

Pharmaceutical Manufacturing Sectors Regulatory-Based Operation Management for Parenteral Preparations

Palanisamy Pethappachetty^{1,*}, Kavya Thirupathi^{1,3}, Phagalavan Moorthy¹, Mohan Kumar²,
Manivasakam Prakash⁴, Anandharaj Govindharaj⁵

¹Department of Pharmaceutics, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University) Yercaud Main Road, Salem, Tamil Nadu, INDIA.

²Department of Pharmaceutical Chemistry, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University) Yercaud Main Road, Salem, Tamil Nadu, INDIA.

³Department of Pharmaceutics, Cherran's College of Pharmacy, Coimbatore, Tamil Nadu, INDIA.

⁴Department of Pharmaceutics, Vellalar College of Pharmacy, Erode, Tamil Nadu, INDIA.

⁵Department of Pharmacy Practice, Vellalar College of Pharmacy, Erode, Tamil Nadu, INDIA.

ABSTRACT

Aim/Background: This research explores the pharmaceutical industry's operations management, focusing on regulatory-based operation management for parenteral preparations. **Materials and Methods:** The study utilizes a comprehensive review of literature and industry practices to examine the application of operations management in the pharmaceutical sector. It incorporates the concepts of Six Sigma and Lean Six Sigma to elucidate the innovative techniques employed for minimizing waste and optimizing production processes. **Results:** The findings highlight the significance of operations management in pharmaceutical manufacturing, particularly in ensuring the rapid and high-quality production of parenteral preparations. The study underscores multinational corporations' successful implementation of operations management and alignment with Six Sigma and Lean Six Sigma principles. **Conclusion:** In conclusion, the research underscores the pivotal role of operations management in the pharmaceutical industry, offering novel solutions for total quality management and emphasizing the distinction between traditional and contemporary operations management.

Keywords: Operations Management, Novel solutions Total Quality Management, Lean Six sigma, Six sigma, Parenteral Preparations.

Correspondence:

Dr. Palanisamy Pethappachetty

Professor, Department of Pharmaceutics,
Vinayaka Mission's College of Pharmacy,
Vinayaka Mission's Research Foundation
(Deemed to be University), Yercaud Main
Road, Salem, Tamil Nadu, INDIA.
Email:palanisamy2907@gmail.com

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INTRODUCTION

Drugs are discovered, researched, and produced in the pharmaceutical business by both public and commercial entities. India is the #1 exporter of generic pharmaceuticals worldwide. It provides 25% of all medicines in the United Kingdom, 40% of the generic demand in the United States, and more than half of the world's need for vaccinations. India is the third-largest volume and fourteenth-largest value manufacturer of medicines in the world. The domestic pharmaceutical industry consists of 10,500 production facilities and 3,000 medical firms. The Indian pharmaceutical business is well-known around the world. To grow its pharmaceutical business, it has a sizable pool of scientists and engineers. They provide over 80% of the AIDS medications. In a cutthroat market, regulatory operations teams are focused

on attaining global expansion, which requires rethinking their operating model by applying strategic resourcing, which balances the demands of maintaining existing product compliance with the needs of new product clearance. The complexity of regulatory standards, which call for more in-depth knowledge and a greater need for employees, forces organizations to adapt their regulatory operations operating model. By providing end-to-end regulatory operations services, from product registration to post-approval maintenance, through a flexible team approach that blends operational and strategic understanding, operation management assures higher efficiency.¹

The Pharmaceutical Industry's History

Since their inception in the nineteenth-century pharmacy, the pharmaceutical and biotech industries have come a long way in the twenty-first century.

The apothecaries and pharmacies of the Middle Ages, which offered a hit-or-miss selection of treatments based on centuries of traditional knowledge, are where the pharmaceutical business emerged.^{1,2}



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However, the origins of the current industrial sector may be traced back to the second part of the nineteenth century. While the scientific revolution of the 17th century encouraged experimentation and reason, and the industrial revolution of the late 18th century altered the means of production, it was not until recently that these two tenets were combined for the benefit of human health. It's possible that the German company Merck was the first to do this. After opening a pharmacy in Darmstadt in 1668, Heinrich Emanuel Merck started his metamorphosis into an industrial and scientific company in 1827 by producing and selling alkaloids. Similar to GlaxoSmithKline, which dates back to 1715, Beecham entered the field of industrial medicine manufacturing in the middle of the nineteenth century, beginning with the production of patented drugs in 1842 and opening the first factory in the world dedicated to the production of only medicines in 1859.¹⁻⁴

Regulatory Strategy and Plan for the World

Having and following a worldwide regulatory strategy might aid your company in increasing both its market share and compliance.

How many of us have entered a new market before being fully aware of the legal requirements and their potential consequences? If this has occurred to you, you are not the only one. By mapping the needs as part of your strategy planning, you may be able to find a lucrative new market or stay away from a costly mistake.

Before moving on, let's confirm that when we use the terms "regulatory strategy" and "regulatory plan," we all mean the same thing.

- **Regulatory Strategy:** This strategy links the company's marketing plan with the legal requirements for releasing a new or updated product on the market. It provides the team with comprehensive direction by outlining the main regulatory components.

- **Regulatory Plan:** Outlines the specific steps that must be followed to carry out the regulatory strategy's objectives. The precise elements required to assemble regulatory submissions are included.

Understanding the advantages is a necessary step in developing a successful worldwide strategy and plan.

Identify each function's purpose

Handle typical problems

The following components need to be included in the plan:

- A piece of machinery or a product is referred to as a "device" or "product."
- Specifies the markets that are of interest, ideally together with a market study to support the market's feasibility.
- The target markets will choose the kind of submission(s).

- Considers any potential relevant life cycle challenges.⁵

A Fresh Approach to Creating a Regulatory Strategy

Obtaining approval or authorization for a new orthopedic product is one example of a regulatory objective that may be achieved through a combination of measures known as a regulatory strategy.

Because regulatory standards are continually expanding and getting more complex, a well-thought-out regulatory strategy and execution may help you fulfill your regulatory objectives while also affording you a competitive advantage. Regulatory implications for a product are identified by collaborative efforts among internal stakeholders, who then gather regulatory information on relevant precedents, record the approach, validate its practicality, and review it as circumstances change.

List the attributes of the product

In order to properly analyze the regulatory implications of the proposed product's intended use, design, and performance, it is important at this stage of strategy creation to completely characterize the proposed product's attributes. Although the regulatory relations team member is usually responsible for establishing the regulatory strategy, it is more likely to correctly represent business goals and be effective if key internal stakeholders are engaged in this stage of the process. Regulatory, Research and Development/Engineering, Marketing, and Medical/Clinical Affairs professionals are common examples of stakeholders. Management of quality, costs, production, and the supply chain are crucial. Crucial external stakeholders include joint venture partners, key vendors, and expert advisors.

Conduct regulatory intelligence gathering

Find out whether there are any regulatory precedents that might affect your regulatory strategy. After accurately identifying product attributes that could have regulatory importance. Although your planned product may not face the same difficulties, you may frequently find comparable things, even in medical specialties outside of orthopedics that can aid with the creation of your plan.

The Food and Drug Administration's website is a great resource for businesses looking for information on how to bring a new product to the US market legally. Companies' 510(k) summaries have come under increased scrutiny from the FDA in recent years for failing to offer sufficient detail. The process of searching the FDA 510(k) database may be sped up with the use of commercial regulatory intelligence products. Detailed descriptions of FDA reviews are given for innovative devices that have received de novo categorization. Summary of Safety and Effectiveness for Premarket Approved Devices from the Food and Drug Administration provides much more detail on the evaluation process. Reading the transcripts of FDA advisory panel meetings may help readers better understand the agency's thinking on

certain products or concerns affecting the medical specialty sector.

Documentation and "Triangulate"

Consider critically validating your product and "triangulating" the many instances mentioned above to determine what problems your product is likely to encounter and how to successfully handle them. Keep in mind what has been accomplished in the past, what has proven successful for other companies, and most crucially, what has failed in the past. Record any critical suppositions, challenges, or problems that need to be verified or addressed, as well as any potential variations in former or present needs during the course of the product development schedule. Establish if your plan should include both short- and long-term goals and whether any short-term wins are required to meet your long-term goals.

Examine the Strategy's Resilience

Consult with the internal stakeholder team to ensure that the plan accurately reflects the project objectives and product qualities that were initially specified. This should be done after the strategy has been created and all essential assumptions and risks have been noted. When the effects of early conclusions regarding the project or product goals become clear, certain modifications should be anticipated.

Create a living process out of the strategy

Keep abreast of any regulatory developments that can have an impact on your project or product since the regulatory environment is continuously evolving. The regulatory environment may change when new guidance documents are released, comparable items are permitted or cleared that increase

the bar for Agency expectations, or clinical results are disclosed in the literature. Remember that there are also internal reasons for change, such as alterations to product functionality or design, or revisions to current items to conform to desired claims in response to competitive activity. Think of your regulatory strategy as a "living process" that changes based on internal and external variables.⁶

Operations Administration (OM)

The goal of Operations Management (OM) is to increase productivity across all areas of an organization. Organizations strive for efficiency in their production processes since it directly affects their bottom line. Maximizing net operational profit is the focus of the management team as they strive to strike a healthy balance between income and expenses. Resources like as employees, supplies, machinery, and computers are just some of the things that fall within the purview of operations management. Managers in charge of operations source materials, manufacture products, and distribute them to customers in response to market demand. Among the many strategic issues that fall within the purview of operations management are the selection of project management techniques, the layout of computer networks, and the size of production facilities. Additional operational concerns include inventory management (including WIP and raw material procurement), quality control, materials handling, and maintenance needs.⁷

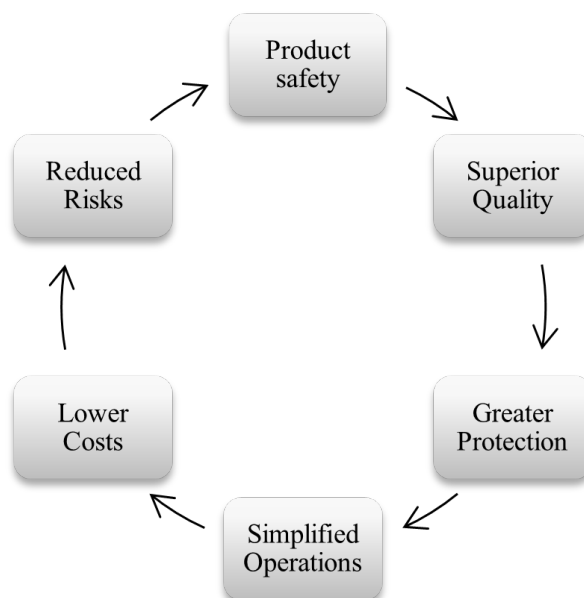


Figure 1: Operation Management in Pharma. Industry.

Operations Management in Pharma Industry and its Recent trends

Regulatory Activities

Experts in regulatory operations coordinate the gathering of documentation and supporting materials for the filing of global applications. Examples of such applications made by pharmaceutical and biotech corporations include: (NDAs) Figure 1.

- Innovative Prescription Drugs for Clinical Study (INDs).
- Marketing Authorization Applications (MAAs); Biologics Licensing Applications (BLAs) (MAAs).

The following are examples for organizations that manufacture medical devices: (PMAs).

- Premarket notifications under 510(k).

For those not familiar with the inner workings of regulatory departments, the handling of regulatory papers may seem simple since they assume that all documents included in regulatory submissions have been reviewed prior to their inclusion in the final submission. However, the opposite is in fact true. All content created by the functional groups that contribute to regulatory submissions, including pharmacology, manufacturing, clinical, and marketing, must go through regulatory operations before being submitted to the designated agency for a specific product to gain approval. The sheer volume of new and updated files that regulatory operations must keep track of might be daunting. Multiple reasons, including the wide variety of document types

and functional origins, make submission processing difficult, including:

- Product line.
- Indication.
- Regulating bodies.
- Nation.

In addition, many submissions need additional copies of certain documents to be filed. Several of the papers included in the submissions are subject to strict reporting obligations (such as safety reports, yearly reports, weekly safety updates, etc.), demonstrating the need of efficient cooperation and transparency. The transparency and accessibility of documents are crucial to the regulatory process.⁸

The Distinction between Regulatory Operations and Regulatory Affairs

In contrast to regulatory operations, which refers to the internal processes and activities associated with keeping a regulatory submission on track, regulatory affairs encompasses all aspects of regulatory compliance and the corresponding interactions with regulators that are necessary throughout the submissions process Figure 2. In the context of the biological sciences, the phrases are often used interchangeably, although a differentiation is often suggested. The Regulatory Affairs Professionals Society (RAPS) defines regulatory affairs as "a profession within the regulated industry whose members are responsible for ensuring that their companies comply with all applicable laws and regulations; working with local, regional, and national regulatory authorities

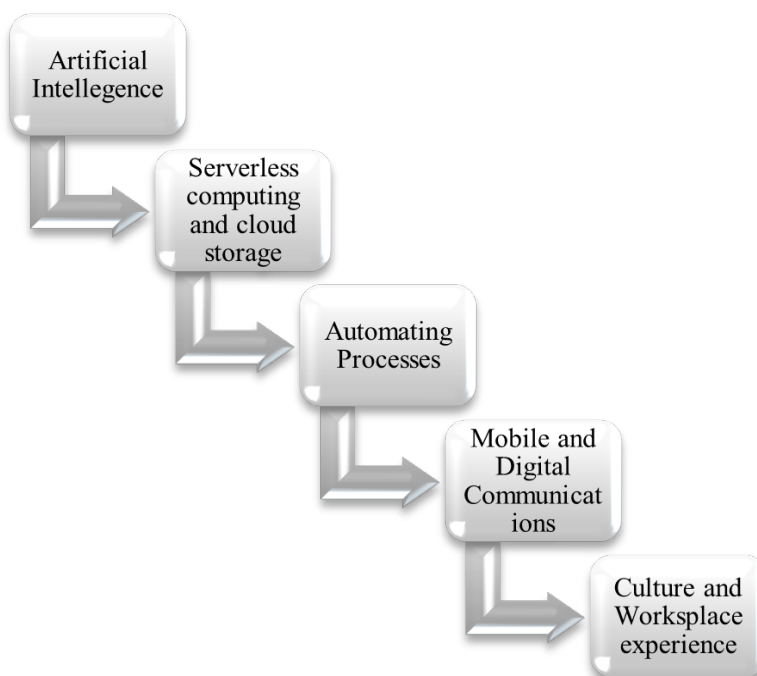


Figure 2: Recent trends in Operations. Management.

and personnel on issues affecting their businesses; and advising their companies on regulatory aspects that may impact their operations." The administrative and logistical aspects of ensuring compliance and timely submissions are handled by the regulatory operations division. Professionals in regulatory operations must not only keep track of standard documents' versions and updates but also be aware of the locations and deadlines for submitting them to regulatory bodies for specific purposes. Without a trustworthy document management system, they cannot be successful.^{7,8}

Operation Management in the Past vs Operation Management Today

Throughout history, technological advancements and the division of labor have helped increase company productivity in commerce and industry. Systematically assessing performance and computing with formulas was a largely unexplored science prior to Frederick Taylor's early contributions to the field. Taylor published his scientific operations management concepts in 1911, which contained four specific components: creating a true management science, Scientific employee selection, training and development of employees, and close communication between management and personnel. The four theories that support contemporary operations management are lean manufacturing, six sigma, Reconfigurable Manufacturing Systems (RMS), and lean manufacturing. PR is a corporate management strategy that focuses on assessing and improving internal business procedures and workflow. 1993 saw the creation of it. BPR's goal is to help companies fundamentally restructure their operations by designing new business procedures from the ground up. Systems for production that may quickly modify their hardware, software, and structural elements are known as reconfigurable manufacturing systems.

This allows systems to quickly adjust their generation capacity and efficiency in response to changes in the market or inside the system itself. Six Sigma is a quality-control approach. Between 1985 and 1987, Motorola mostly engaged on development. The "six" refers to the standard deviations from the mean of the distribution used to establish the control boundaries. The six-sigma approach gained popularity after General Electric's Jack Welch initiated a push to embrace it in 1995. Every six-sigma project in a business has a set of procedures to follow and a set of financial objectives, like increasing profits or reducing expenses. The Six Sigma method makes use of trend charts, estimates of likely defects, and other ratios. Lean manufacturing is a technique for methodically getting rid of waste from the manufacturing process. The lean hypothesis takes into account waste produced by excessive or unbalanced workloads. This concept tries to eliminate as many unneeded resource expenditures as is practical and views the use of resources for any purpose other than producing value for customers as wasteful.⁷⁻¹⁰

Comprehensive Quality Management (Or) Total Quality Management System (TQM)

Comprehensive Quality Management is the process of identifying and limiting or eliminating manufacturing flaws, as well as enhancing supply chain management, and making sure that staff are properly trained. Total quality management aims to make all parties involved in the production process responsible for the overall quality of the finished goods or service. William Deming, a management consultant whose work had a significant impact on Japanese industry, established total quality management. Although they have many similarities, TQM and the Six Sigma improvement process are not the same. The concept of Total Quality Management (TQM) entails monitoring an organization's whole performance. The goal is to continually enhance internal processes to raise the caliber of an organization's outputs, including products and services. The standards for the Total quality management plan can be used to represent both internal goals and any existing industry requirements. Total quality management keeps an eye on all the duties and tasks required to keep a business and its operations operating at the desired degree of perfection. This entails developing and putting into practice a quality strategy, as well as undertaking activities for improvement, planning, and quality assurance.^{11,19}

Principles

1. Customer-centricity;
2. Leadership;
3. Involvement of others;
4. Process-oriented;
5. Using a systematic management strategy;
6. Constant development;
7. Fact-Based Decision-Making Approach.¹²⁻¹⁵

Sigma Six

Companies may utilize the Six Sigma collection of quality assurance tools to lower faults and streamline operations for greater profitability. It was developed in the 1980s by a scientist when they were both employed at Motorola.^{16,17}

It is a scientific and data-driven methodology that looks for and gets rid of little mistakes or faults. By reducing manufacturing failure rates to below 3.4 per million units or events, it also seeks to speed up cycle times. This divergence from the mean is likely to lead to inaccuracy since only 3.4 out of a million occurrences on a bell curve fall outside of six standard deviations. It is a management style that prioritizes qualitative success evaluations above qualitative indicators and statistical enhancements to business processes. As a result, Six Sigma practitioners are businesspeople who employ statistics, financial analysis, and project management to improve

company functionality.¹⁸ Six Sigma is a statistical indicator that assesses the efficiency of a business process. As already said, the program intends to decrease manufacturing defect rates to below 3.4 per million units or events while simultaneously enhancing cycle times. A bell curve's departure from the mean is likely to lead to inaccuracy because only 3.4 out of a million occurrences fall outside of the range of six standard deviations. It is a management concept that prioritizes statistical enhancements to business operations over qualitative success measures. Since statistics, financial analysis, and project management are used to improve company functionality, Six Sigma practitioners are typically entrepreneurs.¹⁸ The effectiveness of a business process is gauged using the statistical metric known as Six Sigma. Like I said before, Numerous businesses, such as Motorola, provide Six Sigma training along with specific credentials like yellow, green, and black belts.^{16,17}

The Six Sigma Five Steps

Followers and practitioners of the Six Sigma process employ the DMAIC technique. Its letters stand for define, measure, analyze, improve, and control.

Businesses employ the DMAIC approach, which is based on statistics, as a theoretical framework for optimizing their operational procedures. The theory states that every problem, no matter how seemingly intractable, can be resolved by a corporation by following the five DMAIC processes:

After reviewing the needs of the firm, a team of people, lead by a Six Sigma champion, chooses one problematic process to work on. This clarifies the issue and goals of the project.

The group evaluates the initial effectiveness of the procedure. These statistical indicators help the team identify possible issue inputs and examine the benchmark performance of the process.

The team then assesses this procedure or factor for failure and puts it to the test to determine if it is the root of the problem. The group uses analytics to identify where process failures are occurring.

The group then works to enhance the system's functionality.

The group adds controls to the process to make sure it doesn't retreat and lose its effectiveness.¹⁸

Lean: A Defined

Toyota created Lean, which was founded on the work of Shewhart and Deming, as a way to increase efficacy and effectiveness by removing waste. He had Toyota as a customer, and Toyota used his lessons as the foundation for its operation management practices. The notion at the heart of Lean is the suppression of unnecessary activity. According to its definition, the Lean methodology is "a collection of instruments that aid in the discovery and continual removal of waste." The waste-involved manufacturing method

demonstrates that factories like Toyota's generate massive amounts of trash due to their focus on mass output. No company has any interest in pursuing this endeavor.^{16,17,19}

The Foundations of Lean Manufacturing

Value: Value is determined by the consumer's priorities, not by the individuals who design or manufacture the goods.

Value Stream: Rather than assessing each stage independently, this activity is involved in producing the product and delivering it to customers.

Flow: The extent to which processes that give the customer value operate smoothly and without interruption, excluding inefficiency and waste.

Pull: How much of the value chain doesn't really produce anything but rather just processes what the client wants.

Perfection: The value that is provided to the consumers is continually evaluated.^{20,21}

SIGMA LEAN

A management approach is called Lean Six Sigma. By decreasing waste and errors and improving task consistency, it seeks to improve product performance. Lean manufacturing is combined with the Six Sigma concept and tools to reduce production and process waste while preserving quality.²²

Differentiating Lean from Six Sigma

Lean and Six Sigma concentrate on variation, or any departure from the target performance, while Muda, Mura, Muri concentrates on waste when it comes to finding issues.

For both studies, many approaches are used. Lean often uses visual tools supported by data analysis. Six Sigma primarily uses statistical methods for analysis and solution formulation, with the help of data visualization. Because the analysis of Lean is easier to understand, this leads to the idea that Lean Six Sigma is superior to Six Sigma.

whereas many people are intimidated by Six Sigma's numerical analyses. Both types of analysis are easy to carry out.

A stream map that has been revised to reflect the value of the Lean solution may result in modifications to the workflow. The Six Sigma solution includes a written control plan for monitoring and setting up processes for responding to variance. This will have an effect and lead to modifications in measuring techniques or systems.

Since the two systems are so similar in so many ways, it was easy to merge them into one paradigm and profit from their interdependence. Lean Six Sigma overcomes the bulk of the problems of earlier, unsuccessful methodologies when used as it is now implemented.²³

The Tenets of Lean Sigma

A control system is part of the solution, which addresses the following factors: a real-world problem can be handled; a team can complete the analysis and it will be process-focused; an analysis based on data; the impact of sigma is understood; the true root cause is treated; and so on.²⁴

Sigma Lean Belts

Due to its use of the name convention for the development of martial arts, the Six Sigma methodology has adopted some of the roles from Lean Six Sigma. Some businesses have their definitions and levels of expertise. It will nonetheless describe the typical amounts. Yellow, Green, Black, and Master Black are the four tiers of Lean Six Sigma belts. Each of these roles is anticipated to have the required education and certification. At the beginning of Lean and Six Sigma, every business established its standards for methodology, tools, and processes. The majority of organizations today, however, rely on an independent certifying body for training and certification. The American Society for Quality and the International Association of Six Sigma are two well-known certificate-issuing bodies.²⁵

Yellow Belt in Lean Six Sigma

A Yellow Belt is a beginner's method for comprehending the Six Sigma adoption principles. Without plunging them into the deep end of the methodological pool, it is intended to educate the fundamentals.²⁶

Green Belt in Lean Six Sigma

Green Belts play a significant role in the process since they spend up to half of their working hours on Six Sigma projects. They are frequently chosen to serve as team leaders in specific fields where they possess in-depth knowledge of the procedure that is being altered as part of the project. A Green Belt certification requires both passing a written test and participating in a Six Sigma project team.²⁷ The project manager will often be a Green Belt. This operates on Lean projects that include the domain of expertise. The personnel are conversant with the structure and methodology of Lean Six Sigma. They can also use the standard statistical methods and analytical tools for Lean Six Sigma. These individuals are in charge of the smaller, more niche project endeavors. This position is often a full-time one.

- Most Green Belts are in charge of a project that aims to enhance one or more parts of the practices used by their organization.
- Large cross-functional initiatives usually include the simultaneous conduct of many studies.
- This individual is responsible for making sure the project's processes are followed and executed appropriately.
- During phase gate reviews, this individual often initiates the presentation and does the analysis.

Black Belt in Lean Six Sigma

People who attain this level typically devote their entire time to Six Sigma projects. Obtaining a Black Belt also involves passing a written exam and finishing two Six Sigma projects. Project teams are led by persons in this position, and green belts are mentored by them.²⁸

Black belts in multiples are typical in organizations. These individuals are in charge of important cross-functional projects.

Their daily tasks include planning a team meeting for one of the projects they are in charge of, monitoring the advancement of many Green Belts, and assisting them as they advance to the next levels, as well as training prospective Yellow and Green Belts and meeting with stakeholders each day to discuss project status.

The individual typically has to oversee many projects at once while simultaneously serving as the boss of a few Green Belt holders who are in charge of their projects. Large, cross-functional initiatives are frequently led by black belts. As project leads, they must organize and plan the work. The most difficult part of those initiatives is often collaborating with stakeholders from various functional areas. Once or twice a year, their duties will vary to ensure that everyone is learning increasingly advanced information.²⁹

Lean Six Sigma Master Black Belt

Black Belt Master is the highest rank. The senior executive in charge of the Lean Six Sigma endeavor will be the sole Master Black Belt in the majority of businesses. Work will be done full-time. This Master Black Belt typically reports to the C-level champion of the Lean Six Sigma Initiative.

- In terms of training and certification, this person has the same credentials as a Black Belt. However, there are differences in the positions and duties.

The project's inception is his responsibility, and he is also in charge of monitoring all ongoing projects, including the pre-planned initiatives.

- These staff members work with human resources to manage the organization's training records by keeping track of all belts.
- If a firm is small, the Master Black Belt position will be assumed by Black Belts from other companies.^{28,29}

Parenteral Arrangements

They are sterile preparations that are injected directly into the circulatory systems of people or animals. They must fulfill the pharmacopeia's quality standards and be safe for their intended usage, just like any other pharmaceutical dosage form. They must not only be sterile but also pyrogen-free. They will either be contained in a glass or a single-dose bottle. Prefilled syringes or pens are used for the packing method that is most frequently

used. The biodistribution will be adjusted, and the circulating half-life will be extended.^{30,31}

Parenteral Preparations' Characteristics

For giving parenteral formulations to people or animals, direct intramuscular or subcutaneous implantation is an option. The minimal compendial requirements are stated below.

- Show no signs of phase separation (emulsions) or the development of aggregates.
- It is very challenging to understand the particle size when using suspension as they will allow sedimenting for easy dispersion after shaking.
- It must be sterile and pyrogen-free, as well as free from visible and invisible particles, as mentioned in the EP, USP, and JP. In parenteral formulations, it may be necessary to employ biocompatible excipients that are chosen based on the specific user and included at the lowest effective concentration.
- It's crucial to remember that excipients shouldn't hinder a drug's ability to perform its intended medical function and shouldn't, at the doses used, be poisonous or significantly irritate the surrounding area.
- Safety and effectiveness will increase.
- There is a reduction in immune recognition.
- Delivery may be readily targeted, pharmacodynamically adjusted formulations; selective release (based on environment and location).^{32,33}

Formulation Difficulties

Achieving compatibility between the drug substance and excipients—avoiding contaminants from drug substance degradation—as well as avoiding adsorption problems during production and packing in the primary containers—represents the key obstacle. The medicinal components in solutions and emulsions must be soluble and stay so for the duration of the product's shelf life. Pro-drug can be employed when drug molecules aren't very soluble. If not, an inclusion complex can be created using a solubility booster like cyclodextrin.

The pH level is one of the most crucial elements of parenteral formulations. The pH levels must be as near to physiological as is practical. In other situations, it can be necessary to strike a balance between maintaining the stability of pharmaceutical materials and physiological pH.

Large-Volume Preparations (LVPs), which should not contain a pH buffer and consist of more than 100 mL of preparation, are classified as parenteral preparations. This is because when the

preparations are injected with the pharmaceutical components, the blood serves as a buffer.

The stability of the medicinal component during drug development is yet another significant challenge that formulators face. Because unstable pharmacological substances are used, the preparation's purity will be compromised.

If the medication ingredient cannot produce "cake" in powder form for injection, a bulking agent may be required. Finally, while deciding on a sterilization method, you should think about the main container type as well as the characteristics of the parenteral preparation (e.g., steam sterilization for aqueous solutions, and dry heat for non-aqueous solutions).

If you want to provide a sterility Assurance Level (ASL) of 10⁻⁶, you need to conduct validation tests to prove that your sterilization method works.

These treatments can be administered intravenously to both humans and animals. It must adhere to ICH recommendations as well as pharmacopeial standards.³²

Parenteral Preparations Processing

Before being injected, all containers, closures, and equipment should be properly cleaned with detergent and tap water. The rubber closures are cleaned using water that has 0.5% sodium pyrophosphate in it.

Material collection: The raw materials needed for the preparation should be retrieved from the warehouse after being accurately weighed. For injection, pyrogen-free water should be utilized.

An aseptic setting should be used for the processing of parenteral products. The components need to be accurately weighed and completely dissolved in the car.

Filtration

The preparations must be filtered with bacteria-proof filters.

Filling the last container with the preparation: The aseptic technique should be used here.

Sealing the container

The container will be promptly sealed when the filling process is finished in an aseptic environment.

Sterilization

For parenteral substances that are thermally stable, autoclaving at various temperatures should be employed.

Several tests are performed on the parenteral formulation to maintain quality control. They do.

Sterility Tests, Clarity Tests, Leakage Tests, Pyrogen Tests, and Assays

Labeling and packaging

These items should be labeled and packaged in an aseptic manner.³⁴

Various Kinds of Parenteral Preparations

These preparations are pharmacological products that are injected into the body and are devoid of impurities. It is either a substance that can be diluted with sterile water or a liquid preparation intended for safe injection (also known as "water for injection"). The stability or effectiveness of the preparation cannot be affected by any other components or substances than water. To increase the stability and effectiveness of the preparation, several substances may be added, but these additives must not be harmful or have any unfavorable side effects. Coloring agents are not allowed in formulations for parenteral use. If parenteral medications are to be stored in multiple-dose containers, antimicrobial preservatives may be added to stop and restrict the development of bacteria in the container. Validating the effectiveness of such preservatives is essential before starting the parenteral production process.^{32,35}

Containers

These substances can be placed in a variety of bottles, vials, ampoules, etc. All of these containers must be transparent to allow for visual inspection of the contents. To ensure that the preparation's quality is not compromised while being stored or used, the container has to be sterile. Parenteral drug storage has traditionally been done using glass, especially borosilicate glass. On the other hand, they are being used increasingly often and come in a variety of forms. The parenteral product's composition affects material choice, and national pharmacopeias (USP), (JP), and (EP) will provide the guidelines for material choice. Quality standards for APIs, drug products, excipients, packaging materials, labels, and storage conditions are all provided by these bodies.

Closure/Sealing

For containers through which injectable samples are to be removed, a special type of seal is required. These must prevent the admission of any germs or microbes, and the closing material must be adequate enough to send a hypodermic needle through them with the least amount of damage. Or material shedding; also, it ought to self-seal when the needle is taken out. Bottle closures are frequently made of elastomers. They are also utilized as ports for plastic bags in another form of primary parenteral packaging, pre-fillable syringe plungers and tip caps, cartridge plungers and seals, and vial stoppers.

Inspection/Quality Control

Each final container should be checked one-by-one for any impurities after the Good Manufacturing Process in order to ensure that the high quality of these parenteral product containers is maintained. Contaminated containers must be rejected and taken away.

Labeling

For parenteral preparations, the name of the preparation, the quantity of the active ingredient, the storage, and the solvent that must achieve the necessary concentration for the product to be given must all be specified. To make it simple to check the products, the label shouldn't completely encircle the bottle.^{32,35}

Types of Parenteral Preparations

Injection

The active ingredient and additional components are dissolved in Water for Injection to create injections. Shaking will spread the particles out in the fluid. To administer a homogenous dosage once the suspension is removed from the container, it must stay stable.

Infusions

This preparation consists of blood as the isotonic component and a sterile aqueous solution as the continuous phase. It is free of bacterial pyrogen and endotoxins. It also doesn't include any antimicrobial preservatives.

Powder that is injectable by shaking the vial, a clear, particle-free solution is produced, and the sterile solids are disseminated throughout the whole volume.

Concentrated injectable solutions

The concentrated solution is diluted with water for injection before administration by injection or intravenous infusion.

Implants

These are inserted into the tissue to prolong the release of the active substance. They are stored separately in sterile containers.³⁵

CONCLUSION

These days, a wide range of businesses are becoming more and more interested in operation management. The products made using this method will be of higher quality, safety, and efficiency than those made using other methods, but the installation costs will be higher. It will be the leader in the pharmaceutical sector in ten years. This approach has previously been used by certain pharmaceutical businesses, who are now providing the best goods with the least amount of waste. This component is connected to the regulatory sector in terms of Operations. When this technology is applied, a large number of items may be created

quickly while retaining the same quality, purity, and effectiveness, which doubles the company's revenue. There have been novel approaches to enhancing operational management and legal compliance.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AIDS: Acquired Immunodeficiency Syndrome; **FDA:** Food and Drug Administration; **OM:** Operations Administration; **WIP:** Work in Progress; **NDA:** New Drug Application; **INDs:** Investigational New Drugs; **MAAs:** Marketing Authorization Applications; **BLAs:** Biologics Licensing Applications; **RAPS:** Regulatory Affairs Professionals Society; **TQM:** Total Quality Management; **USP:** United States Pharmacopeia; **JP:** Japanese Pharmacopoeia; **EP:** European Pharmacopoeia.

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