professionals who are having knowledge or working in pharmaceutical industry in the field of Manufacturing Execution System Software, and Computer System Validation Process. Questions prepared for the interview will not create any bias in the mind

of the participant(Saunders *et al.*, 2023). The questionnaire in this research will be designed in such a way that respondents will be interested in reading it. Provisions for broad answers, and repetitive questions will be avoided in the questionnaire. The selection criteria will be such that all the participants will have adequate knowledge of the pharmaceutical industries and a comparative study will be performed to distinguish the advantages of MES Software and CSV Process over conventional paper documentation(Saunders *et al.*, 2023).

Sample size for the survey questionnaires was calculated by using Sample Size Calculator(calculator.net, 2024). A sample size of 97 was calculated using a confidence level of 95% and margin of error of 10%(calculator.net, 2024).

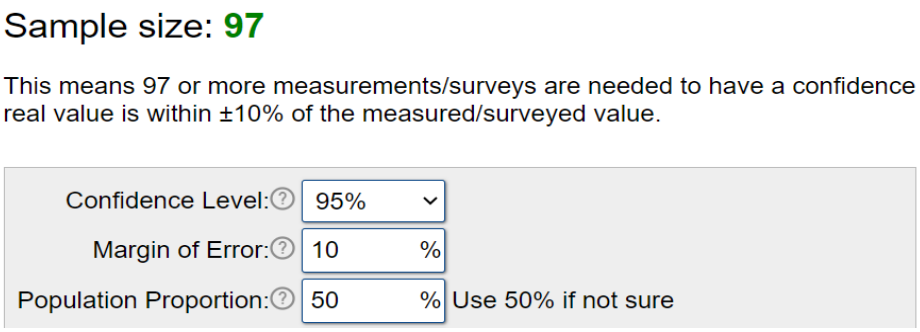

Figure 3.3 Sample Size Calculation (calculator.net, 2024)

3.9 Data Collection

Access of data for the research can be of 4 types: traditional access, internet mediated access, intranet mediated access, and hybrid access(Saunders *et al.*, 2023).

Traditional access involves face to face interviews or collection of data in the form of survey questionnaires in person. This research involves internet mediated access of data: internet mediated access involves collection of data in the form of interviews or questionnaires through internet platform. Intranet mediated access is the collection of data within the organisation by using their company intranet facility. Hybrid access is a combination of internet mediated and traditional access of data(Saunders *et al.*, 2023).

In this research, utmost care will be taken by using suitable language, facilitating replies, developing access only in an incremental pattern, providing a clear account on the purpose of the research(Saunders *et al.*, 2023).

3.10 Data analysis

This research will be conducted as per mixed research methodology. Survey questionnaires containing closed ended questionnaires will be analysed by Likert Scale(Bhandari, 2020) and qualitative data (interviews and open ended survey questionnaires) will be analysed by Thematic Approach or Gioia data analysis tool(Magnani and Gioia, 2023). The collected raw data should be treated so as to make it significant, meaningful and derive inferences and conclusions(Singh, 2006).

3.11 Likert Scale Approach:

Likert scale technique is the evaluation of opinions, behaviour, and attitudes by means of a rating scale(Bhandari, 2020). The technique consists of a question or a statement followed by five-point or seven-point scale of answer statements. The rating scale generally contains five or seven options and the options at both ends are termed as response anchors. The midpoint option on the scale will be usually a neutral response.

The format of a five-point Likert scale will be as follows:

1. Strongly agree
2. Agree
3. Neither agree nor disagree
4. Disagree
5. Strongly disagree

3.12 Gioia methodology:

Gioia methodology is a qualitative approach of data analysis to meet the stringent standards of a trustworthy research and mostly employed for interviews and open-ended survey questionnaires as well(Magnani and Gioia, 2023).

The Gioia approach is based on 3 concepts:

1) Development of a data structure.

Creation of analytical codes and categories, are categorised to form data structures of first order and second order themes.

2) Development of an established model based on the data structure.

Constant comparison of acquired data structure is performed over time and an established model is constructed from the data structure.

3) Describing results in a conclusive narrative.

Detailed data-based narrative will be made using the first order and second order themes of data structures(Magnani and Gioia, 2023).

and should not be published without consent(Saunders *et al.*, 2023).

3.13 Ethical Considerations

Research ethics are the standards of the research behaviour to safeguard the rights of the subjects involved in the research. All social norms should be followed throughout the research. For safeguarding the rights of the subjects, code of ethics is developed. Code of ethics prevent malpractice, harm, poor practices of research and provides quality, integrity, and ethical practice to the research work(Saunders *et al.*, 2023).

Ethics and access are two crucial factors that determines the success of a research. Ethics will be followed while performing both primary and secondary research. Care has to be taken while accessing data for the research, it should fulfil all the ethical requirements. Ethical concerns are high when the research is involved with human participants. This research involves mixed method research methodology and hence all measures will be taken to meet the ethical requirements. Ethical committee approval will be obtained for the commencement of the research and will be documented. Any conflicts of interests, or commercial interests should be declared, researcher must be truthful and honest towards the research. This research will be treated with trust and respect. All measures will be followed to avoid any sort of harm to the subjects which includes violation of confidentiality, mental or social pressure, embarrassment, stress, pain, and discrimination. Privacy of the participants will be maintained; informed consent of the participants will be collected. Participants identity will be kept anonymous and care will be taken from all sorts of abuse (physical, mental or verbal abuses)(Saunders *et al.*, 2023).

Ethical issues associated with internet mediated research(Saunders *et al.*, 2023)

Deception: Collection of data from online communities by researchers without participation or informed consent is termed as “Lurking” and often considered as unethical.

Disrespectful behaviour: All behaviours causing disrespect or harm to the online communities should be avoided.

Informed consent: informed consent of participants should be mandatorily collected while commencing internet mediated online research.

Netiquette: Set of standards to promote courtesy and privacy. All private messages should not be made public and confidentiality should be maintained.

GDPR: After the implementation of General Data Protection Regulation EU 2016/679 (GDPR), both EU and UK GDPR have set clear rules for safeguarding the personal data of the subjects or participants.

Anonymised data: The data regarding name, and other identifiers should be kept anonymous.

3.14 Conceptual Framework

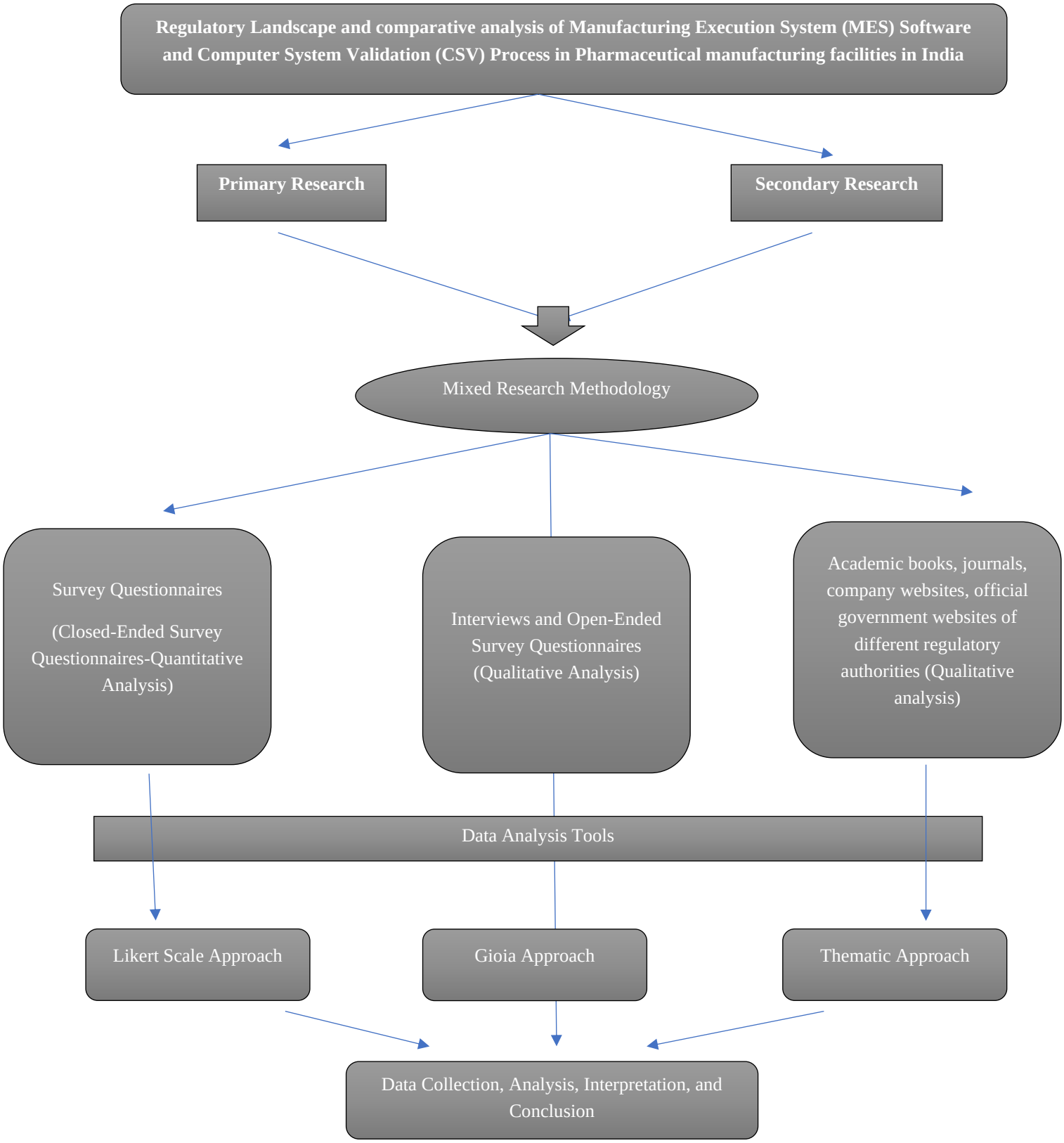

Figure 3.4 Conceptual Framework

CHAPTER 4 – FINDINGS AND ANALYSIS

All the data collected from survey questionnaire was analysed Likert Scale. Qualitative analysis was conducted through Zoom interviews with approximately 8–10 professionals who have knowledge or work expertise in the pharmaceutical industry in the field of Manufacturing Execution System (MES) Software, and computer system validation (CSV) Process. All the recorded interviews were analysed using Gioia Approach.

Quantitative Data Analysis- Analysis of Survey questionnaire by Likert Scale

Likert scale is usually a 5- or 7- point rating scale used to rate the degree to which a participant agrees or disagrees to a particular statement(Sullivan and Artino, 2013). In this research, closed ended questionnaires will be answered by sending survey questionnaires to the participants. A total of 97 survey questionnaires were circulated among 97 participants and 97 responses were collected. Generally, Likert scale is used to interpret opinions, perceptions and attitudes of the research participants. Likert scale can be broadly classified into two: Symmetric Likert scale and Asymmetric Likert scale(Joshi *et al.*, 2015). It generally consists of three or more statements, that usually evaluate an attitude, trait or behaviour. Likert scale was originally developed by Rensis Likert. Likert scale contains 3 parts, "I) Preamble: which is an introductory statement, II) Indicators or items: statements or questions of the scale, and III) Descriptive anchors: Descriptors with score that the participants mark or tick(Alhassn *et al.*, 2022).

Qualitative Data Analysis – Analysis of Interviews by Gioia approach

Qualitative analysis can be performed by 5 approaches(Salamzadeh, 2020):

- Gioia Approach: Theoretical coding structures are extensively employed in this approach for organizing the texts. Interviews and archival data are the primary sources of data in this approach.
- Vignettes Approach: Short stories are developed from the data text in this approach. Usually, Ethnographic data serves as the primary sources of data in this approach.
- Temporal Phases: In this approach, a story will be unfolded over time using the data text. Interviews, archival data, and ethnographic data are used as primary data sources.
- Long data Excerpts: In this approach, data text is represented as conversational exchange structure texts. In this approach long text segments are used to represent the

data. Interviews and ethnographic data are used as primary data sources in this approach.

- Anthropological approach: In this approach, the overall research context will be organised in the text. Ethnographic data are the primary data sources used in this approach.

The abbreviation of Gioia Methodology is GM. It is a data analysis tool used to meet the rigorous standards of a trustworthy research. Gioia methodology is extensively used to analyse the data of the qualitative research(Salamzadeh, 2020). The Gioia Methodology is based on three principles(Kaspar, 2024):

- Data structure development Initially all the collected data will be organised and categorised in a structural way to facilitate data analysis.
- Grounded Model development: Based on the categorised data structure, a grounded model will be developed and ultimately it will be a theoretical framework of the data structure.
- Presenting all the findings: All the findings will be articulated in a conclusive manner.

Gioia Methodology helps the researcher to develop new ideas and theories while performing data interpretation. This methodology makes the overall research study credible and trustworthy(Kaspar, 2024). A total of 3 coding structures will be used in this approach. First-order codes, second-order codes, and third-order codes. First-order codes are basically the summary of the responses of the participants asked during the interview. Second-order codes are used for distillation of first-order codes and third-order codes will distil the second-order codes and generally it is singular ideas or concepts.

Zoom interviews conducted with professionals who are having knowledge or work expertise in pharmaceutical industry in the field of MES Software, and CSV Process. Interviews of 12 participants were completed. 6 participants were experts having Manufacturing Execution System (MES) Software experience and 6 were Computer System Validation consultants. Gioia approach is used to develop new concepts. Gioia is used to develop a systematic research approach. First step is the development of data structure by the use of analytical codes and categories containing information and theory centred themes. Second phase is the development of a grounded model using data structure followed by the final presentation of narrative which is based on the grounded theory model(Magnani and Gioia, 2023).

4.1 Demographic Representation of Respondents from the Survey Questionnaire

4.1.1 The various groups/segments of the respondent from the survey questionnaire

Table 4.1.1 Distribution of respondents according to the various groups/segments

Respondents	Male	Female	Total
Quality Assurance (QA)	13 (13.4%)	0	13 (13.4%)
Quality Control (QC)	4 (4.1%)	8 (8.2%)	12 (12.4%)
Production department	10 (10.3%)	0	10 (10.3%)
Microbiology department	6 (6.2%)	6 (6.2%)	12 (12.4%)
Engineering department	8 (8.2%)	3 (3.1%)	11 (11.3%)
Warehouse department	5 (5.2%)	8 (8.2%)	13 (13.4%)
Research and Development	10 (10.3%)	3 (3.1%)	13 (13.4%)
Environment Health and Safety	9 (9.3%)	4 (4.1%)	13 (13.4%)
Total	65 (67.0%)	32 (33.0%)	97 (100%)

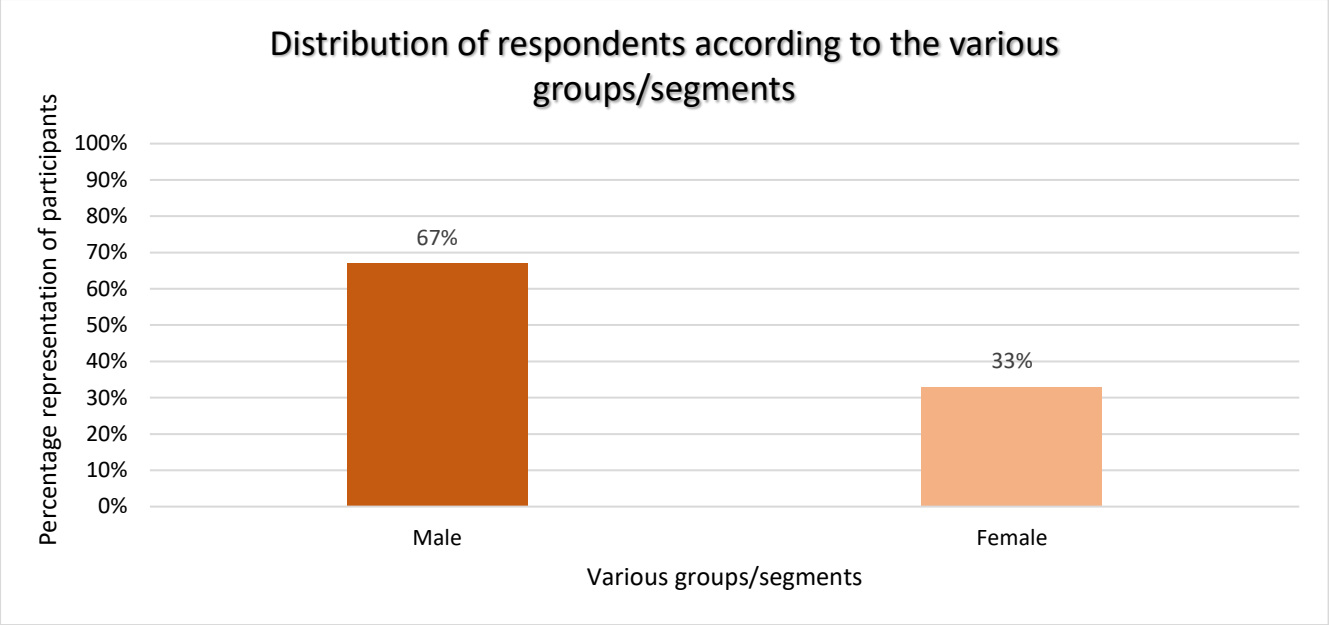

Figure 4.1.1 Clustered column chart representing the percentage distribution of respondents according to their department of expertise.

Table 4.1.1 and figure 4.1.1 above display the distribution of respondents according to their department of expertise. Each department or area of expertise has a proportionate representation among the respondents. Closed-ended survey questionnaires were circulated to 97(100%) participants. Quality Assurance, Warehouse, Research and Development, and Environment Health and Safety have the highest representation with 13(13.4%) each, while Production department has the lowest representation with 10(10.3%). 11(11.3%) respondents of the Engineering department answered to the survey. Microbiology and Quality Control responded equally with 12(12.4%).

4.1.2 The work experience level of the respondent from the survey questionnaire

Table 4.1.2 Distribution of respondents according to their work experience level

Respondents	Less than 1Yr	1Yr- 3Yr	3Yr-5Yr	5Yr-15Yr	Above 15Yr	Total
Quality Assurance (QA)	0	1 (1.0%)	2 (2.1%)	8 (8.2%)	2 (2.1%)	13 (13.4%)
Quality Control (QC)	3 (3.1%)	5 (5.2%)	2 (2.1%)	2 (2.1%)	0	12 (12.4%)

Production department	0	0	2 (2.1%)	7 (7.2%)	1 (1.0%)	10 (10.3%)
Microbiology department	1 (1.0%)	2 (2.1%)	4 (4.1%)	3 (3.1%)	2 (2.1%)	12 (12.4%)
Engineering department	6 (6.2%)	1 (1.0%)	0	2 (2.1%)	2(2.1%)	11 (11.3%)
Warehouse department	7 (7.2%)	3 (3.1%)	2 (2.1%)	0	1 (1.0%)	13 (13.4%)
Research and Development	0	3 (3.1%)	4 (4.1%)	5 (5.2%)	1 (1.0%)	13 (13.4%)
Environment Health and Safety	1 (1.0%)	2 (2.1%)	5 (5.2%)	3 (3.1%)	2 (2.1%)	13 (13.4%)
Total	**18 (18.6%)**	**17 (17.5%)**	**21 (21.6%)**	**30 (30.9%)**	**11 (11.3%)**	**97 (100%)**

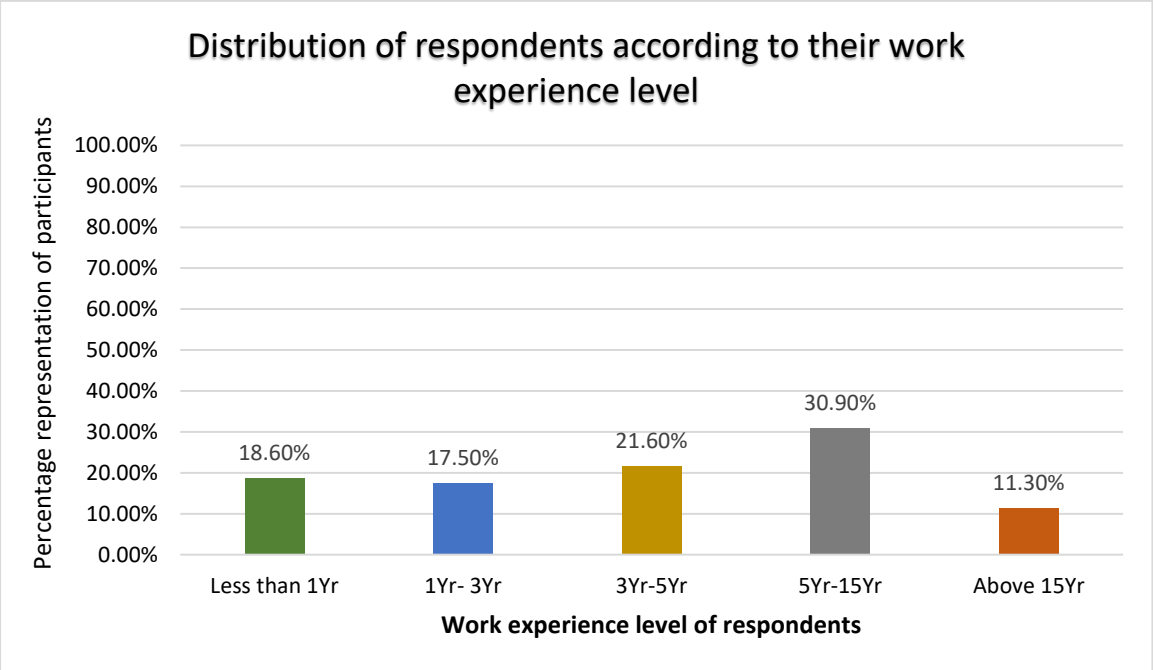

Figure 4.1.2 Clustered column chart representing the distribution of respondents according to their work experience level

Table 4.1.2 and Figure 4.1.2 represents the distribution of respondents according to their work experience level. Out of the 13(13.4%) from the Quality Assurance, 8(8.2%) were from 5Yr-15Yr which was the highest concentration. The total distribution of experience ranges from 1Yr to above 15 Yr. In the case of Quality Control, there is a wide range of experience, with the 1 to 3 years 5(5.2%) showing the highest concentration. Production accounts for the 10(10.3%) of participants with the largest concentration in the 5 to 15 years group. Microbiology accounts for 12(12.4%) of participants with the largest concentration in the 3 to 5 years group. Engineering department accounts for 11(11.3%) of participants with the largest concentration 6(6.2%) responses in the Less than 1 year category. Warehouse department, Research and Development, and Environment Health and Safety departments accounts for 13(13.4%) each of 97(100%) participants.

4.1.3 The Educational Qualification of the respondent from the survey questionnaire

Table 4.1.3 The Educational Qualification of the respondent from the survey questionnaire

Respondents	Doctorate PhD	Postgraduate	Undergraduate	Others	Total
Quality Assurance (QA)	0	9 (9.3%)	3 (3.1%)	1 (1.0%)	13 (13.4%)
Quality Control (QC)	0	9 (9.3%)	3 (3.1%)	0	12 (12.4%)
Production department	0	6 (6.2%)	3 (3.1%)	1 (1.0%)	10 (10.3%)
Microbiology department	1 (1.0%)	8 (8.2%)	3 (3.1%)	0	12 (12.4%)
Engineering department	0	8 (8.2%)	2(2.1%)	1 (1.0%)	11 (11.3%)
Warehouse department	2(2.1%)	6 (6.2%)	5 (5.2%)	0	13 (13.4%)

Research and Development	1 (1.0%)	4 (4.1%)	8 (8.2%)	0	13 (13.4%)
Environment Health and Safety	0	7 (7.2%)	6 (6.2%)	0	13 (13.4%)
Total	**4 (4.1%)**	**57 (58.8%)**	**33 (34.0%)**	**3 (3.1%)**	**97 (100%)**

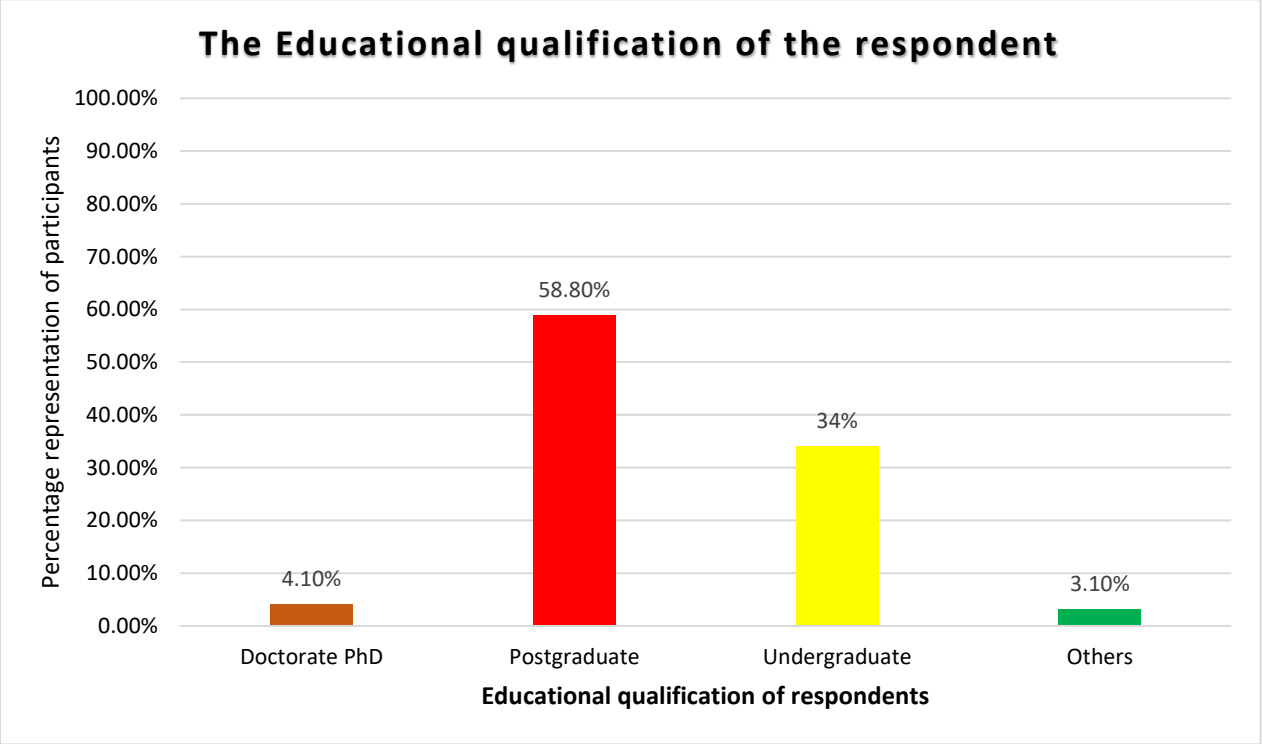

Figure 4.1.3 Clustered column chart representing the percentage distribution of respondents according to their educational qualification

Table 4.1.3 and Figure 4.1.3 represents the percentage distribution of respondents according to their educational qualification. Out of the 97(100%) participants, 57(58.80%) were Postgraduates, 33 respondents were holding Undergraduate degree and 4(4.10%) of them were

having Doctorate PhD. 3(3.10%) of the respondents who participated in the survey were having diploma qualification.

4.2 Analysis of the objectives gained from the Survey Questionnaire

4.2.1 Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.

Question asked to the Participants regarding regulatory landscape: Under what regulatory system does your company operates?

Table 4.2.1 The distribution of various regulatory systems under which participants operates in the pharmaceutical manufacturing facilities based in India.

Regulatory Authorities	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total
U.S. Food and Drug Administration (US FDA), United States	10 (3.4%)	3 (1.0%)	6 (2.1%)	7 (2.4%)	1 (0.3%)	2 (0.7%)	7 (2.4%)	4 (1.4%)	40 (13.7%)
Medical and Healthcare Products Regulatory Agency (MHRA), United Kingdom	12 (4.1%)	2 (0.7%)	8 (2.7%)	5 (1.7%)	5 (1.7%)	2 (0.7%)	2 (0.7%)	6 (2.1%)	42 (14.4%)
The European Medicines Agency (EMA), Europe	10 (3.4%)	2 (0.7%)	4 (1.4%)	4 (1.4%)	3 (1.0%)	2 (0.7%)	5 (1.7%)	7 (2.4%)	37 (12.7%)
Pharmaceuticals and Medical Devices Agency (PMDA), Japan	3 (1.0%)	0	1 (0.3%)	2 (0.7%)	2 (0.7%)	0	1 (0.3%)	1 (0.3%)	10 (3.4%)
The Central Drugs Standard Control Organization (CDSCO), India	10 (3.4%)	8 (2.7%)	3 (1.0%)	7 (2.4%)	3 (1.0%)	3 (1.0%)	5 (1.7%)	8 (2.7%)	47 (16.1%)
The National Health Surveillance Agency (ANVISA), Brazil	8 (2.7%)	0	3 (1.0%)	1 (0.3%)	1 (0.3%)	2 (0.7%)	1 (0.3%)	3 (1.0%)	19 (6.5%)
Therapeutic Goods Administration (TGA), Australia	8 (2.7%)	1 (0.3%)	4 (1.4%)	1 (0.3%)	3 (1.0%)	1 (0.3%)	0	5 (1.7%)	23 (7.9%)
World Health Organization (WHO)	9 (3.1%)	2 (0.7%)	3 (1.0%)	3 (1.0%)	1 (0.3%)	3 (1.0%)	8 (2.7%)	4 (1.4%)	33 (11.3%)

South African Health Products Regulatory Authority (SAHPRA), Africa	**5 (1.7%)**	**0**	**3 (1.0%)**	**0**	**1 (0.3%)**	**0**	**2 (0.7%)**	**0**	**11 (3.8%)**
Health Canada, Canada	**6 (2.1%)**	**0**	**4 (1.4%)**	**0**	**2 (0.7%)**	**3 (1.0%)**	**0**	**2 (0.7%)**	**17 (5.8%)**
The National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria	**4 (1.4%)**	**1 (0.3%)**	**1 (0.3%)**	**2 (0.7%)**	**2 (0.7%)**	**1 (0.3%)**	**2 (0.7%)**	**0**	**13 (4.5%)**
Total	**85**	**19**	**40**	**32**	**24**	**19**	**33**	**40**	**292 (100%)**

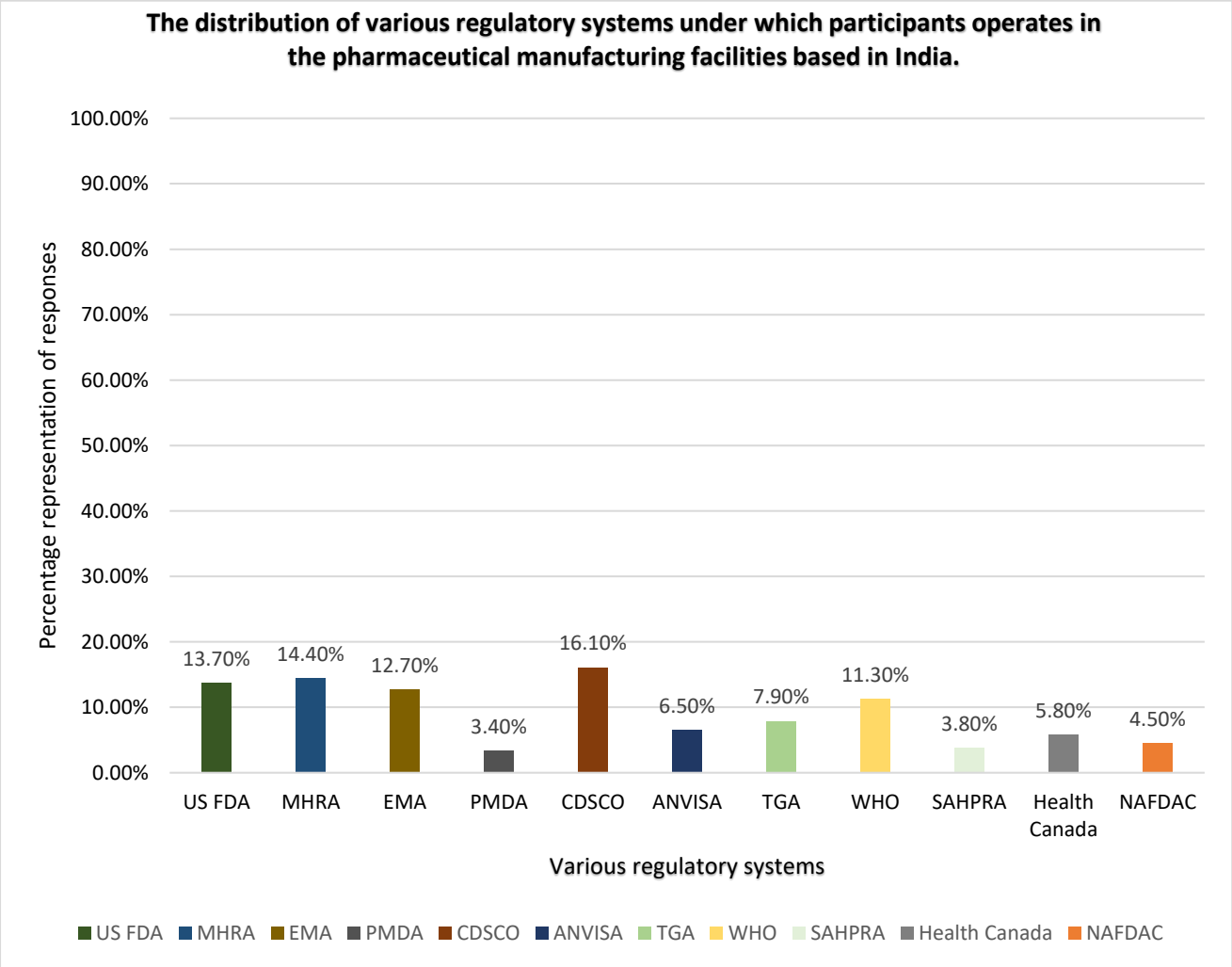

Figure 4.2.1 Regulatory landscape: Clustered column chart representing the distribution of various regulatory landscape under which participants operates in the pharmaceutical manufacturing facility.

Table 4.2.1 and Figure 4.2.1 represents the distribution of various regulatory landscape under which participants operates in the pharmaceutical manufacturing facility. 40(13.7%) of the total participants operates under US FDA, United States. 42(14.4%) of the participants operates under MHRA, United Kingdom. 37(12.7%) of the respondents operates under EMA, Europe. The highest percentage was recorded for CDSCO, India 47(16.1%) and lowest for PMDA, Japan by 10(3.4%) participants. 19(6.5%) of the total participants operates under ANVISA, Brazil. 23(7.9%) of the total participants operates under TGA, Australia and 33(11.3%) of the total participants operates under WHO. 11(3.8%) of the total participants operates under SAHPRA, Africa whereas 17(5.8%) of the total participants operates under Health Canada, Canada. 13(4.2%) of respondents operates under NAFDAC, Nigeria. Other regulatory authorities the participants recorded are NDA-Uganda, TFDA-Tanzania, MCAZ- Zimbabwe, PPB-Kenya, FDA-Ghana, MHSS-Namibia, MOH-Sri Lanka, FDA- Philippines, MOH-Yemen and NMPB-Sudan.

Table 4.2.1 Regulatory system influence: Influence of regulatory systems on the implementation of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities in India.

Regulatory System under which different pharmaceutical manufacturing facilities operates in India	**No of companies functioning with Manufacturing Execution System (MES) Software**
The Central Drugs Standard Control Organization (CDSCO), India	38 (15.4%)
Medical and Healthcare Products Regulatory Agency (MHRA), United Kingdom	37 (15.0%)
The European Medicines Agency (EMA), Europe	31 (12.6%)
The National Health Surveillance Agency (ANVISA), Brazil	15 (6.1%)
Therapeutic Goods Administration (TGA), Australia	22 (8.9%)
South African Health Products Regulatory Authority (SAHPRA), Africa	7 (2.8%)
Health Canada, Canada	16 (6.5%)
The National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria	8 (3.2%)
U.S. Food and Drug Administration (US FDA), United States	36 (14.6%)

National Medicines and Poisons Board (NMPB)-Sudan	1 (0.4%)
National Drug Authority (NDA), Uganda	1 (0.4%)
Tanzania Medicines and Medical Devices Authority (TMDA), Tanzania	1 (0.4%)
Medicines Control Authority of Zimbabwe (MCAZ) Zimbabwe	1 (0.4%)
Ministry of Public Health and Population (MOH)-Yemen	1 (0.4%)
Pharmacy and Poisons Board (PPB) Kenya	1 (0.4%)
Food and Drugs Authority FDA Ghana	1 (0.4%)
Ministry of Health & Social Services (MHSS) Namibia	1 (0.4%)
Sri Lankan Ministry of Health (MoH)	1 (0.4%)
Food and Drug Administration (FDA)- Philippines	1 (0.4%)
Total	247 (100%)

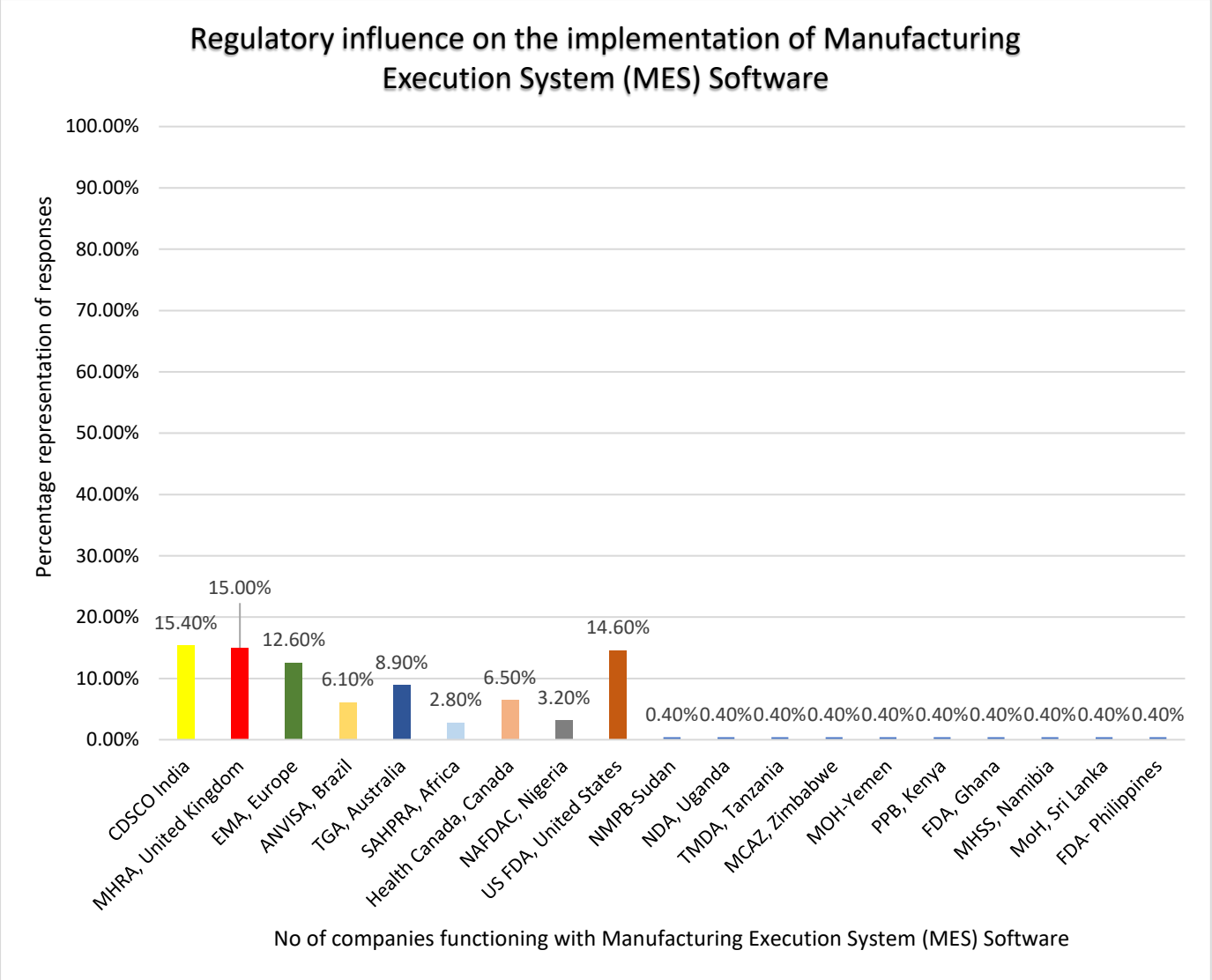

Figure 4.2.1 Regulatory influence: Influence of regulatory systems on the implementation of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities in India.

Out of the 247(100%) total responses, 37(15.0%) of the pharmaceutical manufacturing facilities working under MHRA, United Kingdom are using MES Software along with 36(14.6%) under the US FDA of United States. 31(12.6%) of the pharmaceutical manufacturing facilities working under EMA, Europe are also functioning with the integration of MES Software. Companies functioning under TGA of Australia also shows promising use of MES Software with 22(8.9%).

Question asked to the Participants: Is your company using Manufacturing Execution System (MES) software?

Table 4.2.1 MES implementation: The response of the participants stating whether their company is operating under Manufacturing Execution System (MES) software.

Respondents	Yes	No	Total
Quality Assurance (QA)	11 (11.3%)	2 (2.1%)	13 (13.4%)
Quality Control (QC)	10 (10.3%)	2 (2.1%)	12 (12.4%)
Production department	9 (9.3%)	1 (1.0%)	10 (10.3%)
Microbiology department	10 (10.3%)	2 (2.1%)	12 (12.4%)
Engineering department	11 (11.3%)	0	11 (11.3%)
Warehouse department	9 (9.3%)	4 (4.1%)	13 (13.4%)
Research and Development	11 (11.3%)	2 (2.1%)	13 (13.4%)
Environment Health and Safety	11 (11.3%)	2 (2.1%)	13 (13.4%)
Total	**82 (84.5%)**	**15 (15.5%)**	**97 (100%)**

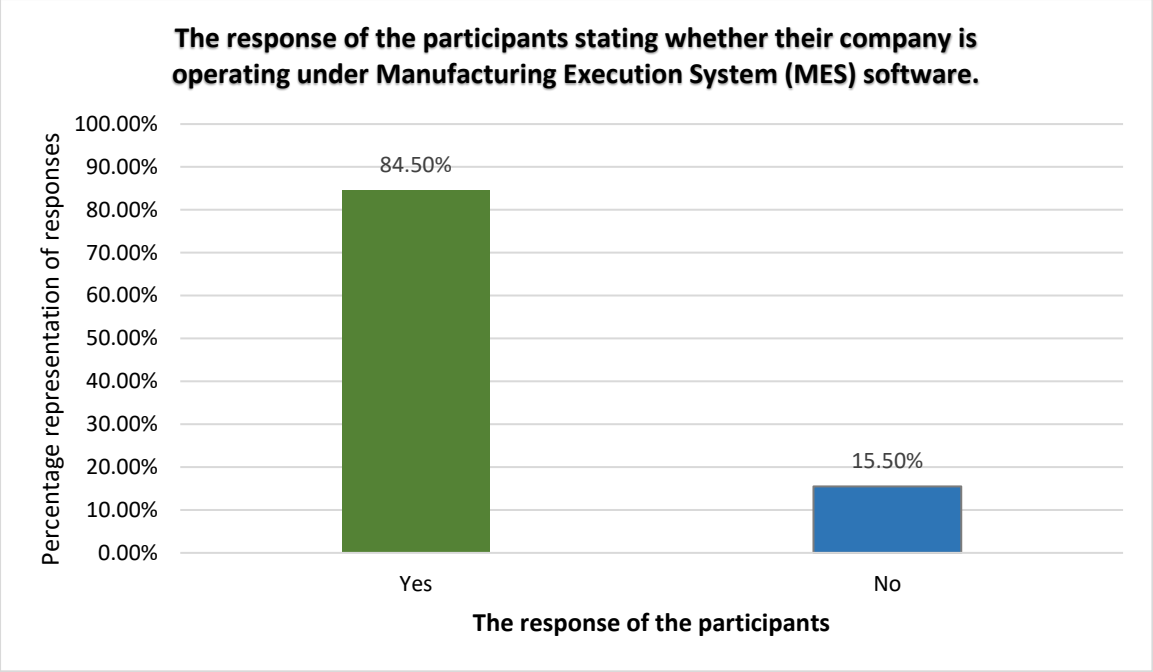

Figure 4.2.1 MES implementation: Clustered Column Chart representing the response of the participants stating whether their company is operating under Manufacturing Execution System (MES) software.

Table 4.2.1 and Figure 4.2.1 represents the distribution of companies operating under Manufacturing Execution System (MES) software. The table describes that 82(84.5%) of the companies are using Manufacturing Execution System (MES) software. However, 15(15.5%) of the companies are not using Manufacturing Execution System (MES) software.

Question asked to participant regarding MES: Do you agree or disagree that regulatory authorities have a crucial role in the implementation of Manufacturing Execution System (MES) Software in pharmaceutical manufacturing facilities through their regulatory guidelines?

Table 4.2.1 MES: Perception of participants on their agreement and disagreement that the regulatory authorities have a crucial role in the implementation of Manufacturing Execution System (MES) Software.

Respondents	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	Total
Quality Assurance (QA)	10 (10.3%)	2 (2.1%)	1 (1.0%)	0	0	13 (13.4%)
Quality Control (QC)	6 (6.2%)	5 (5.2%)	1 (1.0%)	0	0	12 (12.4%)
Production	8 (8.2%)	2 (2.1%)	0	0	0	10 (10.3%)
Microbiology	6 (6.2%)	4 (4.1%)	2 (2.1%)	0	0	12 (12.4%)
Engineering	5 (5.2%)	4 (4.1%)	1 (1.0%)	0	1 (1.0%)	11 (11.3%)
Warehouse	3 (3.1%)	6 (6.2%)	4 (4.1%)	0	0	13 (13.4%)
Research and Development	11 (11.3%)	2 (2.1%)	0	0	0	13 (13.4%)
Environment Health and Safety	8 (8.2%)	2 (2.1%)	2 (2.1%)	0	1 (1.0%)	13 (13.4%)
Total	**57 (58.8%)**	**27 (27.8%)**	**11 (11.3%)**	**0**	**2 (2.1%)**	**97 (100 %)**

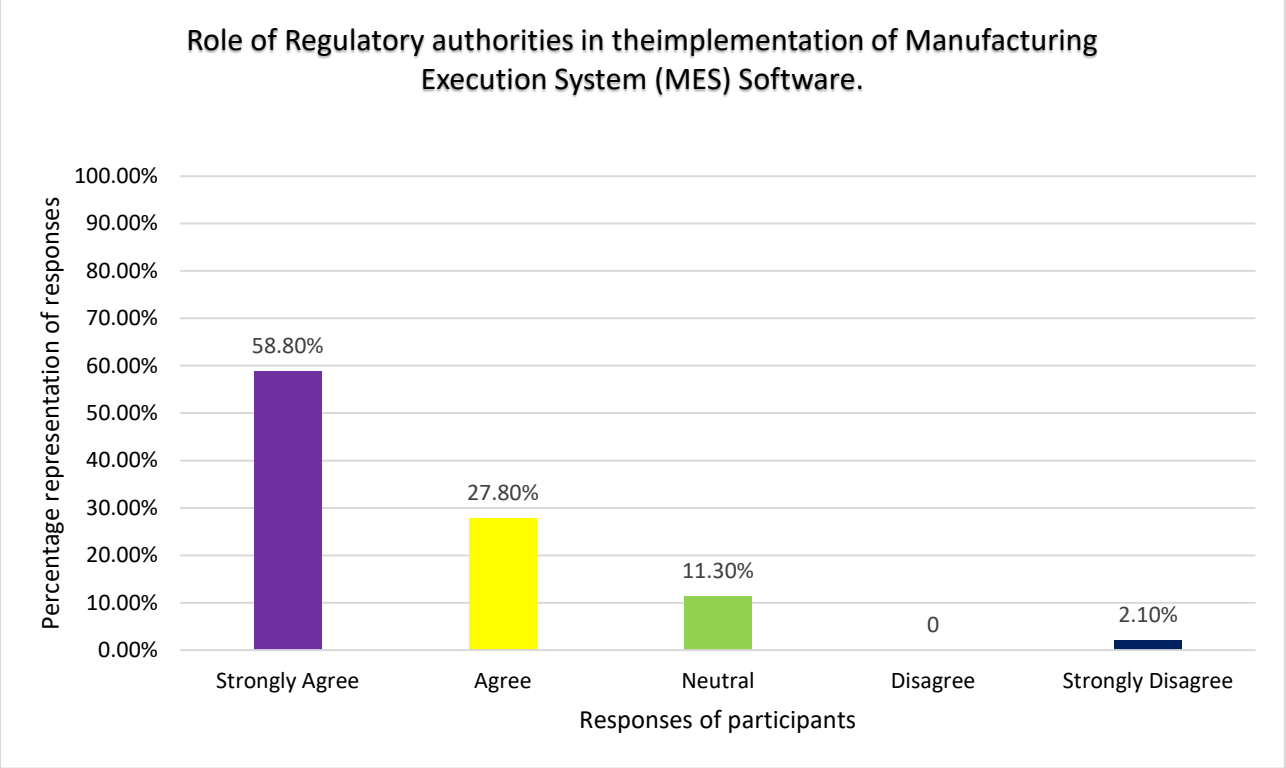

Figure 4.2.1 MES: Clustered column chart representing the crucial role of regulatory authorities in the implementation of Manufacturing Execution System (MES) Software.

Table 4.2.1 MES and Figure 4.2.1 MES represents the crucial role of regulatory authorities in the implementation of MES Software. 57 (58.80%) respondents strongly agree that regulatory authorities do have a crucial role in the implementation of MES Software.27(27.80%) respondents agree to the statement that regulatory authorities do have a crucial role in the implementation of MES Software and 2(2.10%) respondents strongly disagreed to the survey question. 11(11.30%) participants were neutral to the statement.

Question asked to the participant regarding Computer System Validation (CSV) Process:

Do you agree or disagree that regulatory authorities have a crucial role in the implementation of Computer System Validation (CSV) Process in pharmaceutical manufacturing facilities through their regulatory guidelines?

Table 4.2.1 CSV Perception of participants on their agreement and disagreement that the regulatory authorities have a crucial role in the implementation of Computer System Validation (CSV) Process.

Respondents	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	Total

Quality Assurance (QA)	12 (12.4%)	1 (1.0%)	0	0	0	13 (13.4%)
Quality Control (QC)	6 (6.2%)	4 (4.1%)	2 (2.1%)	0	0	12 (12.4%)
Production	7 (7.2%)	3 (3.1%)	0	0	0	10 (10.3%)
Microbiology	5 (5.2%)	5 (5.2%)	0	0	2 (2.1%)	12 (12.4%)
Engineering	4 (4.1%)	5 (5.2%)	2 (2.1%)	0	0	11 (11.3%)
Warehouse	4 (4.1%)	5 (5.2%)	4 (4.1%)	0	0	13 (13.4%)
Research and Development	12 (12.4%)	1 (1.0%)	0	0	0	13 (13.4%)
Environment Health and Safety	7 (7.2%)	5 (5.2%)	0	0	1 (1.0%)	13 (13.4%)
Total	**57 (58.8%)**	**29 (29.9%)**	**8 (8.2%)**	**0**	**3 (3.1%)**	**97 (100 %)**

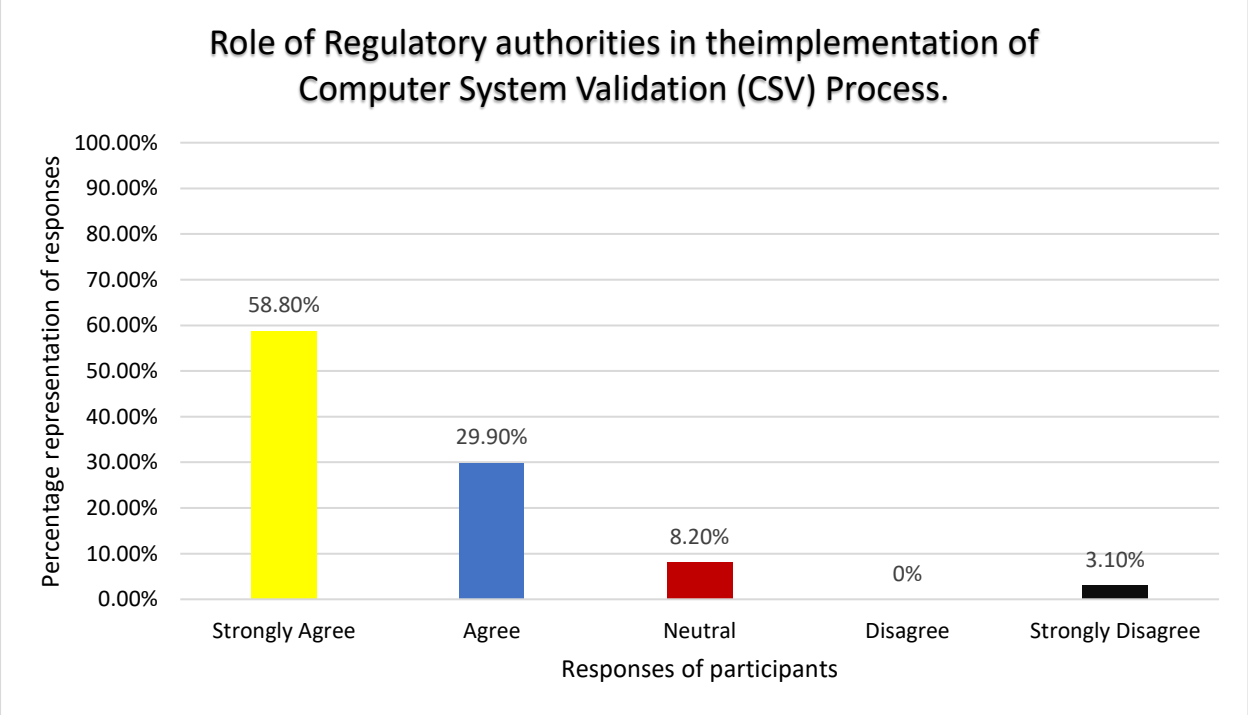

Figure 4.2.1 CSV Clustered Column chart representing the crucial role of regulatory authorities in the implementation of Computer System Validation (CSV) Process.

Table 4.2.1 CSV and Figure 4.2.1 CSV represents the crucial role of regulatory authorities in the implementation of CSV Process. 57 (58.80%) respondents strongly agree that regulatory authorities do have a crucial role in the implementation of CSV Process.29(29.90%) respondents agree to the statement that regulatory authorities do have a crucial role in the implementation of CSV Process and 3(3.10%) respondents strongly disagreed to the survey question. 8(8.20%) participants were neutral to the statement.

4.2.2 Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.

Question asked to the participant: In your opinion, what are the advantages in implementation of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities?

Table 4.2.2 MES Advantages: Perception of participants on the advantages in the implementation of Manufacturing Execution System (MES) Software

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 195 (100%)
Eliminating human errors	3 (1.5%)	3 (1.5%)	1 (0.5%)	5 (2.6%)	2 (1.0%)	1 (0.5%)	5 (2.6%)	4 (2.1%)	24 (12.3%)
Traceability of process	3 (1.5%)	4 (2.1%)	1 (0.5%)	2 (1.0%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)	16 (8.2%)
Paperless	2 (1.0%)	4 (2.1%)	2 (1.0%)	3 (1.5%)	2 (1.0%)	2 (1.0%)	2 (1.0%)	4 (2.1%)	21 (10.8%)
Reduce inventory	3 (1.5%)	3 (1.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.5%)	2 (1.0%)	13 (6.7%)
Improved productivity	1 (0.5%)	2 (1.0%)	1 (0.5%)	4 (2.1%)	2 (1.0%)	2 (1.0%)	4 (2.1%)	2 (1.0%)	18 (9.2%)
Timely approval of batches	3 (1.5%)	3 (1.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	5 (2.6%)	2 (1.0%)	17 (8.7%)
Reduces shift handover time	3 (1.5%)	3 (1.5%)	1 (0.5%)	2 (1.0%)	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	13 (6.7%)

Deviation management	3 (1.5%)	1 (0.5%)	1 (0.5%)	2 (1.0%)	1 (0.5%)	0	0	2 (1.0%)	10 (5.1%)
All of the above	11 (5.6%)	7 (3.6%)	9 (4.6%)	6 (3.1%)	6 (3.1%)	8 (4.1%)	7 (3.6%)	9 (4.6%)	63 (32.3%)

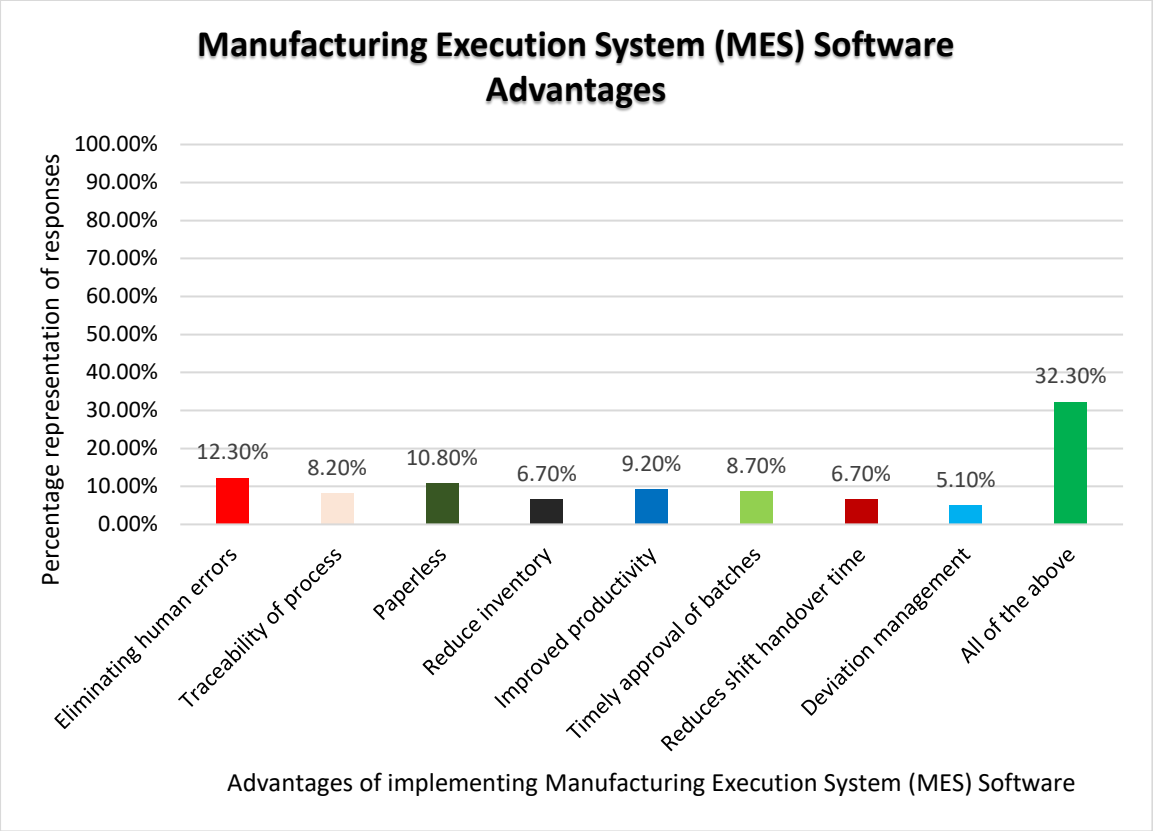

Figure 4.2.2 MES Advantages: Clustered Column Chart representing the perception of participants on the advantages in the implementation of Manufacturing Execution System (MES) Software

Table 4.2.2 MES and Figure 4.2.2 MES represents the Perception of participants on the advantages in the implementation of MES Software. 63(32.3%) of the total respondents believed that all of the given advantages including eliminating human errors, traceability of process, paperless, reduce inventory, improved productivity, Timely approval of batches, reduces shift handover time, and deviation management have significant impact on the implementation of MES Software.

Question asked to the participant: In your opinion, what are the advantages in implementation of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities?

Table 4.2.2 CSV Advantages: Perception of participants on the advantages in the implementation of Computer System Validation (CSV) Process.

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 180 (100%)
Accurate results by Computer System	2 (1.1%)	3 (1.7%)	2 (1.1%)	4 (2.2%)	4 (2.2%)	5 (2.8%)	5 (2.8%)	3 (1.7%)	28 (15.6%)
Maintains data integrity	2 (1.1%)	3 (1.7%)	3 (1.7%)	4 (2.2%)	3 (1.7%)	5 (2.8%)	6 (3.3%)	1 (0.6%)	27 (15.0%)
Patient safety	2 (1.1%)	2 (1.1%)	1 (0.6%)	3 (1.7%)	3 (1.7%)	2 (1.1%)	3 (1.7%)	1 (0.6%)	17 (9.4%)
Risk management of Computer System	2 (1.1%)	3 (1.7%)	1 (0.6%)	1 (0.6%)	4 (2.2%)	2 (1.1%)	2 (1.1%)	1 (0.6%)	16 (8.9%)
Boosts Operational efficiency	2 (1.1%)	3 (1.7%)	2 (1.1%)	3 (1.7%)	1 (0.6%)	2 (1.1%)	2 (1.1%)	0	15 (8.3%)
Prevents Computer System malfunctions	2 (1.1%)	2 (1.1%)	2 (1.1%)	2 (1.1%)	1 (0.6%)	2 (1.1%)	1 (0.6%)	1 (0.6%)	13 (7.2%)
All of the above	13 (7.2%)	8 (4.4%)	7 (3.9%)	7 (3.9%)	5 (2.8%)	8 (4.4%)	6 (3.3%)	10 (5.6%)	64 (35.6%)

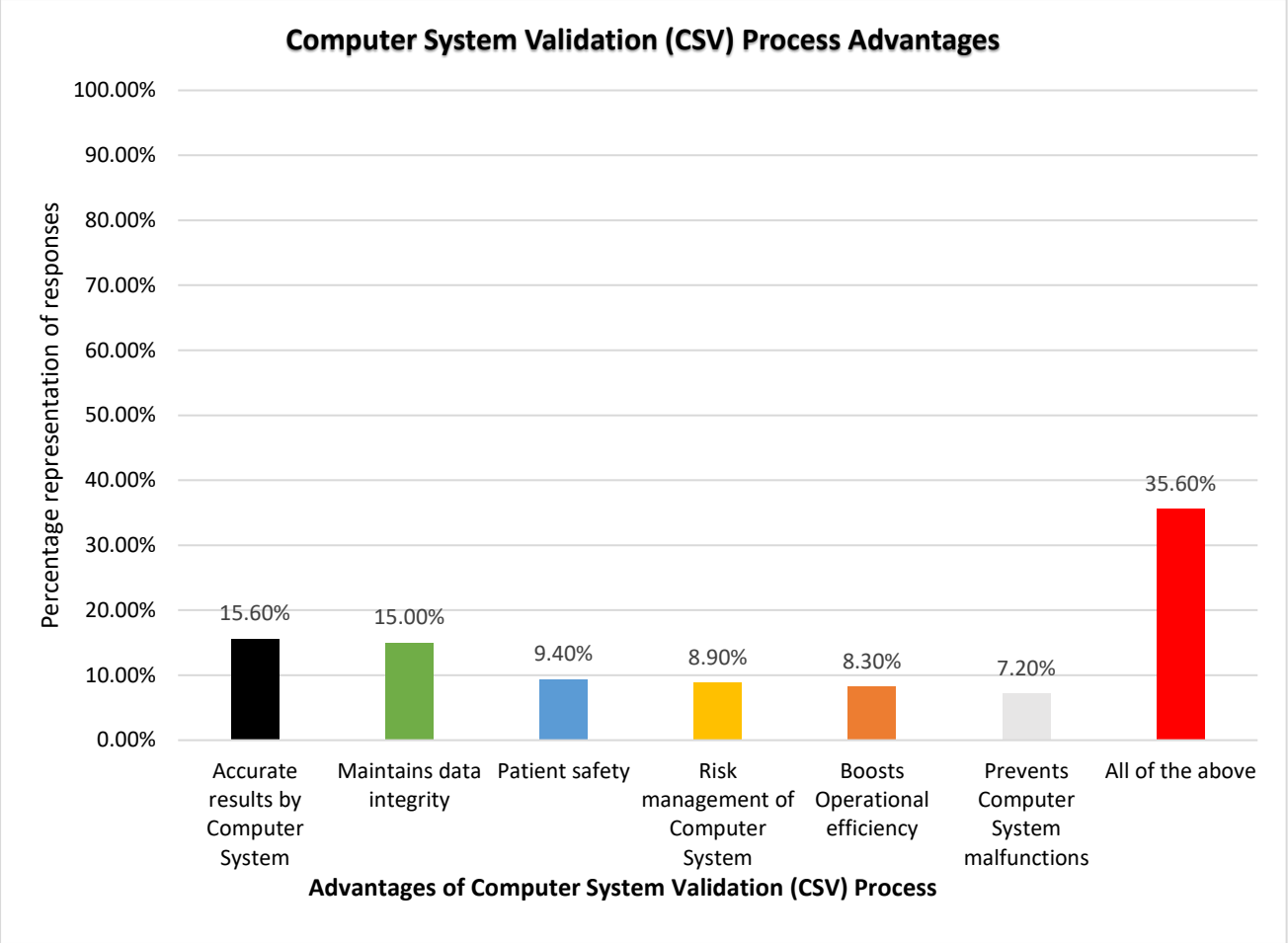

Figure 4.2.2 CSV Advantages: Clustered Column Chart representing the perception of participants on the advantages in the implementation of Computer System Validation (CSV) Process.

Table 4.2.2 CSV and Figure 4.2.2 CSV represents the Perception of participants on the advantages in the implementation of CSV Process in different pharmaceutical manufacturing facilities. 64(35.6%) of the total respondents believed that all of the given advantages including accurate results by Computer System, maintains data integrity, patient safety, risk management of Computer System, boosts operational efficiency, and prevents computer system malfunctions have significant impact on the implementation of MES Software.

Question asked to the participant: In your opinion, what are the disadvantages in implementation of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities?

Table 4.2.2 MES disadvantages: Perception of participants on the disadvantages in the implementation of Manufacturing Execution System (MES) Software

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 169 (100%)
Costly in nature	6 (3.6%)	6 (3.6%)	4 (2.4%)	6 (3.6%)	4 (2.4%)	1 (0.6%)	7 (4.1%)	6 (3.6%)	40 (23.7%)
Complexity of software	3 (1.8%)	3 (1.8%)	0	3 (1.8%)	1 (0.6%)	1 (0.6%)	5 (3.0%)	2 (1.2%)	18 (10.7%)
Time consuming process	1 (0.6%)	2 (1.2%)	1 (0.6%)	0	2 (1.2%)	3 (1.8%)	3 (1.8%)	1 (0.6%)	13 (7.7%)
Improper training	1 (0.6%)	3 (1.8%)	2 (1.2%)	1 (0.6%)	3 (1.8%)	5 (3.0%)	4 (2.4%)	5 (3.0%)	24 (14.2%)
Regular support from IT department regardless of shift	5 (3.0%)	4 (2.4%)	1 (0.6%)	2 (1.2%)	2 (1.2%)	3 (1.8%)	2 (1.2%)	4 (2.4%)	23(13.6%)
Network and connectivity lag	3 (1.8%)	4 (2.4%)	4 (2.4%)	4 (2.4%)	2 (1.2%)	2 (1.2%)	3 (1.8%)	4 (2.4%)	26 (15.4%)
All of the above	7 (4.1%)	4 (2.4%)	2 (1.2%)	3 (1.8%)	5 (3.0%)	3 (1.8%)	0	1 (0.6%)	25 (14.8%)

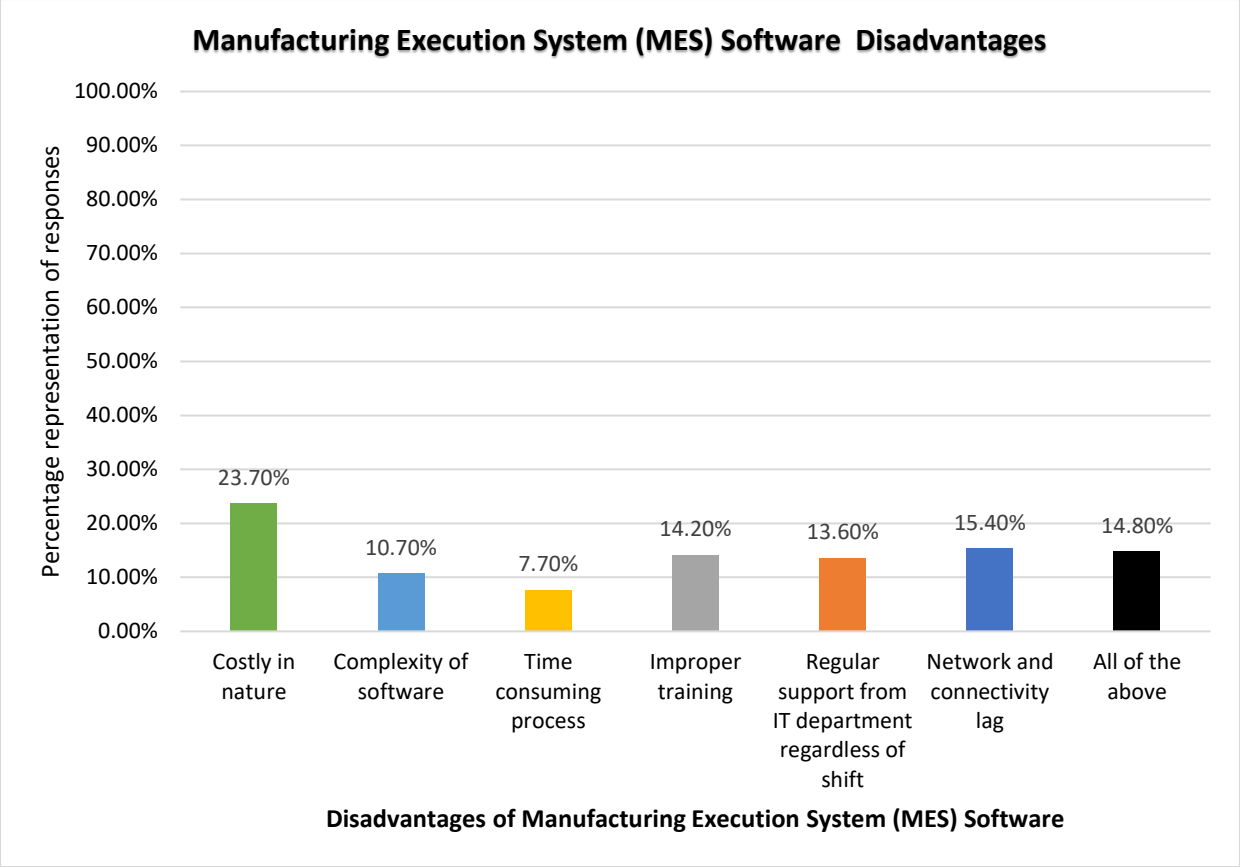

Figure 4.2.2 MES disadvantages: Clustered Column Chart representing the perception of participants on the disadvantages in the implementation of Manufacturing Execution System (MES) Software

Table 4.2.2 MES and Figure 4.2.2 MES illustrates the key disadvantages in the implementation of MES Software in different pharmaceutical manufacturing facilities. Costly in nature has the highest response rate of 40(23.7%) followed by Network and connectivity lag with 26(15.4%) response rate. Other disadvantages include: Cybersecurity issues, need for relying back to paper documentation in case of software bug or network error.

Question asked to the participant: In your opinion, what are the disadvantages in implementation of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities?

Table 4.2.2 CSV disadvantages: Perception of participants on the disadvantages in the implementation of Computer System Validation (CSV) Process

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 132 (100%)
Burden on internal resources	4 (3.0%)	2 (1.5%)	0	2 (1.5%)	1 (0.8%)	4 (3.0%)	1 (0.8%)	2 (1.5%)	16 (12.1%)
Expensive nature	5 (3.8%)	2 (1.5%)	5 (3.8%)	3 (2.3%)	6 (4.5%)	5 (3.8%)	11 (8.3%)	8 (6.1%)	45 (34.1%)
Generate large volume of data in form of reports	2 (1.5%)	3 (2.3%)	0	2 (1.5%)	1 (0.8%)	3 (2.3%)	3 (2.3%)	2 (1.5%)	16 (12.1%)
Evidence based approach	1 (0.8%)	3 (2.3%)	1 (0.8%)	2 (1.5%)	1 (0.8%)	3 (2.3%)	0	1 (0.8%)	12 (9.1%)
Involves more tests and test evidence	2 (1.5%)	1 (0.8%)	2 (1.5%)	2 (1.5%)	2 (1.5%)	0	2 (1.5%)	0	11 (8.3%)
All of the above	6 (4.5%)	7 (5.3%)	4 (3.0%)	4 (3.0%)	4 (3.0%)	4 (3.0%)	1 (0.8%)	2 (1.5%)	32 (24.2%)

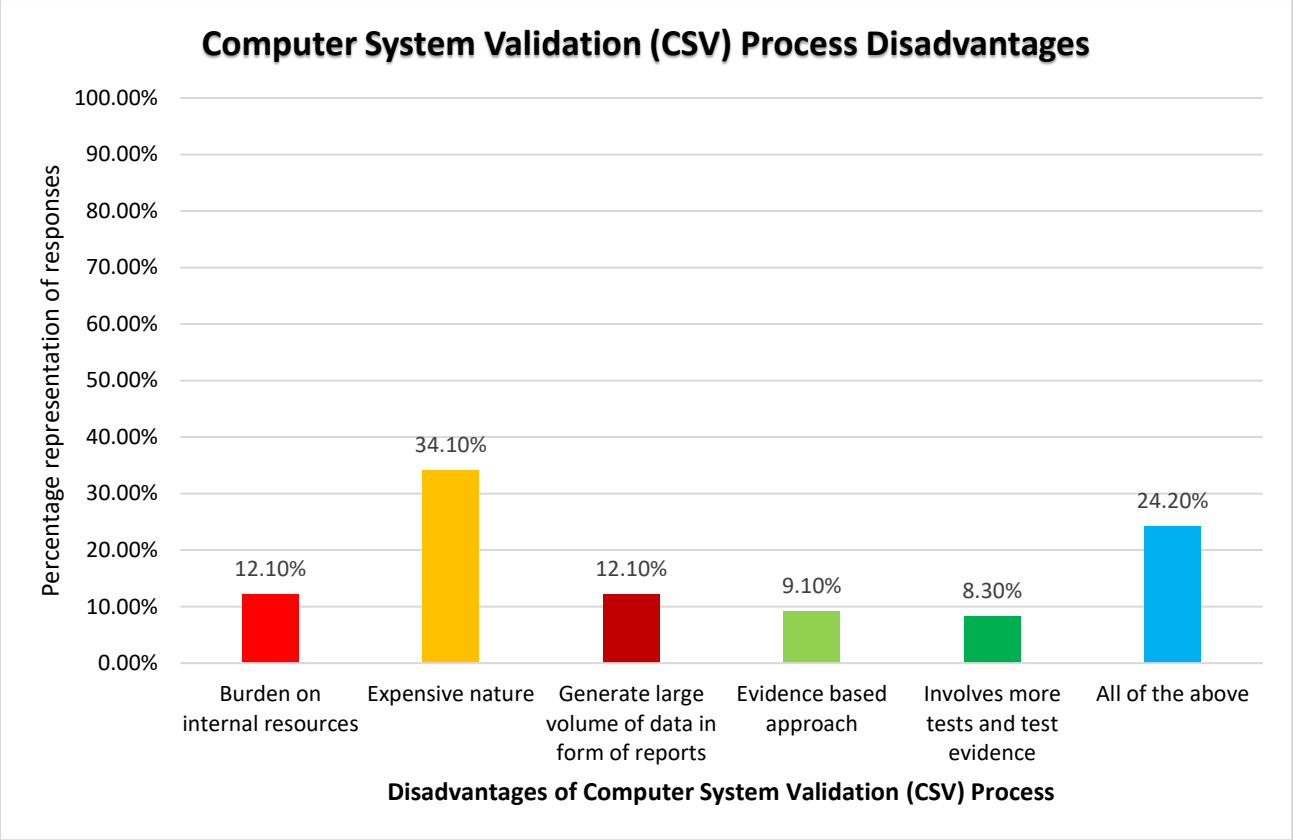

Figure 4.2.2 CSV disadvantages: Clustered Column Chart representing the perception of participants on the disadvantages in the implementation of Computer System Validation (CSV) Process.

Table 4.2.2 CSV and Figure 4.2.2 CSV illustrates the key disadvantages in the implementation of CSV Process in different pharmaceutical manufacturing facilities. 45(34.1%) of the respondents believe that expensive nature is the biggest disadvantage of the CSV Process implementation. 32(24.2%) of the participants have an opinion that all the factors like burden on internal resources, expensive nature, generate large volume of data in form of reports, evidence-based approach, and involves more tests and test evidence have a strong negative impact on the implementation of CSV Process.

4.2.3 Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.

Question asked to the participant: What are the types of Manufacturing Execution System (MES) software that are operating in your work place?

Table 4.2.3 MES Types of Manufacturing Execution System (MES) software used by the pharmaceutical professionals in different manufacturing facilities.

Respondents	Hitachi	Laurel	POMS Aquila	PAS-X	Sepasoft	Epicor	Aveva	Siemens	AIMSCO	Traditional paper documentation
Quality Assurance (QA)	3 (1.9%)	7 (4.3)	1 (0.6%)	2 (1.2%)	1 (0.6%)	1 (0.6%)	0	4 (2.5%)	0	3 (1.9%)
Quality Control (QC)	3 (1.9%)	4 (2.5%)	2 (1.2%)	0	2 (1.2%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	6 (3.7%)
Production	1 (0.6%)	7 (4.3%)	0	1 (0.6%)	0	1 (0.6%)	0	2 (1.2%)	0	2 (1.2%)
Microbiology	4 (2.5%)	7 (4.3%)	1 (0.6%)	5 (3.1%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	3 (1.9%)	0	2 (1.2%)
Engineering	2 (1.2%)	6 (3.7%)	2 (1.2%)	1 (0.6%)	3 (1.9%)	1 (0.6%)	0	1 (0.6%)	0	0
Warehouse	3 (1.9%)	7 (4.3%)	1 (0.6%)	3 (1.9%)	3 (1.9%)	2 (1.2%)	1 (0.6%)	4 (2.5%)	1 (0.6%)	1 (0.6%)
Research and Development	5 (3.1%)	7 (4.3%)	1 (0.6%)	2 (1.2%)	0	0	1 (0.6%)	3 (1.9%)	0	2 (1.2%)
Environment Health and Safety	2 (1.2%)	6 (3.7%)	1 (0.6%)	2 (1.2%)	0	1 (0.6%)	1 (0.6%)	1 (0.6%)	0	3 (1.9%)
Total: 162 (100%)	23 (14.2%)	51 (31.5%)	9 (5.6%)	16 (9.9%)	10 (6.2%)	8 (4.9%)	5 (3.1%)	19 (11.7%)	2 (1.2%)	19 (11.7%)

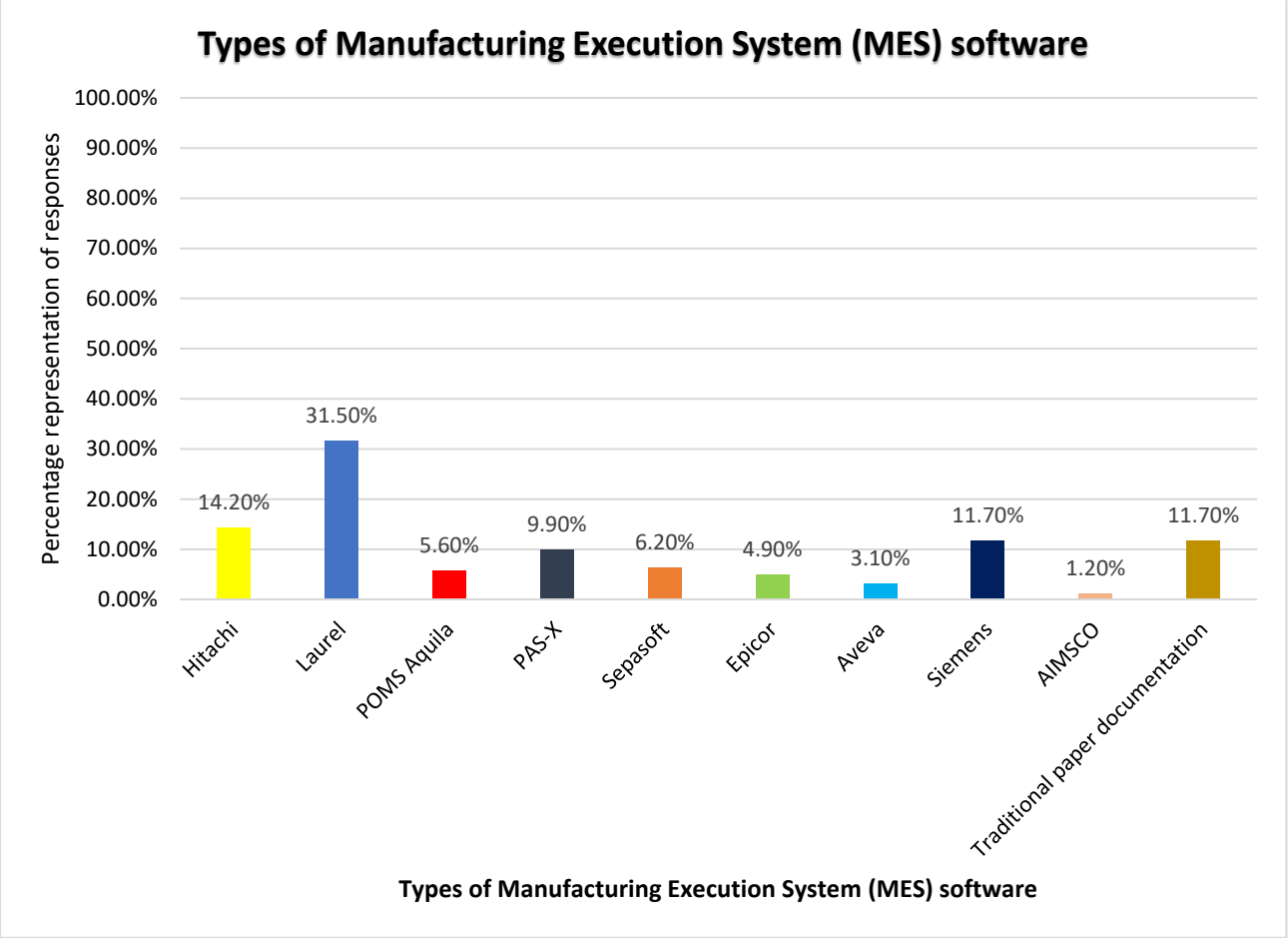

Figure 4.2.3 Clustered Column Chart illustrating various types of Manufacturing Execution System (MES) software used by the pharmaceutical professionals in different manufacturing facilities.

Table 4.2.3 and Figure 4.2.3 illustrates various types of MES software used by the pharmaceutical professionals in different manufacturing facilities. QA participants are familiar with all MES software except Aveva, and AIMSCO. They also have used Leucine and Atachi systems. QC respondents are familiar with all MES software except PAS-X. Laurel, Hitachi, PAS-X, Epicor, and Siemens are the MES software that production respondents are familiar with. Majority of the Production 7(4.3%) are familiar with Laurel MES software and 2(1.2%) is still using traditional paper documentation. 7(4.3%) of Microbiology respondents are using Laurel software followed by PAS-X 5(3.1%) and Hitachi 4(2.5%). In addition, they also operated Emerson Syncade. 6(3.7) % of the Engineering respondents reported that they are more familiar with Laurel MES software. Majority of the Warehouse personnel were familiar with Laurel MES software 7(4.3%) followed by 4(2.5%) with Siemens MES software. Research and Development respondents reported majority are using Laurel MES software with

a response rate of 7(4.3%). Environment Health and Safety respondents are also primarily using Laurel MES software with a response rate of 6(3.7%). In addition, they also operated Emerson Syncade.

Table 4.2.3 MES Others: Other types of Manufacturing Execution System (MES) Software used by pharmaceutical professionals in different manufacturing facilities.

Respondents	Atachi	Leucine	Emerson Syncade
Quality Assurance (QA)	1 (0.6%)	1 (0.6%)	0
Quality Control (QC)	0	0	0
Production	0	0	0
Microbiology	0	0	1 (0.6%)
Engineering	0	0	0
Warehouse	0	0	0
Research and Development	0	0	1 (0.6%)
Environment Health and Safety	0	0	1 (0.6%)
Total: 162(100%)	1 (0.6%)	1 (0.6%)	3 (1.9%)

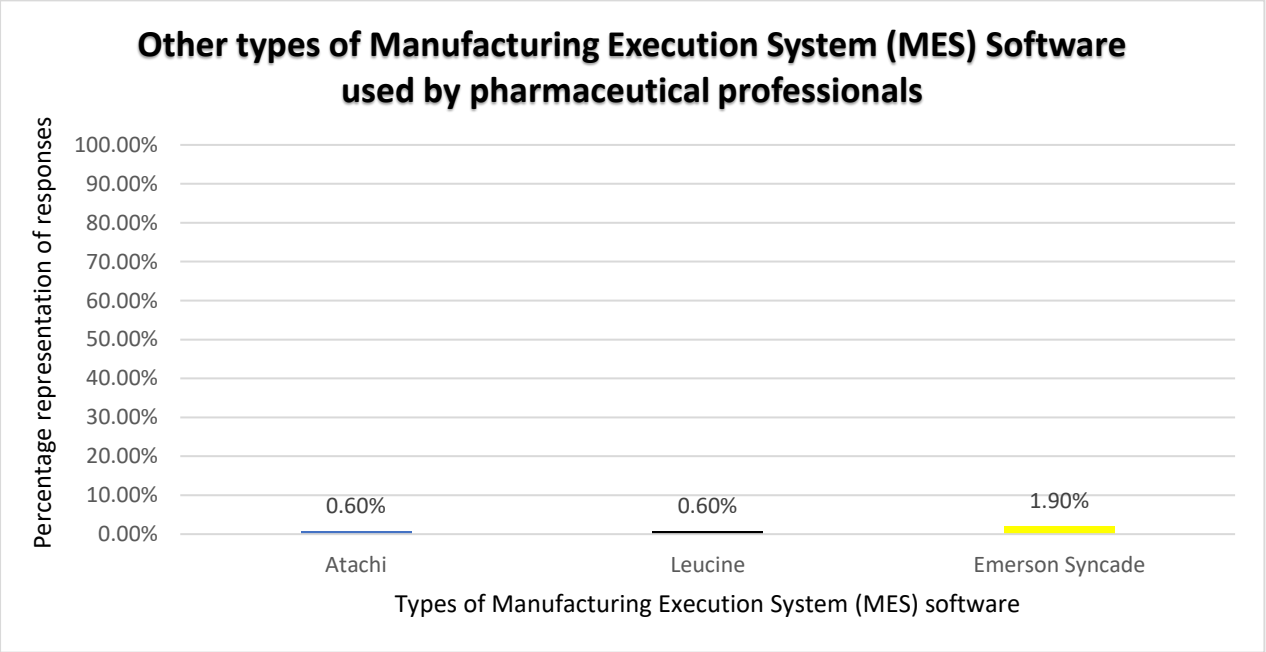

Figure 4.2.3 MES Others: Clustered Column Chart illustrating other types of Manufacturing Execution System (MES) software used by the pharmaceutical professionals in different manufacturing facilities

Apart from the Manufacturing Execution System (MES) software mentioned in the table 4.2.3, personnel from the quality Assurance, microbiology, research and development, and environment health and safety also have experience in Atachi 1(0.6%), Emerson

Syncade 3(1.9%) and Leucine Manufacturing Execution System (MES) software 1(0.6%).

4.2.4 Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.

Question asked to the participant: In your opinion, what are the challenges that would be influencing adaptation of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities?

Table 4.2.4 MES: Perception of participants on the challenges that would be influencing adaptation of Manufacturing Execution System (MES) Software

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total:137 (100%)
Financial hurdles	2 (1.5%)	1 (0.7%)	1 (0.7%)	5 (3.6%)	2 (1.5%)	2 (1.5%)	10 (7.3%)	7 (5.1%)	30 (21.9%)
Infrastructural limitations	2 (1.5%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	3 (2.2%)	2 (1.5%)	3 (2.2%)	2 (1.5%)	15 (10.9%)
Technological backwardness	1 (0.7%)	1 (0.7%)	2 (1.5%)	3 (2.2%)	2 (1.5%)	0	0	1 (0.7%)	10 (7.3%)
Strict regulatory framework	1 (0.7%)	1 (0.7%)	1 (0.7%)	2 (1.5%)	0	0	1 (0.7%)	2 (1.5%)	8 (5.8%)
Time consuming process	0	1 (0.7%)	0	1 (0.7%)	2 (1.5%)	2 (1.5%)	4 (2.9%)	1 (0.7%)	11 (8.0%)
Complexity in nature	1 (0.7%)	3 (2.2%)	1 (0.7%)	0	0	3 (2.2%)	1 (0.7%)	1 (0.7%)	10 (7.3%)

Huge organizational change required	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	2 (1.5%)	0	1 (0.7%)	2 (1.5%)	9 (6.6%)
All of the above	10 (7.3%)	7 (5.1%)	6 (4.4%)	4 (2.9%)	5 (3.6%)	7 (5.1%)	2 (1.5%)	3 (2.2%)	44 (32.1%)

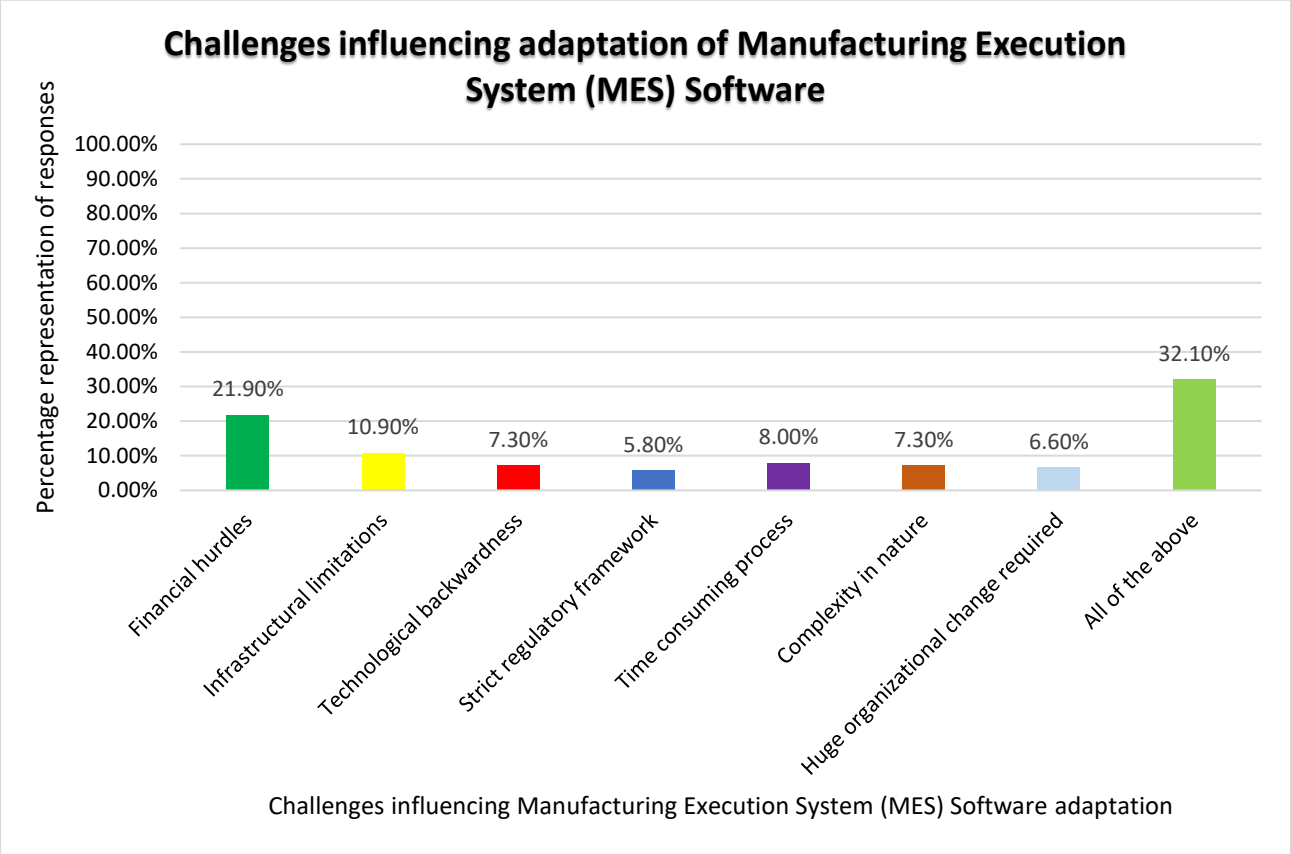

Figure 4.2.4 MES: Clustered Column Chart representing the perception of participants on the challenges that would be influencing adaptation of Manufacturing Execution System (MES) Software.

Table 4.2.4 MES and Figure 4.2.4 MES represents the challenges that would be influencing adaptation of MES Software. Majority 44(32.1%) of the participants all the challenges including financial hurdles, infrastructural limitations, technological backwardness, strict regulatory framework, time consuming process, complexity in nature, huge organizational change required are having profound impact on the adaptation of MES Software.

Question asked to the participant: In your opinion, what are the challenges that would be influencing adaptation of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities?

Table 4.2.4 CSV: Perception of participants on the challenges that would be influencing adaptation of Computer System Validation (CSV) Process

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 149 (100%)
Regulatory compliance	0	0	1 (0.7%)	4 (2.7%)	4 (2.7%)	2 (1.3%)	4 (2.7%)	0	15 (10.1%)
Training cost	0	2 (1.3%)	2 (1.3%)	2 (1.3%)	4 (2.7%)	1 (0.7%)	5 (3.4%)	1 (0.7%)	17 (11.4%)
Time consuming process	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	2 (1.3%)	2 (1.3%)	1 (0.7%)	10 (6.7%)
Excess validation documentation	0	2 (1.3%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	2 (1.3%)	3 (2.0%)	11 (7.4%)
Cybersecurity challenges	1 (0.7%)	2 (1.3%)	0	1 (0.7%)	6 (4.0%)	0	2 (1.3%)	8 (5.4%)	20 (13.4%)
Technical complexity	2 (1.3%)	3 (2.0%)	0	3 (2.0%)	1 (0.7%)	3 (2.0%)	3 (2.0%)	2 (1.3%)	17 (11.4%)
Regular upgrades and	2 (1.3%)	1 (0.7%)	0	1 (0.7%)	2 (1.3%)	0	2 (1.3%)	3 (2.0%)	11 (7.4%)

modification									
All of the above	11 (7.4%)	7 (4.7%)	8 (5.4%)	5 (3.4%)	5 (3.4%)	7 (4.7%)	2 (1.3%)	3 (2.0%)	48 (32.2%)

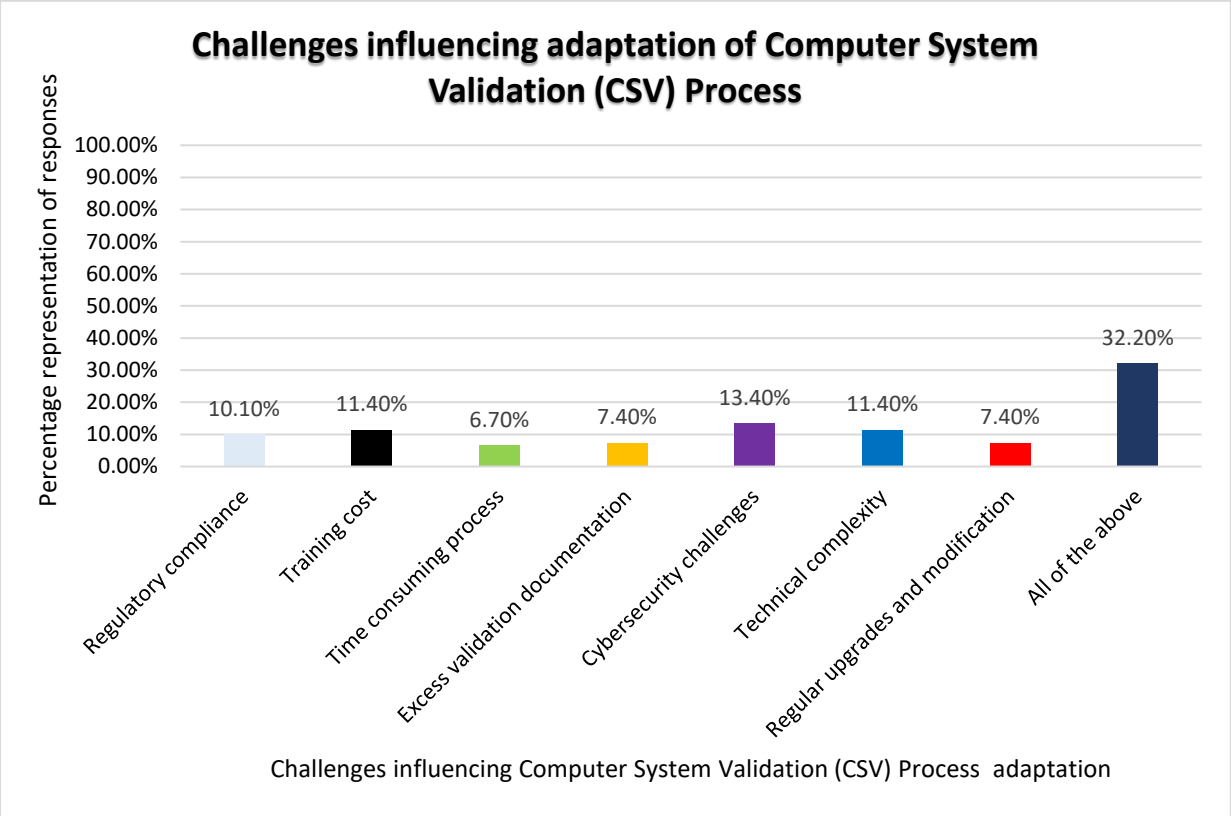

Figure 4.2.4 CSV: Clustered Column Chart representing the challenges that would be influencing adaptation of Computer System Validation (CSV) Process

Table 4.2.4 CSV and Table 4.2.4 CSV illustrates the challenges that would be influencing adaptation of CSV Process. 48(32.2%) of the participants believe that all of the challenges including regulatory compliance, training cost, time consuming process, excess validation documentation, Cybersecurity challenges, technical complexity, and regular upgrades and modification have a vital role in the adaptation of CSV Process.

Question asked to the participant: In your opinion what type of support Government authorities should initiate for the implementation of innovative computerization technologies?

Table 4.2.4 Government measures: supportive schemes the Government authorities should initiate for the implementation of innovative computerization technologies

Respondents	**Quality Assurance (QA)**	**Quality Control (QC)**	**Production department**	**Microbiology department**	**Engineering department**	**Warehouse department**	**Research and Development**	**Environment Health and Safety**	**Total: 131 (100%)**
Technological support	2 (1.5%)	2 (1.5%)	4 (3.1%)	3 (2.3%)	3 (2.3%)	2 (1.5%)	1 (0.8%)	1 (0.8%)	18 (13.7%)
Infrastructural support	1 (0.8%)	2 (1.5%)	2 (1.5%)	5 (3.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0	13 (9.9%)
Tax credits	2 (1.5%)	4 (3.1%)	0	1 (0.8%)	2 (1.5%)	1 (0.8%)	0	2 (1.5%)	12 (9.2%)
Incentives	1 (0.8%)	0	1 (0.8%)	2 (1.5%)	1 (0.8%)	4 (3.1%)	1 (0.8%)	2 (1.5%)	12 (9.2%)
Subsidies	0	3 (2.3%)	1 (0.8%)1	4 (3.1%)	2 (1.5%)	1 (0.8%)	1 (0.8%)	2 (1.5%)	14 (10.7%)
All of the above	7 (5.3%)	8 (6.1%)	5 (3.8%)	6 (4.6%)	7 (5.3%)	7 (5.3%)	12 (9.2%)	10 (7.6%)	62 (47.3%)

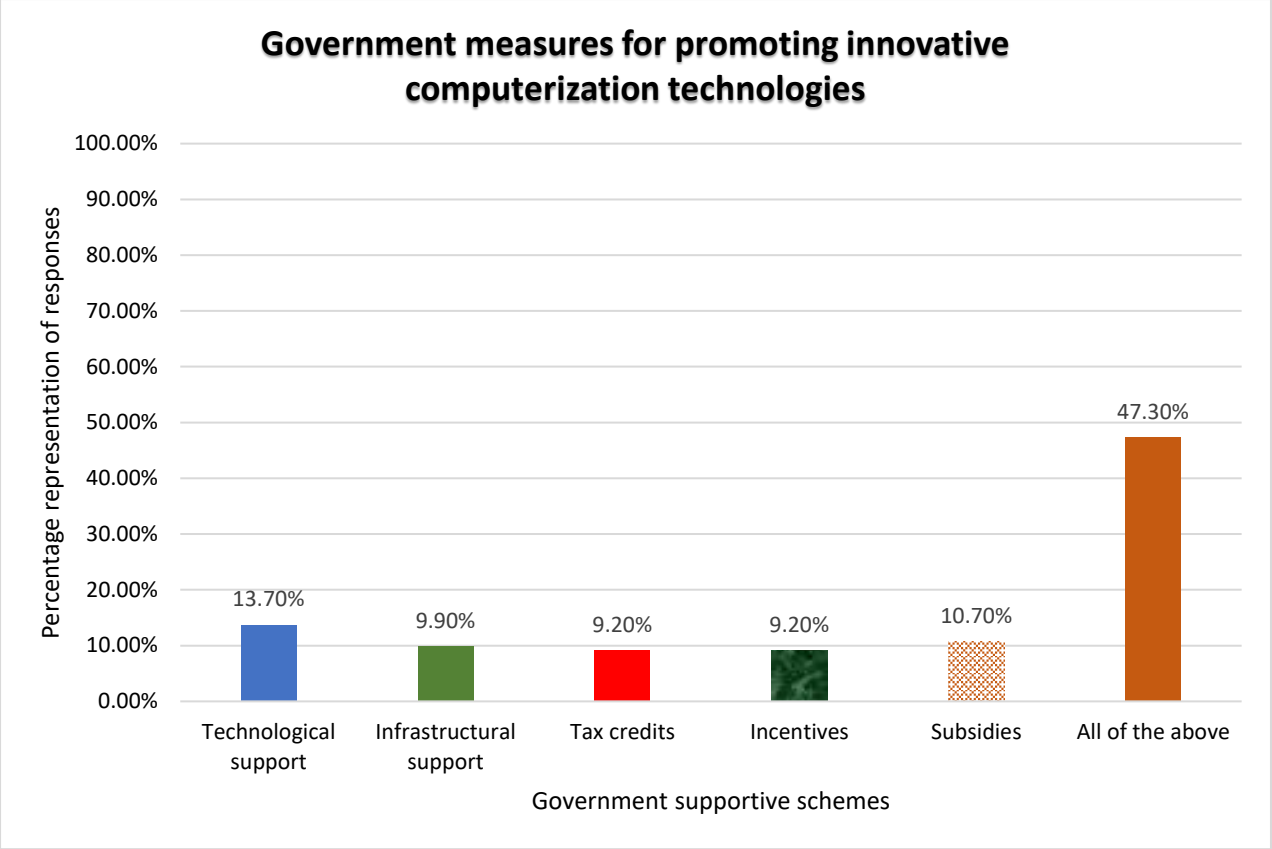

Figure 4.2.4 Government measures: Clustered Column Chart representing the supportive schemes the Government authorities should initiate for the implementation of innovative computerization technologies.

Table 4.2.4 Government measures and Figure 4.2.4 Government measures represents the supportive schemes the Government authorities should initiate for the implementation of innovative computerization technologies. From the response, it is clear that majority 62(47.3%) of the participants believe that all the factors mentioned is mandatorily required for implementation of innovative computerization technologies.

4.2.5 Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.

Question asked to the participant: In your opinion, what are the most common safety attributes of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities?

Table 4.2.5 MES: Perceptions on the most common safety attributes of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities.

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total:127 (100%)
User Specific Credentials	1 (0.8%)	2 (1.6%)	0	4 (3.1%)	2 (1.6%)	3 (2.4%)	1 (0.8%)	1 (0.8%)	14 (11.0%)
Electronic Signatures	1 (0.8%)	1 (0.8%)	2 (1.6%)	3 (2.4%)	1 (0.8%)	1 (0.8%)	0	3 (2.4%)	12 (9.4%)
Audit trails	1 (0.8%)	5 (3.9%)	0	3 (2.4%)	1 (0.8%)	1 (0.8%)	2 (1.6%)	2 (1.6%)	15 (11.8%)
Online data capturing	1 (0.8%)	2 (1.6%)	0	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	8 (6.3%)
Traceability	1 (0.8%)	4 (3.1%)	0	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	10 (7.9%)
All of the above	13 (10.2%)	7 (5.5%)	8 (6.3%)	6 (4.7%)	7 (5.5%)	7 (5.5%)	11 (8.7%)	9 (7.1%)	68 (53.5%)

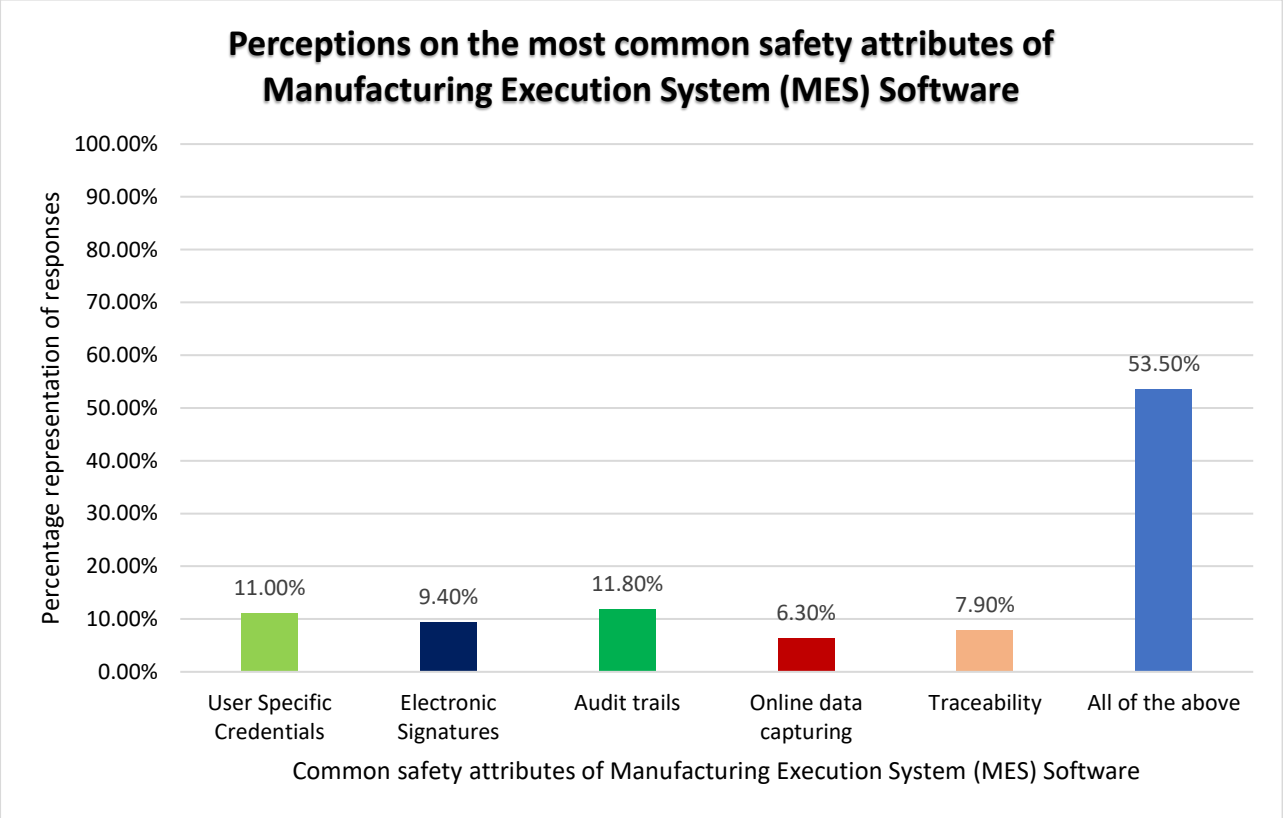

Figure 4.2.5 Safety attribute MES: Clustered Column Chart representing the perceptions on the most common safety attributes of Manufacturing Execution System (MES) Software in different pharmaceutical manufacturing facilities

Table 4.2.5 Safety attributes MES and Figure 4.2.5 Safety attributes MES describes the common safety attributes of MES Software in different pharmaceutical manufacturing facilities. A solid response rate of 68(53.5%) indicates that all common safety attributes like

user specific credentials, electronic signatures, audit trails, online data capturing, and traceability are useful in the MES Software.

Question asked to the participant: In your opinion, what are the most common safety attributes of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities?

Table 4.2.5 CSV: Perceptions on the most common safety attributes of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities.

Respondents	Quality Assurance (QA)	Quality Control (QC)	Production department	Microbiology department	Engineering department	Warehouse department	Research and Development	Environment Health and Safety	Total: 137 (100%)
Data management and data integrity	1 (0.7%)	2 (1.5%)	1 (0.7%)	5 (3.6%)	2 (1.5%)	2 (1.5%)	2 (1.5%)	4 (2.9%)	19 (13.9%)
System validation and testing	1 (0.7%)	1 (0.7%)	1 (0.7%)	4 (2.9%)	1 (0.7%)	0	1 (0.7%)	0	9 (6.6%)
Security and access control	1 (0.7%)	4 (2.9%)	0	3 (2.2%)	1 (0.7%)	3 (2.2%)	3 (2.2%)	4 (2.9%)	19 (13.9%)
Disaster Recovery and Business Continuity	1 (0.7%)	3 (2.2%)	0	4 (2.9%)	0	3 (2.2%)	3 (2.2%)	3 (2.2%)	17 (12.4%)
Training and user support	1 (0.7%)	4 (2.9%)	0	1 (0.7%)	1 (0.7%)	0	2 (1.5%)	0	9 (6.6%)
All of the above	13 (9.5%)	8 (5.8%)	8 (5.8%)	6 (4.4%)	7 (5.1%)	7 (5.1%)	8 (5.8%)	7 (5.1%)	64 (46.7%)

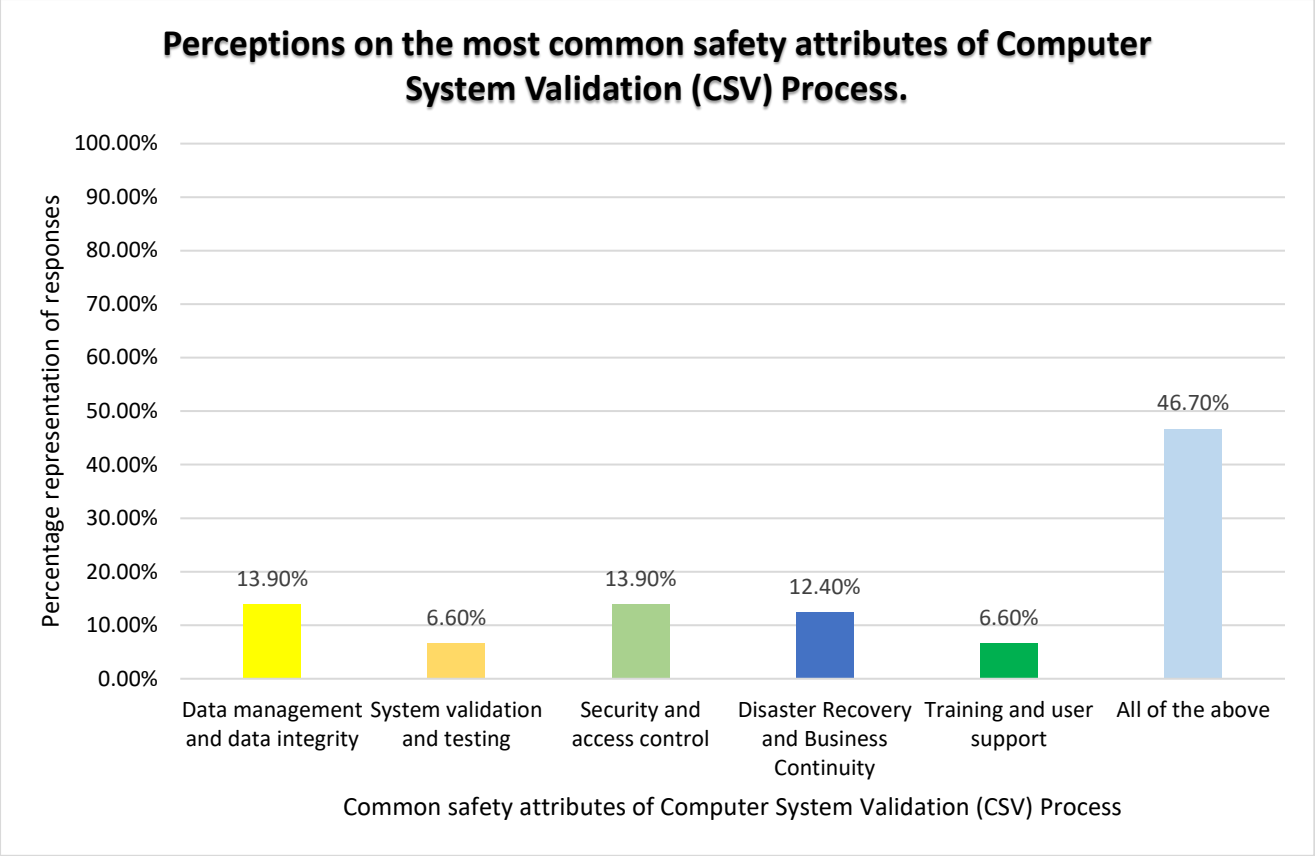

Figure 4.2.5 Safety attribute CSV: Clustered Column Chart representing the perceptions on the most common safety attributes of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities

Table 4.2.5 safety attribute CSV and Figure 4.2.5 Safety attribute CSV explains the common safety attributes of CSV Process in different pharmaceutical manufacturing facilities. A valid response of 64(46.7%) by the participants indicates all the common safety attributes like data management and data integrity, system validation and testing, security and access control, disaster recovery and business continuity, and training and user support are mandate for the implementation of CSV Process in different pharmaceutical manufacturing facilities.

4.3 Qualitative Data Analysis of Interviews

Interview Participants: Equal proportions of experts having knowledge or work expertise in pharmaceutical industry in the field of MES Software, and CSV Process were interviewed. Interview with equal proportion of participants have several advantages. Balanced evaluation to derive unique and meaningful conclusion is possible by interviewing equal proportions of participants. Another advantage is the prevention of bias during the analysis phase of the research study.

4.3.1 Table 1: Coding of the Participants

Table 1 is the coding of the participants. The table information on the Participant ID, designation and the interview status.

Participant ID	Participant's Designation	Interview Status
1. Shankar Suyodha CSV Consultant, Cognizant	**CSVP1**	**Completed**
2. Naveen K CSV Consultant, Cognizant	**CSVP2**	**Completed**
3. Hariprasad Reddy CSV Consultant, HCL	**CSVP3**	**Completed**
4. Suman Devraj D CSV Consultant, Sartorius	**CSVP4**	**Completed**
5. Prabhukumar Rayapuri CSV Consultant, Cognizant	**CSVP5**	**Completed**
6. Raveendra Talari CSV Consultant, HCL	**CSVP6**	**Completed**
7. Manjunatha Reddy Sirumala MES Expert, Tenshi Kaizen	**MESP1**	**Completed**
8. Vijay Wankhade Patil MES Expert, Medreich Ltd	**MESP2**	**Completed**
9. Stephan Francis MES Expert, Medreich Ltd	**MESP3**	**Completed**
10. Merin C Jose MES Expert, Sance Laboratories	**MESP4**	**Completed**
11. Vimal Rajeev MES Expert, Sance Laboratories	**MESP5**	**Completed**
12. Saravanan Muthaiyan MES Expert, Strides Shasun Ltd	**MESP6**	**Completed**

4.3.1 Table 2: Summary of the responses using first-order coding

Table 2 is based the on the summary of the responses provided by the participants during the interview and based on the responses are first-order codes.

Participant ID	Research questions and objectives	Responses
CSVP1	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: We have different regulatory bodies like EMA, TGA, PMDA. But above all these regulatory bodies we have US FDA which serves as a benchmark. User access, System control, multifactor authentication, and GAMP guidelines will give elaborate details on the CSV Process.** **OI Q2: We do have strict regulatory systems like USFDA 21 CFR Part 11, EudraLex, PIC/S guidelines. To maintain validated GxP environment we need to perform data integration, data separation, data migration, installation qualification, operational qualification, and performance qualification based on application complexity. Risks increases with the complexity of the application. To mitigate the risks strict regulatory systems and approach guidelines are needed.** **OII Q3: Human errors are seriously monitored by the US FDA regulatory bodies. Main advantages include error free data entry, and moreover the system will perform as expected by the regulatory bodies and business requirements.** **OIII Q4: We should not decide which software suits our need merely by its brand or market value. Patient safety, Product quality, Data integrity, Regulatory aspects should be taken into consideration while selecting appropriate software. Based upon risk assessment and evaluation of process we should decide whether the application is fit for the intended purpose. Regardless of the types of MES application, vendor assessment should be performed. Usually, all sorts of MES application fall under category 4 unless it is a customizable application. If it is customized, it is a category 5 application.** **OIV Q5: Cost effectiveness, integration of MES system into the legacy systems are time consuming. If the systems are manufactured before 1984, then it is considered as legacy systems. Training, Resource allocations as per regulatory requirements.** **OV Q6: Identity Access Management, masked up passwords, multifactor authentication. During the vendor assessment all the safety requirements should be verified.**

CSVP2	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: Yes, there are various regulatory systems which details about Computer System Validation Process like EMA (EudraLex Annex 11), US FDA (21 CFR Part 11), PIC/S, ISO Guidelines, GAMP guidelines. These regulatory systems guide in the implementation of MES Software and CSV Process.** **OI Q2: Obviously, strict regulatory guidelines are needed for the effective implementation of MES Software and CSV Process. Guidelines should give adequate information regarding the process of performing validation, personnel responsible for performing validation.** **OII Q3: Advantages includes manipulation of the data and data integrity issues can be avoided. Excessive manpower can be reduced in the process saving the cost. Disadvantages includes Complexity in handling and understanding the process, expensive nature in implementation of the software.** **OIII Q4: Plenty of vendors are available in the market. Caution should be given on the regulatory guidelines that the vendor follows, reputation of the firm, technical support by the vendor, Previous experience profile of the vendor should be analysed, cost effectiveness of the software should be also taken into consideration.** **OIV Q5: Third party team may be needed for the implementation of the software (especially for the integration of the software and the equipment), technical support and availability of the vendor unit.** **OV Q6: Better risk assessment and a good mitigation plan can definitely solve the safety concerns. If not procedure in the SOP should be revised.**
CSVP3	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES)**	**OI Q1: Yes, to some extent. We have regulatory guidelines like 21 CFR and EU Annex 11, GAMP guidelines. The software's and activities will be validated as per these guidelines.** **OI Q2: Yes, it is mentioned in GAMP-5 edition 2. It is emphasizing to use MES Software rather than the traditional paper documentation.** **OII Q3: The main advantages include adherence to data integrities, reduce manpower, good for regulatory submissions, easy to use, reduces the errors.**

	Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry. **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OIII Q4: It should be user friendly, adhere to regulatory agencies, adhere to QMS (Quality Management System) activities.** **OIV Q5: Causes more cost to the company, more training should be given to the people involved in the operations, and time consuming are the main challenges to the company.** **OV Q6: Before implementing CSV Process, we should have Standard Operating Procedures on the data backup, data retrieval and archival. Should be continuously monitored, periodically taken backup, disaster recoveries or contingency plan should be available and made effective.**
CSVP4	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and**	**OI Q1: Yeah correct, regulatory requirements are very essential in pharmaceutical companies. US FDA, EMA are having specific requirements as per current Good Manufacturing Practices regarding implementation of MES Software and CSV Process.** **OI Q2: CSV is completely based upon the regulatory requirements. Recently the US FDA have released the draft for introduction of Computer System Assurance (CSA) which will replace the Computer System Validation in the future. Unlike CSV Process, CSA have less documentation.** **OII Q3: Advantages includes improved efficiency, productivity, real time data capturing, reducing costs and resources, offering competitive advantages to companies due to the popularity of digitalisation in the pharmaceutical manufacturing facilities. Disadvantages includes, installation costs of hardware/software, complexity in training, resistance from the end users since they are more addicted to traditional paper works.** **OIII Q4: Depends on the product which the company is manufacturing, and also on the regulatory authority the company follows. As per GAMP-5 guidelines, MES Software are categorised from 1-5.**

	Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India. **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OIV Q5: Installation costs will be high for hardware and software, Strong technical data backup, server availabilities, data storage locations and complex trainings for end users. CSV Process requires specific team and skilled personnel. Regular maintenance of the system including change controls and updates of the software.** **OV Q6: Yeah, definitely it will help to address safety concerns but not completely. Based on innovative technologies machine learning, and automated hazards can be identified earlier.**
CSVP5	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: Regulatory authorities are encouraging the use of MES Software and CSV Process, because the data is very secure and will be digitally available, hence there is no chance of data integrity.** **OI Q2: Yes, it is required, regulatory systems like MHRA, US FDA are suggesting the use of MES Software and CSV Process mainly for achieving regulatory compliance and reducing data integrity issues. There are some companies in India who are supplying medicines domestic or to Indian market who needs to adapt these digital technologies.** **OII Q3: Advantages: Data will be digitally captured and no scope for data integrity, on time documentation, improve the quality of documentation, and traceability. Disadvantages are very less but it is a time-consuming process.** **OIII Q4: User friendly, easy to use.** **OIV Q5: Training of users, Personnel should have a thorough knowledge on the usage of the MES Software, otherwise wrong data entries may lead to data integrity and deviations.** **OV Q6: All safety concerns cannot be addressed but by procedure controls we can reduce the safety concerns. CSV Process will not assure 100 % mitigation of safety concerns. Additional procedure controls will be performed in such cases.**

CSVP6	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: The regulatory systems like US FDA and MHRA are encouraging the implementation of MES Software and CSV Process.** **OI Q2: For any application, it is mandatory to comply with regulatory standards and guidelines.** **Deliverables for category 3 software: Impact assessment, Qualification Plan, URS, FS (Functional Specification), Vendor assessment, IQ, OQ, Traceability matrix, and validation summary. Configuration specification additionally done for category 4. Code review and design specification needs to be additionally performed for category 5 software.** **OII Q3: Advantages: avoid data integrity, track any errors or changes, online activities with electronic signatures, online data capturing, reduction in manpower, contemporaneous data entry. Disadvantages are very less.** **OIII Q4: Quality software with reasonable price.** **OIV Q5: Software integration with equipment configuration is a complex process, based on experience other challenges can be resolved.** **OV Q6: A backup of electronic data will be always there for MES Software. Generally, it is stored in a disaster recovery server. In case of any natural calamities like fire, spillage, all data will be stored in a recovery backup server. The GAMP guidelines are saying to include such backup servers like disaster recovery servers.**
MESP1	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES)**	**OI Q1: Every country is having their own specific regulatory systems with different policies and regulations. 21 CFR of US FDA suggests the use of electronic signatures and electronic records.** **OI Q2: Yes, it is required, different countries have specific guidelines. They should monitor and give detailed guidelines on how the software is working.** **OII Q3: Advantages: Reduce data integrity issues, easy to access, reduction in cost, traceability of batches, environmentally friendly. Disadvantages: Security issues like software data breach, training takes more time, small**

	Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry. **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**companies cannot afford expensive software packages, equipment integration and automation is difficult.** **OIII Q4: Cost effectiveness, User friendly interface of the software, based on security features which prevents all sorts of manual errors.** **OIV Q5: Continuous Software support is required, Expensive nature.** **OV Q6: The safety concerns can be addressed only up to 70% but disadvantages like security issues, software may get corrupted, malfunctions. Equipment integration and automation is difficult.**
MESP2	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and**	**OI Q1: Regulatory systems across the globe like US FDA, MHRA, ANVISA, TGA and EMA are serious about data integrity issues and are strongly encouraging the implementation of MES Software and CSV Process.** **OI Q2: Strict regulatory system is essential for MES and CSV Process implementation.** **OII Q3: Advantages: Reduces the data integrity issues and human errors, retention and retrieval of documents Disadvantages: Software is expensive.** **OIII Q4: Usability of the software should be good and should be affordable.** **OIV Q5: Cost of the software, In India there are so many small-scale companies and their budget won't be sufficient to purchase such costly software's.** **OV Q6: Safety concerns cannot be solved completely, but by periodic validations and encouraging such innovative technologies safety concerns can be resolved to a major extend.**

	Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India. **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	
MESP3	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: Yes, the strict regulatory systems like US FDA, EMA, and PMDA has a positive role in the implementation of MES Software.** **OI Q2: Yes, strict guidelines are needed for the implementation of MES Software and CSV Process.** **OII Q3: Advantages: Reduces the data integrity issues, regulatory compliance, positively impact on Quality Management System and document management. Disadvantages includes cost of training, cost of maintenance of the software.** **OIII Q4: Cost effectiveness, comply with the international regulatory guidelines and easy to use.** **OIV Q5: Cost of the software, updating of software, training costs.** **OV Q6: No, we cannot completely solve the safety concerns but by ensuring calibrations and periodic validations we can solve most of the safety concerns.**

MESP4	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OI Q1: Yes, Like US FDA, PMDA TGA have strict guidelines and promoting electronic documentation so that the regulatory filing will be easy.** **OI Q2: Yes, strict regulatory system like US FDA, PMDA, TGA promotes electronic documentation. But in India, CDSCO is the regulatory system and it give only limited information regarding the electronic documentation. Small scale pharmaceutical manufacturing facilities in India should also promote and implement the use of MES Software. The guidelines of CDSCO should be revised in the future and should give more importance to the computerization technologies.** **OII Q3: Advantages: Automation: easy to trace data, using audit trails, efficiency is very high, inventory management, real-time monitoring which is online data entry, data retrievability and traceability. Disadvantage is the costly nature of the software.** **OIII Q4: Cost of the software should be affordable, efficiency, traceability of the software, user friendliness of the software.** **OIV Q5: High cost for installation and updating the software, Complexity in nature.** **OV Q6: No, all the safety concerns cannot be completely solved. Proper validations and updation we can resolve the safety concerns to a greater extend.**
MESP5	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES)**	**OI Q1: Yes, because different regulatory systems like TGA, and EMA are encouraging the use of electronic documentation. It will decrease all the disadvantages of the traditional paper works we are currently using. By this ultimately it helps to enhance the quality of the product we are currently manufacturing.** **OI Q2: Strict regulatory system is essential for the MES and CSV implementation. In other countries they are following strict guidelines but in India there is no proper regulatory system but in future they will promote the implementation of MES Software and CSV Process.**

	Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry. **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India.** **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**OII Q3: Advantages are it decreases the integrity issues of data, minimize user error in the manufacturing process. Disadvantage will be the expensive nature of the software for small scale pharmaceutical companies.** **OIII Q4: Based on the requirement and budget of the company, should be affordable** **OIV Q5: Cost of the software will be high, strong IT team is needed for technological support.** **OV Q6: Regular and periodic validation of computer systems can solve the safety concerns to a major extend.**
MESP6	**Objective I: Comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process in different Pharmaceutical manufacturing facilities with different Regulatory Landscape in India.** **Objective I Research question 1 (OI Q1):** Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view? **OI Q2:** Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process? **Objective II: Evaluate Advantages and Disadvantages in the implementation of Manufacturing Execution Systems (MES) Software and Computer System Validation (CSV) Process technologies in the Pharmaceutical industry.** **OII Q3:** What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities? **Objective III: To examine the different types of Manufacturing Execution System (MES) Software available across the industry.** **OIII Q4:** There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software? **Objective IV: To analyse the challenges in the implementation of Manufacturing Execution System (MES) Software and**	**OI Q1: Regulatory systems now a days recommending the digitalisation of documentation and online entries. CDSCO of India not promoting digitalisation but other regulatory systems like US FDA, ANVISA, TGA, MHRA are demanding the digitalisation of documents.** **OI Q2: Definitely effective guidelines are required for the implementation of MES Software and CSV Process.** **OII Q3: Advantages are Tracking, Traceability, avoid data integrities, all in process checks can be documented contemporaneously, online data entries. Disadvantages are the development of software bugs.** **OIII Q4: User friendly and cost-effective system.** **OIV Q5: Cost of the software. It is difficult for the small-scale companies in India to install such costly software but the multinational companies in India under the USFDA, MHRA regulations are currently capable of implementing such innovative technologies.** **OV Q6: Still some safety concerns will exist but by the implementation of MES Software and CSV Process safety concerns can be improved.**

	Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities in India. **OIV Q5:** What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India? **Objective V: Highlight Challenges concerning data safety in the use of Manufacturing Execution System (MES) software and Computer System Validation (CSV) Process.** **OV Q6:** Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	

4.3.1 Table 3: Segregation of responses using the first-order codes

Table 3 is the segregation of the responses provided by the participants during the interview based on the responses of first-order codes.

Research Questions	First Order Codes
Objective 1 Research question 1 (OI Q1): Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view?	**CSVP1: We have different regulatory bodies like EMA, TGA, PMDA. But above all these regulatory bodies we have US FDA which serves as a benchmark. User access, System control, multifactor authentication, and GAMP guidelines will give elaborate details on the CSV Process.** **CSVP2: Yes, there are various regulatory systems which details about Computer System Validation Process like EMA (EudraLex Annex 11), US FDA (21 CFR Part 11), PIC/S, ISO Guidelines, GAMP guidelines. These regulatory systems guide in the implementation of MES Software and CSV Process.** **CSVP3: Yes, to some extent. We have regulatory guidelines like 21 CFR and EU Annex 11, GAMP guidelines. The software's and activities will be validated as per these guidelines.** **CSVP4: Yeah correct, regulatory requirements are very essential in pharmaceutical companies. US FDA, EMA are having specific requirements as per current Good Manufacturing Practices regarding implementation of MES Software and CSV Process.** **CSVP5: Regulatory authorities are encouraging the use of MES Software and CSV Process, because the data is very secure and will be digitally available, hence there is no chance of data integrity.** **CSVP6: The regulatory systems like US FDA and MHRA are encouraging the implementation of MES Software and CSV Process.** **MESP1: Every country is having their own specific regulatory systems with different policies and regulations. 21 CFR of US FDA suggests the use of electronic signatures and electronic records.** **MESP2: Regulatory systems across the globe like US FDA, MHRA, ANVISA, TGA and EMA are serious about data integrity issues and are strongly encouraging the implementation of MES Software and CSV Process.** **MESP3: Yes, the strict regulatory systems like US FDA, EMA, and PMDA has a positive role in the implementation of MES Software.**

	MESP4: Yeah correct, regulatory requirements are very essential in pharmaceutical companies. US FDA, EMA are having specific requirements as per current Good Manufacturing Practices regarding implementation of MES Software and CSV Process. **MESP5: Yes, because different regulatory systems like TGA, and EMA are encouraging the use of electronic documentation. It will decrease all the disadvantages of the traditional paper works we are currently using. By this ultimately it helps to enhance the quality of the product we are currently manufacturing.** **MESP6: Regulatory systems now a days recommending the digitalisation of documentation and online entries. CDSCO of India not promoting digitalisation but other regulatory systems like US FDA, ANVISA, TGA, MHRA are demanding the digitalisation of documents.**
OI Q2: Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process?	**CSVP1: We do have strict regulatory systems like USFDA 21 CFR Part 11, EudraLex, PIC/S guidelines. To maintain validated GxP environment we need to perform data integration, data separation, data migration, installation qualification, operational qualification, and performance qualification based on application complexity. Risks increases with the complexity of the application. To mitigate the risks strict regulatory systems and approach guidelines are needed.** **CSVP2: Obviously, strict regulatory guidelines are needed for the effective implementation of MES Software and CSV Process. Guidelines should give adequate information regarding the process of performing validation, personnel responsible for performing validation.** **CSVP3: Yes, it is mentioned in GAMP-5 edition 2. It is emphasizing to use MES Software rather than the traditional paper documentation.** **CSVP4: CSV is completely based upon the regulatory requirements. Recently the US FDA have released the draft for introduction of Computer System Assurance which will replace the Computer System Validation in the future. Unlike CSV Process, CSA have less documentation.** **CSVP5: Yes, it is required, regulatory systems like MHRA, US FDA are suggesting the use of MES Software and CSV Process mainly for achieving regulatory compliance and reducing data integrity issues. There are some companies in India who are supplying medicines domestic or to Indian market who needs to adapt these digital technologies.** **CSVP6: For any application, it is mandatory to comply with regulatory standards and guidelines.** **Deliverables for category 3 software: Impact assessment, Qualification Plan, URS, FS, Vendor assessment, IQ, OQ, Traceability matrix, and validation summary. Configuration specification additionally done for category 4. Code review and design specification needs to be additionally performed for category 5 software.** **MESP1: Yes, it is required, different countries have specific guidelines. They should monitor and give detailed guidelines on how the software is working.** **MESP2: Strict regulatory system is essential for MES and CSV Process implementation.** **MESP3: Yes, strict guidelines are needed for the implementation of MES Software and CSV Process.** **MESP4: Yes, strict regulatory system like US FDA, PMDA, TGA promotes electronic documentation. But in India, CDSCO is the regulatory system and it give only limited information regarding the electronic documentation. Small scale pharmaceutical manufacturing facilities in India should also promote and implement the use of MES Software. The guidelines of CDSCO should be revised in the future and should give more importance to the computerization technologies.**

	MESP5: Strict regulatory system is essential for the MES and CSV implementation. In other countries they are following strict guidelines but in India there is no proper regulatory system but in future they will promote the implementation of MES Software and CSV Process. **MESP6: Definitely effective guidelines are required for the implementation of MES Software and CSV Process.**
OII Q3: What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities?	**CSVP1: Human errors are seriously monitored by the US FDA regulatory bodies. Main advantages include error free data entry, and moreover the system will perform as expected by the regulatory bodies and business requirements.** **CSVP2: Advantages includes manipulation of the data and data integrity issues can be avoided. Excessive manpower can be reduced in the process saving the cost. Disadvantages includes Complexity in handling and understanding the process, expensive nature in implementation of the software.** **CSVP3: The main advantages include adherence to data integrities, reduce manpower, good for regulatory submissions, easy to use, reduces the errors.** **CSVP4: Advantages includes improved efficiency, productivity, real time data capturing, reducing costs and resources, offering competitive advantages to companies due to the popularity of digitalisation in the pharmaceutical manufacturing facilities. Disadvantages includes, installation costs of hardware/software, complexity in training, resistance from the end users since they are more addicted to traditional paper works.** **CSVP5: Advantages: Data will be digitally captured and no scope for data integrity, on time documentation, improve the quality of documentation, and traceability. Disadvantages are very less but it is a time-consuming process.** **CSVP6: Advantages: avoid data integrity, track any errors or changes, online activities with electronic signatures, online data capturing, reduction in manpower, contemporaneous data entry. Disadvantages are very less.** **MESP1: Advantages: Reduce data integrity issues, easy to access, reduction in cost, traceability of batches, environmentally friendly. Disadvantages: Security issues like software data breach, training takes more time, small companies cannot afford expensive software packages, equipment integration and automation is difficult.** **MESP2: Advantages: Reduces the data integrity issues and human errors, retention and retrieval of documents Disadvantages: Software is expensive.** **MESP3: Advantages: Reduces the data integrity issues, regulatory compliance, positively impact on Quality Management System and document management. Disadvantages includes cost of training, cost of maintenance of the software.** **MESP4: Advantages: Automation: easy to trace data, using audit trails, efficiency is very high, inventory management, real-time monitoring which is online data entry, data retrievability and traceability. Disadvantage is the costly nature of the software.** **MESP5: Advantages are it decreases the integrity issues of data, minimize user error in the manufacturing process. Disadvantage will be the expensive nature of the software for small scale pharmaceutical companies.** **MESP6: Advantages are Tracking, Traceability, avoid data integrities, all in process checks can be documented contemporaneously, online data entries. Disadvantages are the development of software bugs.**
OIII Q4: There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software?	**CSVP1: We should not decide which software suits our need merely by its brand or market value. Patient safety, Product quality, Data integrity, Regulatory aspects should be taken into consideration while selecting appropriate software. Based upon risk assessment and evaluation of process we should decide whether the application is fit for the intended purpose. Regardless of the types of MES application, vendor assessment should be performed. Usually, all sorts of MES application fall under category 4 unless it is a customizable application. If it is customized, it is a category 5 application.**

	CSVP2: Plenty of vendors are available in the market. Caution should be given on the regulatory guidelines that the vendor follows, reputation of the firm, technical support by the vendor, Previous experience profile of the vendor should be analysed, cost effectiveness of the software should be also taken into consideration. **CSVP3: It should be user friendly, adhere to regulatory agencies, adhere to QMS activities.** **CSVP4: Depends on the product which the company is manufacturing, and also on the regulatory authority the company follows. As per GAMP-5 guidelines, MES Software are categorised from 1-5.** **CSVP5: User friendly, easy to use.** **CSVP6: Quality software with reasonable price.** **MESP1: Cost effectiveness, User friendly interface of the software, based on security features which prevents all sorts of manual errors.** **MESP2: Usability of the software should be good and should be affordable.** **MESP3: Cost effectiveness, comply with the international regulatory guidelines and easy to use.** **MESP4: Cost of the software should be affordable, efficiency, traceability of the software, user friendliness of the software.** **MESP5: Based on the requirement and budget of the company, should be affordable** **MESP6: User friendly and cost-effective system.**
OIV Q5: What do you think are the main challenges in implementing MES Software and CSV Process in different pharmaceutical manufacturing facilities in India?	**CSVP1: Cost effectiveness, integration of MES system into the legacy systems are time consuming. If the systems are manufactured before 1984, then it is considered as legacy systems. Training, Resource allocations as per regulatory requirements.** **CSVP2: Third party team may be needed for the implementation of the software (especially for the integration of the software and the equipment), technical support and availability of the vendor unit.** **CSVP3: Causes more cost to the company, more training should be given to the people involved in the operations, and time consuming are the main challenges to the company.** **CSVP4: Installation costs will be high for hardware and software, Strong technical data backup, server availabilities, data storage locations and complex trainings for end users. CSV Process requires specific team and skilled personnel. Regular maintenance of the system including change controls and updates of the software.** **CSVP5: Training of users, Personnel should have a thorough knowledge on the usage of the MES Software, otherwise wrong data entries may lead to data integrity and deviations.** **CSVP6: Software integration with equipment configuration is a complex process, based on experience other challenges can be resolved.** **MESP1: Continuous Software support is required, Expensive nature.** **MESP2: Cost of the software, In India there are so many small-scale companies and their budget won't be sufficient to purchase such costly software's.**

	MESP3: Cost of the software, updating of software, training costs. **MESP4: High cost for installation and updating the software, Complexity in nature.** **MESP5: Cost of the software will be high, strong IT team is needed for technological support.** **MESP6: Cost of the software. It is difficult for the small-scale companies in India to install such costly software but the multinational companies in India under the USFDA, MHRA regulations are currently capable of implementing such innovative technologies.**
OV Q6: Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**CSVP1: Identity Access Management, masked up passwords, multifactor authentication. During the vendor assessment all the safety requirements should be verified.** **CSVP2: Better risk assessment and a good mitigation plan can definitely solve the safety concerns. If not procedure in the SOP should be revised.** **CSVP3: Before implementing CSV Process, we should have Standard Operating Procedures on the data backup, data retrieval and archival. Should be continuously monitored, periodically taken backup, disaster recoveries or contingency plan should be available and made effective.** **CSVP4: Yeah, definitely it will help to address safety concerns but not completely. Based on innovative technologies machine learning, and automated hazards can be identified earlier.** **CSVP5: All safety concerns cannot be addressed but by procedure controls we can reduce the safety concerns. CSV Process will not assure 100 % mitigation of safety concerns. Additional procedure controls will be performed in such cases.** **CSVP6: A backup of electronic data will be always there for MES Software. Generally, it is stored in a disaster recovery server. In case of any natural calamities like fire, spillage, all data will be stored in a recovery backup server. The GAMP guidelines are saying to include such backup servers like disaster recovery servers.** **MESP1: The safety concerns can be addressed only up to 70% but disadvantages like security issues, software may get corrupted, malfunctions. Equipment integration and automation is difficult.** **MESP2: Safety concerns cannot be solved completely, but by periodic validations and encouraging such innovative technologies safety concerns can be resolved to a major extend.** **MESP3: No, we cannot completely solve the safety concerns but by ensuring calibrations and periodic validations we can solve most of the safety concerns.** **MESP4: No, all the safety concerns cannot be completely solved. Proper validations and updation we can resolve the safety concerns to a greater extend.** **MESP5: Regular and periodic validation of computer systems can solve the safety concerns to a major extend.** **MESP6: Still some safety concerns will exist but by the implementation of MES Software and CSV Process safety concerns can be improved.**

4.3.1 Table 4: Second-Order Codes

Second-Order Codes based on the distillation of First-Order Codes

Research Questions	Second-Order Codes
Objective I Research question 1 (OI Q1): Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities in India? If yes, please explain your view?	**1. Strict regulatory systems are very essential for the implementation of MES Software and CSV Process.** **2. Provides security and integrity to the data.** **3. Enhances the quality of the product.** **4. Delivering safe medicine for consumers.**
OI Q2: Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process?	**1. Risk mitigation of computerized system through strict regulatory system and approach guidelines.** **2. Need for detailed and clear regulatory guidelines.** **3. All segments of pharmaceutical industries in India should promote electronic batch documentation.** **4. Proposal for the inclusion of Computer System Assurance by US FDA in "General Principles of Software" guidelines.** **5. Helps in reducing data integrity issues**
OII Q3: What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities?	**Advantages:** **1. Error free data.** **2. Adherence to regulatory systems.** **3. Manpower reduction.** **4. Easy regulatory submissions.** **5. Competitive advantage to pharmaceutical manufacturing facilities.** **6. Ease to track and trace the data.** **7. Improved efficiency and productivity** **8. Online data capturing.** **Disadvantages:** **1. Time consuming and complexity of processes.** **2. Equipment integration challenges.** **3. Resistance from users who are used to traditional paper documentation.** **4. Software/Hardware, training, and maintenance costs are high.** **5. Software bugs may appear during the manufacturing process causes time delay.**
OIII Q4: There are the different types of MES software available across the industry, what do you think will be the selection criteria for an ideal software?	**1. Product quality, Data integrity, and Regulatory aspects are to be given high priority while selecting MES Software.** **2. Software should be cost effective and should be user friendly.** **3. Risk assessment and critical thinking are two important factors to be considered for the CSV Process implementation.** **4. Vendor assessment is crucial in MES Software implementation.**
OIV Q5: What do you think are the main challenges in implementing MES Software and CSV Process in different	**1. A competent and skilled team is needed for effective CSV Process implementation.** **2. Time consuming process and rigorous training for end-users.** **3. CSV Process requires strong data backup and server availabilities.** **4. Extend of technical support offered by CSV consultants.** **5. Installation of MES Software are often very expensive.**

pharmaceutical manufacturing facilities in India?	**6. Constant IT support needed for smooth functioning.**
OV Q6: Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**1. CSV Process ensures all computerized systems involved in critical manufacturing processes are in validated state and performs accurately.** **2. Strong data backup, disaster recovery server and contingency plans are essential.** **3. By procedure controls and data migration tests, quality of data migrated from legacy systems to new computerized systems can be evaluated.** **4. Periodic validations and updation of MES Software is mandatory requirement for effectively addressing all safety concerns.**

4.3.1 Table 5: Third-Order Codes

Third-Order Codes based on distillation of Second-Order Codes

Research Questions	Third-Order Codes
Objective I Research question 1 (OI Q1): Do you think different regulatory systems can influence the implementation of MES Software and CSV Process in different pharmaceutical facilities? If yes, please explain your view?	**1. Strict regulatory systems with detailed guidelines.** **2. Data security and integrity.** **3. Product quality** **4. Safe medicine to consumers.**
OI Q2: Do you think a strict regulatory system with detailed guidelines are needed for the effective implementation of MES Software and CSV Process?	**1. Risk mitigation through clear and detailed regulatory guidelines.** **2. Constant revision of guidelines by US FDA.** **3. Irrespective of the market, India should promote data reliable digitalisation techniques.**
OII Q3: What are the advantages and disadvantages of implementing MES Software and CSV Process in pharmaceutical manufacturing facilities?	**Advantages** **1. Assuring data integrity** **2. Process performance** **3. Better traceability** **4. Regulatory compliance and easy filings.** **5. Staff reduction** **Disadvantages** **1. CSV is a tedious and costly process.** **2. Financial burden imposed by MES Software.** **3. End user resistance.** **4. Software bugs/glitches.**

OIII Q4: There are the different types of MES Software available across the industry, what do you think will be the selection criteria for an ideal software?	**1. Vendor assessment is very crucial in MES Software selection.** **2. Affordability and usability.** **3. Risk assessment and critical thinking have crucial role in CSV Process adoption.**
OIV Q5: What do you think are the main challenges in implementing MES Software and CSV Process?	**1. Expert IT team and skilled CSV consultants are required for hassle-free adoption of MES Software and CSV Process.** **2. MES Software may present financial tension onto the pharmaceutical companies.** **3. Time consuming and training complexity.** **4. Availability of reliable data backup and disaster recovery servers.**
OV Q6: Do you think all the safety concerns can be completely solved by MES Software and CSV Process? If No, how it can be managed efficiently?	**1. CSV Process validates computerized systems and their performance.** **2. Procedure controls and contingency plans are crucial in CSV Process adoption.** **3. Unreliable data backup and missing disaster recovery servers presents huge safety concerns.** **4. Regular validation and updation of software with adherence to regulatory requirements.**

4.3.2 Table 1: Summary of the responses collected from the 12 interviewees.

Interview statement	**No of participants in favour**	**Percentage out of 12 (100%) participants**
Need for strict regulatory system.	11 out of 12	91.2%
Helps in reducing data integrity issues.	11 out of 12	91.2%
Better traceability of documents.	6 out of 12	50%
Need for reliable data backup and disaster recovery servers.	3 out of 12	25%
Need for affordable MES Software.	8 out of 12	66.7%
Causing financial burden to the different pharmaceutical manufacturing facilities.	9 out of 12	75%

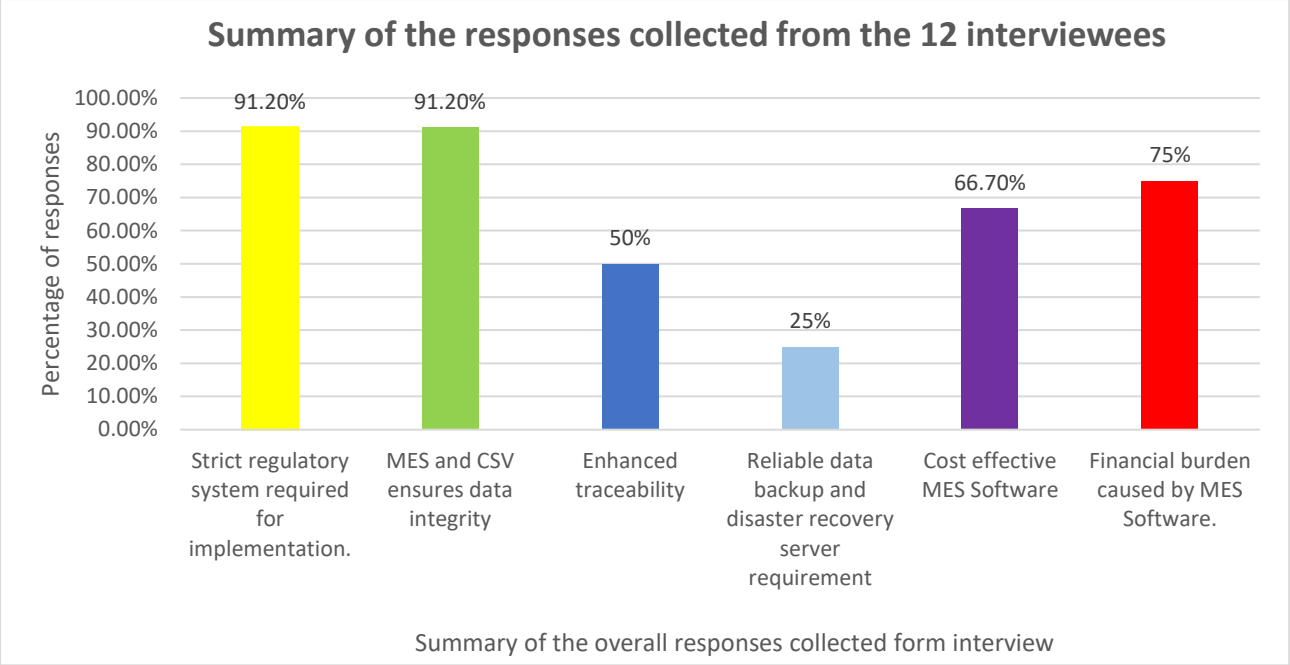

Figure 4.3.2 Summary of the responses collected from 12 interviewees.

4.3.3 Data interpretation

4.3.3 Objective I: Interpretation based on the survey questionnaire

From the response obtained from the survey questionnaire, it is evident that majority of the pharmaceutical manufacturing facilities working in India are under the strict regulatory systems like US FDA, EMA, MHRA, TGA, and ANVISA. However, there are a few small-scale pharmaceutical manufacturing facilities in India who supply medicine to the domestic market and to the third countries like Africa, Nigeria, Zimbabwe, Uganda, Philippines, Sudan, Tanzania, Kenya, Ghana, Namibia, and Sri Lanka. Strict regulatory bodies like US FDA, MHRA, TGA, EMA are encouraging the use of electronic data systems. Majority of the company operates under strict regulatory systems like USFDA, EMA, MHRA, TGA. 84.5% of the pharmaceutical manufacturing facilities are using the Manufacturing Execution System (MES) Software, but still 15.5% of the small-scale pharmaceutical manufacturing facilities are using traditional paper documentation. Also from the survey response, it is clear that regulatory systems have a crucial role in the implementation of Manufacturing Execution System (MES) Software, and Computer System Validation (CSV) Process.

4.3.3 Objective I: Interpretation based on the research question 1 and research question 2

The response from the research question 1 reveals that all the participants believe that strict regulatory systems are mandatory for the effective implementation of Manufacturing Execution System (MES) Software, and Computer System Validation (CSV) Process. Both are highly efficient in ensuring data integrity and security. Strict monitoring by regulatory systems like US FDA, EMA, MHRA, TGA will improve the manufacturing processes and the product quality. Ultimately, it will assure the patient safety. From the research question 2, strict and clear regulatory guidelines are essential for the risk assessment and mitigation of the associated risks with the computerized systems. Also, the small-scale pharmaceutical manufacturing facilities in India should promote digitalization. One of the respondents CSVP4, emphasized in future US FDA is replacing Computer System Validation (CSV) Process with Computer System Assurance (CSA) Process. A strong regulatory system will constantly revise it is guidelines and make it in line with the current Good Manufacturing Practices.

4.3.3 Objective II: Interpretation based on the survey questionnaire and research question 3

The responses from the survey questionnaire and research question indicated that Manufacturing Execution System (MES) Software offers various advantages like elimination of human errors, enhanced traceability, paperless documentation, inventory control, improved productivity, timely approval of batches, reduced shift handover time, regulatory compliance, easy regulatory filings and effective deviation management. It was also evident form the responses that various advantages like accurate results by the computer system, data integrity, patient safety, risk management, operational efficiency, prevention of computer system malfunctions can be achieved by the Computer System Validation (CSV) Process. Apart from the advantages, majority of the survey participants had an opinion that the expensive nature is a common disadvantage for both Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process. From the response of the CSVP4, the implementation of MES Software have to face resistance form the end users who are used to the traditional paper documentation. MESP6 had an opinion about the glitches or bugs of the software may present some difficulties in the proper functioning of manufacturing processes.

4.3.3 Objective III: Interpretation based on the survey questionnaire

From the response of the survey, Laurel MES which is basically an Indian based Manufacturing Execution System (MES) Software leads the survey table. The main reason might be the affordability of the software to the small and medium scale pharmaceutical manufacturing facilities in India. Laurel MES is affordable at the same time adhere to strict regulatory guidelines like US FDA 21 CFR part 11. There are other MES users like Hitachi MES (Japan), Werum Pas-X (Germany), and Emerson Syncade MES (United States). It is also notable that 11.7% responses indicate the use of traditional paper documentation.

4.3.3 Objective III: Interpretation based on the research question 4

Based on the research question 4, it is again emphasizing that the implementation of Manufacturing Execution System (MES) Software is dependent on the affordability of the software. Also, the participants are also stating that vendor assessment and risk assessment is crucial factors in Manufacturing Execution System (MES) Software selection.

4.3.3 Objective IV: Interpretation based on the survey questionnaire

There are various challenges and barriers that may arise during the implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process. The results of the survey indicated that out of 137 responses of the survey, 32.7% of the responses stated that financial hurdles, infrastructural limitations, technological backwardness, strict regulatory framework, time consuming, complexity, and need for huge organisational change are equally raising challenges to the Manufacturing Execution System (MES) Software adoption in pharmaceutical manufacturing facilities. A solid 21.9% of responses have an opinion that financial hurdles specifically have impact on the Manufacturing Execution System (MES) Software implementation. Majority of the survey responses pointed out that all challenges like regulatory compliance, training cost, time consuming, excess documentation, cybersecurity challenges, complexity, regular upgrades and modifications have equal impact on the Computer System Validation (CSV) Process adoption.

To overcome these challenges 47.3% of respondents, believe that the Government of India should strongly support pharmaceutical manufacturing facilities in India by offering technological, and infrastructural supports. Furthermore, they should also provide monetary assistance like tax credits, incentives, and subsidies.

4.3.3 Objective IV: Interpretation based on the research question 5

Apart from the challenges mentioned above, the participants of the interview specified the challenges of having a reliable data backup and disaster recovery servers. Also, the availability of skilled Computer System Validation Consultants and a strong IT team presents challenges to the Computer System Validation (CSV) Process and Manufacturing Execution System (MES) Software respectively.

4.3.3 Objective V: Interpretation based on the survey questionnaire and research question 6

Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process provides immense safety features to the pharmaceutical manufacturing facilities. 53.5% of responses states that user specific credentials, electronic signatures, audit trails, online data capturing and traceability have immense impact on the Manufacturing Execution System (MES) Software implementation. Out of the 137 responses, 46.7% had an opinion that all of the safety features like data management and data integrity, system validation and testing, security access and control, disaster recovery and business continuity, training and user support will influence the safety concerns in different pharmaceutical manufacturing facilities. The response from the interviews indicates the importance of having good procedural controls and contingency plans in the Computer System Validation (CSV) Process for risk mitigation. In addition, regular validation and upgrade of Manufacturing Execution System (MES) Software is really important for clarifying the safety concerns associated with Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process.

CHAPTER 5 - CONCLUSION AND FUTURE RECOMMENDATIONS

Strict regulatory systems are really essential in providing safe medicine for consumers. Good documentation of a pharmaceutical manufacturing facility is the ultimate evidence that all the procedures in the manufacturing process had been completed as per current Good Manufacturing Practices, and will produce drug products having quality, safety, and efficacy and helps in delivering safe medicine to the consumers.

5.1 Summary Findings from Primary Research

The first objective mainly focusses on the comparative analysis of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process adoption under different regulatory system in Pharmaceutical manufacturing facilities in India. Findings from the survey reveals that majority of the pharmaceutical manufacturing facilities operating in India follows strict regulatory systems like US FDA, MHRA, EMA, ANVISA, TGA, and Health Canada. At the same time, India has several small-scale pharmaceutical manufacturing facilities for supplying drug products to domestic markets and third countries like Africa, Nigeria, Zimbabwe, Uganda, Philippines, Sudan, Tanzania, Kenya, Ghana, Namibia, and Sri Lanka which are not highly regulated as the former regulatory systems.

Second objective mainly focusses on the advantages and disadvantages of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process. Both of them share common advantages like prevention of data integrity issues, increased efficiency and productivity. Manufacturing Execution System (MES) Software provides better traceability, archival and retention of batch documents whereas CSV Process prevents the malfunctions and assures accuracy of the computer systems functioning in the pharmaceutical manufacturing facilities. The results of the research study shows that the common disadvantage of MES Software and CSV Process are the costly nature of implementation.

Third objective points out the popularity of Laurel Manufacturing Execution System (MES) Software, which is an Indian based software widely used in pharmaceutical manufacturing facilities in India. The reason might be the affordability and the adherence with strict regulatory guidelines. From the interview also it was evident that the Manufacturing Execution System (MES) Software should be cost effective and should have all the security features.

The findings of the fourth objective details about the challenges involved in the adoption of Manufacturing Execution System (MES) Software which includes financial hurdles,

infrastructural limitations, technological backwardness, strict regulatory framework, time consuming, complexity, and need for huge organisational change. The challenges need to be resolved in Computer System Validation (CSV) Process involves regulatory compliance, training cost, time consuming, excess documentation, cybersecurity challenges, complexity, regular upgrades and modifications. It is notable that Government has a crucial role in resolving these challenges and tensions. By leveraging stable monetary supportive schemes, technological and infrastructural assistance, the small-scale pharmaceutical manufacturing facilities in India can easily implement such innovative technologies. In addition, with the financial support from the Government they could use advanced Software like Emerson Syncade, Werum Pas-X and Hitachi MES.

The fifth objective details about the various safety features of Manufacturing Execution System (MES) Software like audit trails, date and time stamped online entries, electronic signatures, user-specific credentials, multi factor authentication and masking of passwords. Computer System Validation (CSV) Process is also encouraged by all strict regulatory systems since they assure that all the computer systems performing critical operations in the pharmaceutical manufacturing facilities are in a state of validation and error free. Reliable data backup and disaster recovery server availability are two essential checkpoints in the Computer System Validation (CSV) Process. It ensures all the data processed in the pharmaceutical manufacturing facilities are protected from means of physical damages like fire, spillage, chemical hazards as well as cyberattacks like viruses, malwares, internet of thing attack, password attack, phishing, backdoor trojan. Findings shown that periodic validation and software updation are to be mandatorily followed for clarifying all sorts of safety concerns related with the MES Software and CSV Process. From the responses of the survey, it was evident that the Pharmaceutical manufacturing facilities in India are facing financial challenges for adopting such advanced technologies. This can be tackled by the financial support aided by the Government including tax credits, incentives, and subsidies.

5.2 Summary Findings from Secondary Research

Strict and accepted regulatory systems have advanced technologies and are continuously promoting digitalization. Through strict regulatory audits and inspections regulatory systems like US FDA, EMA, TGA, MHRA constantly monitors the pharmaceutical manufacturing facilities. By these measures they assuring the quality, safety and efficacy of medicines produced in Pharmaceutical industries in India. Strict regulatory systems are promoting the use

of digitalisation elements like MES Software and CSV Process due to the data transparency and integrity they bring out. Also, the finding reveals that still fifteen percent of the small-scale companies are operating under traditional paper documentation. The research study clarifies that the CDSCO of India has not much influence or strict emphasize in implementation of advanced technologies. CDSCO of India only provides limited amount of information about the computerization technologies. There are needs for supportive measures for implementation of Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process by the Indian regulatory system. From the secondary research it was evident that the US FDA, EMA, and PMDA who are the benchmarks of the health regulatory systems have detailed guidelines and instructions regarding the implementation of computerisation technologies in the Pharmaceutical manufacturing facilities. However, The CDSCO guidelines of India needs to be strengthened and should promote the use of advanced technologies. The current CDSCO guidelines are found to be weak and the respective guidelines and annexures demands a revision in the future.

5.3 Future Recommendations

The research study was a cross sectional study conducted over a period of 3 months. From the research study it was evident that Data Safety and Integrity can be achieved in the Pharmaceutical manufacturing facilities by the effective implementation of MES Software and CSV Process. Breach of the data or data alterations are serious threat in Pharmaceutical manufacturing facilities since, it involves production of life saving drugs to the consumers. It is recommended to extend the research study by increasing the study population in the future to find out new perspectives about the Manufacturing Execution System (MES) Software and Computer System Validation (CSV) Process implementation in different pharmaceutical manufacturing facilities under different regulatory systems. The research study will help the fellow researchers as well as the small-scale industries in India to explore more benefits of the Manufacturing Execution System (MES) Software and to understand the importance and relevance of Computer System Validation (CSV) Process in different pharmaceutical manufacturing facilities.

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