



# Enhancing Safety and Compliance in Syringe Manufacturing: A Study of Risk Management Strategies Based on ISO 14971

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## Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

## Article Information

DOI: <https://doi.org/10.9734/jamps/2024/v26i7702>

## Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/119790>

Original Research Article

Received: 29/05/2024  
Accepted: 30/07/2024  
Published: 03/08/2024

## ABSTRACT

Ensuring the safety and compliance of syringes is crucial in the medical device industry to mitigate risks and uphold quality standards. This research paper examines effective risk management strategies for syringe manufacturers, grounded in the principles outlined in ISO 14971. The ISO 14971 standard provides a systematic framework for identifying, evaluating, and controlling risks throughout the product lifecycle. By integrating these strategies into manufacturing processes, syringe manufacturers can enhance product safety, achieve regulatory compliance, and improve

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overall quality. This study synthesizes current practices and case studies to illustrate the practical application of ISO 14971 in enhancing safety and compliance within the syringe manufacturing industry.

**Keywords:** Syringe manufacturing; risk management; safety; compliance.

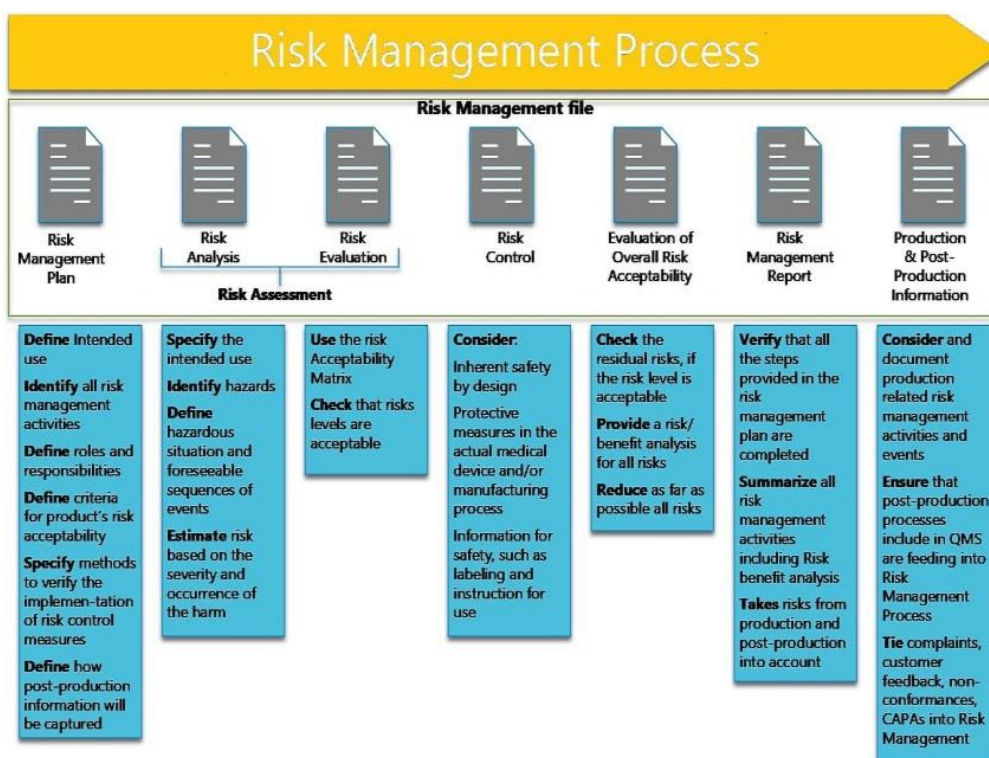
## 1. INTRODUCTION

In the realm of medical devices, syringes stand as indispensable tools, pivotal in administering medications, vaccines, and therapeutic agents. The reliability, safety, and compliance of these devices are paramount to ensure the well-being of patients and the efficacy of healthcare delivery systems worldwide. As such, the manufacturing processes of syringes must adhere rigorously to stringent standards to mitigate potential risks and ensure regulatory compliance.

ISO 14971 emerges as a cornerstone in this endeavor, providing a structured framework for managing risks associated with medical devices throughout their entire lifecycle. This international standard is recognized globally and serves as a guiding principle for manufacturers in identifying, evaluating, and controlling risks inherent in their products. By systematically assessing risks from design to disposal, ISO 14971 not only enhances product safety but also aids in achieving

regulatory approvals and maintaining market competitiveness [1].

This paper aims to delve into the critical intersection of safety, compliance, and risk management in syringe manufacturing, with a specific focus on the principles outlined in ISO 14971. Through a comprehensive review of literature, case studies, and practical applications, this study seeks to elucidate effective strategies that syringe manufacturers can adopt to enhance safety, ensure compliance with regulatory requirements, and ultimately improve patient outcomes. By exploring these themes, this research aims to provide valuable insights into the implementation and benefits of ISO 14971 in the context of syringe manufacturing, thereby contributing to the ongoing discourse on quality assurance and risk management in the medical device industry. Risk Management Process is demonstrated in the below given Fig.1.



**Fig. 1. Risk management process**

## 2. RISK MANAGEMENT IN MEDICAL DEVICE MANUFACTURING

- **ISO 14971 Overview:** ISO 14971 provides a systematic approach to identifying, assessing, and mitigating risks associated with medical devices. Its application spans across all stages of the device lifecycle, from initial conception and design to manufacturing, distribution, and disposal [2].
- **Integration of Risk Management Practices:** Effective risk management practices involve hazard identification, risk assessment, risk control measures, and monitoring. These practices are essential for ensuring product safety, regulatory compliance, and overall quality management.

Risk management in medical device manufacturing is critical to ensure the safety, efficacy, and compliance of devices throughout their lifecycle as mentioned in Fig. 2 Process flow diagram for Syringe Manufacturing [3]. Here's how it is typically approached [4,5]

### ➤ Risk Assessment:

- **Hazard Identification:** Identify potential hazards associated with the device, its materials, components, and manufacturing processes. This includes physical, chemical, biological, and usability hazards.
- **Risk Analysis:** Evaluate the identified hazards to assess the likelihood of occurrence and the severity of their

potential consequences if they were to occur. Use tools such as FMEA (Failure Modes and Effects Analysis) or FMECA (Failure Modes, Effects, and Criticality Analysis) to systematically analyze risks.

- **Risk Evaluation:** Determine the level of risk posed by each identified hazard based on the results of the risk analysis. Prioritize risks based on their severity and likelihood to determine which require immediate attention.

### ➤ Risk Control:

- **Risk Control Measures:** Implement measures to mitigate or eliminate identified risks. This may include design controls, process controls, quality assurance procedures, and validation activities. For example, using specific materials that are biocompatible, implementing sterilization processes, or ensuring proper assembly techniques.
- **Verification and Validation:** Verify and validate the effectiveness of risk control measures through testing, analysis, and other verification activities to ensure they adequately mitigate identified risks.
- **Document Control:** Maintain documentation of risk assessments, risk control measures implemented, and verification/validation activities to demonstrate compliance with regulatory requirements.

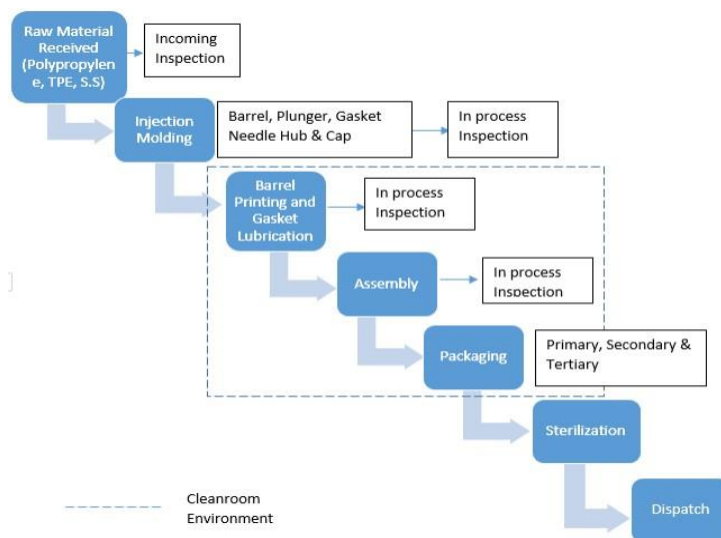


Fig. 2. Process flow diagram for syringe manufacturing

➤ **Risk Management throughout the Lifecycle:**

- **Design and Development:** Incorporate risk management activities into the design and development process of the medical device to identify and mitigate risks early [6].
- **Manufacturing:** Implement robust manufacturing processes and controls to ensure consistent quality and safety of the device during production.
- **Distribution and Use:** Consider risks associated with packaging, labeling, transportation, storage, and use of the device by healthcare providers and patients.

➤ **Regulatory Compliance:**

- Ensure compliance with relevant regulations and standards (e.g., ISO 13485, FDA QSR) that require manufacturers to establish and maintain a risk management system for medical devices.
- Prepare documentation and evidence of risk management activities for regulatory submissions and audits.

➤ **Post-Market Surveillance:**

- Monitor and evaluate feedback from users, complaints, adverse events, and other sources to identify potential new risks or changes in existing risks associated with the device [7].
- Implement corrective and preventive actions (CAPAs) as needed to address identified risks and improve device safety and performance.

➤ **Continuous Improvement:**

- Establish mechanisms for ongoing review and improvement of the risk management process based on feedback, data analysis, and lessons learned from post-market surveillance and quality management activities.
- Foster a culture of quality and safety within the organization to continuously enhance risk management practices and ensure the delivery of safe and effective medical devices to patients.

By integrating risk management into every phase of medical device manufacturing, from design

through post-market surveillance, manufacturers can effectively identify, assess, control, and mitigate risks to ensure patient safety and regulatory compliance.

### 3. SYRINGE MANUFACTURING PROCESSES

➤ **Risk Assessment in Raw Material**

Risk assessment in raw materials for syringes involves evaluating potential hazards and their likelihood of occurrence throughout the supply chain. Here are key steps and considerations for conducting such an assessment:

1. **Identifying Raw Materials:** Determine the specific raw materials used in syringe production. This typically includes plastics (such as polypropylene or polycarbonate), rubber (for gaskets and seals), metals (for needles or components) and silicon for lubrication.
2. **Hazard Identification:** Identify potential hazards associated with each raw material. Hazards could include chemical substances (e.g., toxic additives, residues from manufacturing processes), physical hazards (e.g., sharp edges, brittleness), and biological hazards (e.g., contamination from microbes, pyrogenic, sensitization).
3. **Risk Evaluation:** Evaluate the risks associated with each identified hazard. This involves assessing the likelihood of the hazard occurring and the severity of its potential impact. Consider factors such as exposure levels, frequency of use, and intended applications of the syringes.
4. **Regulatory Compliance:** Ensure compliance with relevant regulations and standards (e.g., ISO standards, FDA regulations). Different countries may have specific requirements for materials used in medical devices to ensure safety and efficacy.
5. **Supplier Assessment:** Assess the reliability and quality assurance measures of raw material suppliers. This includes reviewing supplier qualifications, certifications (e.g., ISO certifications) and auditing their manufacturing processes.
6. **Material Testing:** Conduct testing and analysis of raw materials to confirm their quality and safety. This may involve chemical analysis, mechanical testing (e.g., strength, durability), and biological testing to detect contaminants.

7. **Traceability and Documentation:** Establish systems for traceability of raw materials throughout the production process. Maintain comprehensive documentation of raw material specifications, test results, and supplier information for regulatory purposes and quality control.
8. **Risk Mitigation Strategies:** Develop strategies to mitigate identified risks. This could include implementing quality control measures during manufacturing, establishing contingency plans for supply chain disruptions, and conducting regular audits of suppliers.
9. **Monitoring and Review:** Implement ongoing monitoring and review processes to ensure that raw material risks are effectively managed over time. This includes updating risk assessments based on new information or changes in manufacturing processes.

By systematically assessing risks associated with raw materials used in syringe production, manufacturers can enhance product safety, comply with regulatory requirements, and maintain quality standards throughout the supply chain.

#### ➤ Risk Assessment in Injection Molding

A predominant method for syringe production, injection molding involves precise molding of plastic materials into syringe components such as barrels and plungers. Quality control measures in injection molding are crucial to ensure dimensional accuracy, material integrity, and sterility [8,9]. Turtle diagram for Injection Molding Process Risks is demonstrated in Fig. 3.

##### • Hazard Identification

- Potential hazards specific to injection molding of syringes (e.g., material contamination, mold design flaws)
- Factors affecting product quality and safety (e.g., material selection, process parameters)

##### • Risk Analysis

- Methods for assessing risks associated with injection molding (e.g., Failure Mode and Effects Analysis - FMEA)

- Quantitative and qualitative approaches to evaluating risk severity, probability, and detectability

#### ➤ Risk Control Measures

##### • Process Control

- Implementing robust process controls to minimize variability (e.g., temperature, pressure, injection speed)
- Monitoring and optimizing process parameters to ensure consistent product quality

##### • Material Selection and Quality Assurance

- Selecting suitable materials for syringe components (e.g., barrel, plunger)
- Establishing material specifications and conducting quality checks to mitigate material-related risks

#### ➤ Design Considerations for Injection Molded Syringes

##### • Design for Manufacturability (DFM)

- Design guidelines to optimize moldability and minimize risks during injection molding
- Considering features such as wall thickness, draft angles, and part geometry

##### • Tooling and Mold Design

- Importance of proper tooling design to prevent defects and ensure mold integrity
- Incorporating features for ease of manufacturing and maintenance

#### ➤ Quality Control and Assurance

##### • Process Validation

- Validation protocols for injection molding processes to demonstrate consistency and capability
- Conducting mold qualification and process validation studies

##### • Inspection and Testing

- Inspection techniques for verifying part quality and identifying defects (e.g., visual inspection, dimensional checks)

- Testing methods (e.g., leak testing, functional testing) to ensure syringe performance and reliability
- **Regulatory Compliance and Standards**
  - **Adherence to Regulatory Requirements**
    - Ensuring compliance with applicable regulatory standards (e.g., FDA regulations, ISO 13485)
    - Documentation and traceability of risk management activities for regulatory audits

**Assembly and Packaging:** The assembly process involves the integration of syringe components, including needles, caps, and labels, while packaging ensures sterility and protection during transportation and storage.

➤ **Risk Assessment in Assembly and Packaging**

Risk assessment in the assembly and packaging of syringes is critical to ensure the safety, efficacy, and quality of medical devices. Here's how risk assessment can be applied specifically to the assembly and packaging process of syringes: Turtle diagram for Assembly and Packaging Process Risks is demonstrated in Fig. 4 & Fig. 5.

- **Hazard Identification:**
  - **Physical Hazards:** Such as breakage or malfunction of syringe components during assembly.
  - **Chemical Hazards:** Including risks from materials used in syringe construction or from contaminants introduced during assembly or packaging.
  - **Biological Hazards:** Ensuring sterility throughout the process to prevent microbial contamination.
  - **Operational Hazards:** Risks related to human error during assembly or packaging.
- **Risk Analysis:**
  - Assess the likelihood of each identified hazard occurring during assembly and packaging.
  - Evaluate the severity of potential harm or impact on patients or users if a hazard materializes.
  - Consider the detectability of hazards through quality control measures and inspection processes.

- **Risk Evaluation:**

- Prioritize risks based on their severity and likelihood to determine which require immediate attention.
- Determine acceptable risk levels for different hazards based on regulatory requirements and industry standards.

- **Risk Control Measures:**

- Implement design controls to ensure syringe components fit together correctly and reliably during assembly.
- Use materials that are compatible with the intended use and ensure they do not introduce harmful substances into the syringe or its contents.
- Establish and validate processes for maintaining sterility throughout assembly and packaging.
- Implement quality assurance checks, such as visual inspection, functional testing, and microbial testing, at critical points in the assembly and packaging process.
- Provide training to personnel involved in assembly and packaging to reduce the risk of human error.

- **Documentation and Monitoring:**

- Maintain comprehensive documentation of the risk assessment process, including hazard identification, risk analysis, risk evaluation, and risk control measures implemented.
- Regularly monitor and review the effectiveness of risk control measures through audits, inspections, and feedback mechanisms.
- Update risk assessments as needed in response to changes in materials, processes, regulations, or feedback from post-market surveillance [10].

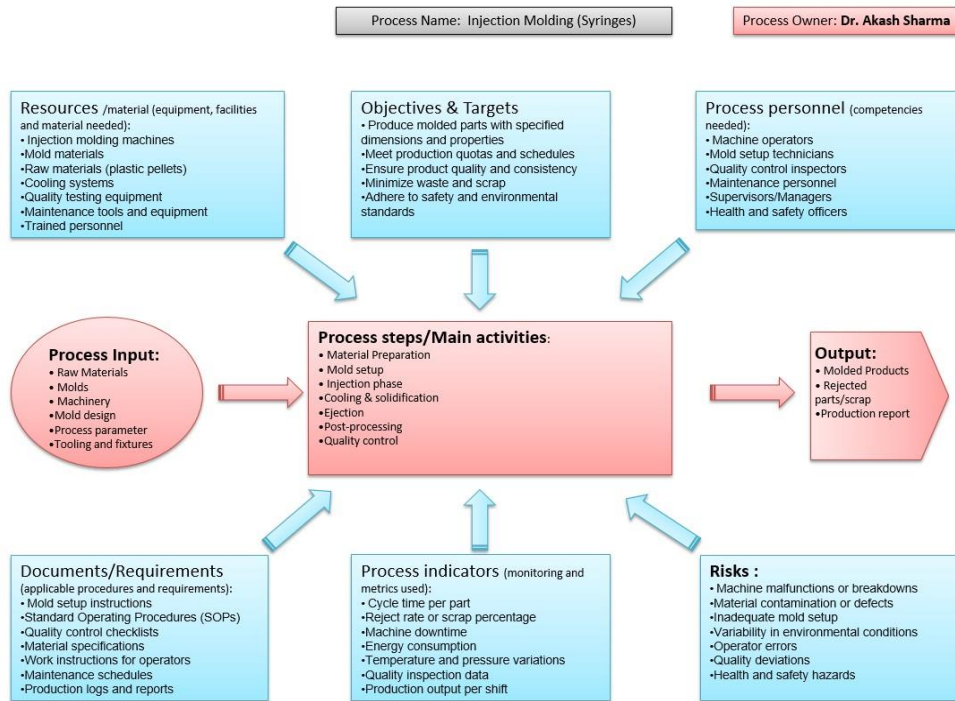
### 3.1 Ethylene Oxide (EO) Sterilization Process:

- **Overview and Importance:** Ethylene oxide (EO) sterilization is a widely utilized method in the medical device industry due to its effectiveness in sterilizing heat-sensitive devices such as syringes. The process involves exposing syringes to EO gas under controlled conditions to eliminate microorganisms and ensure product sterility [11].

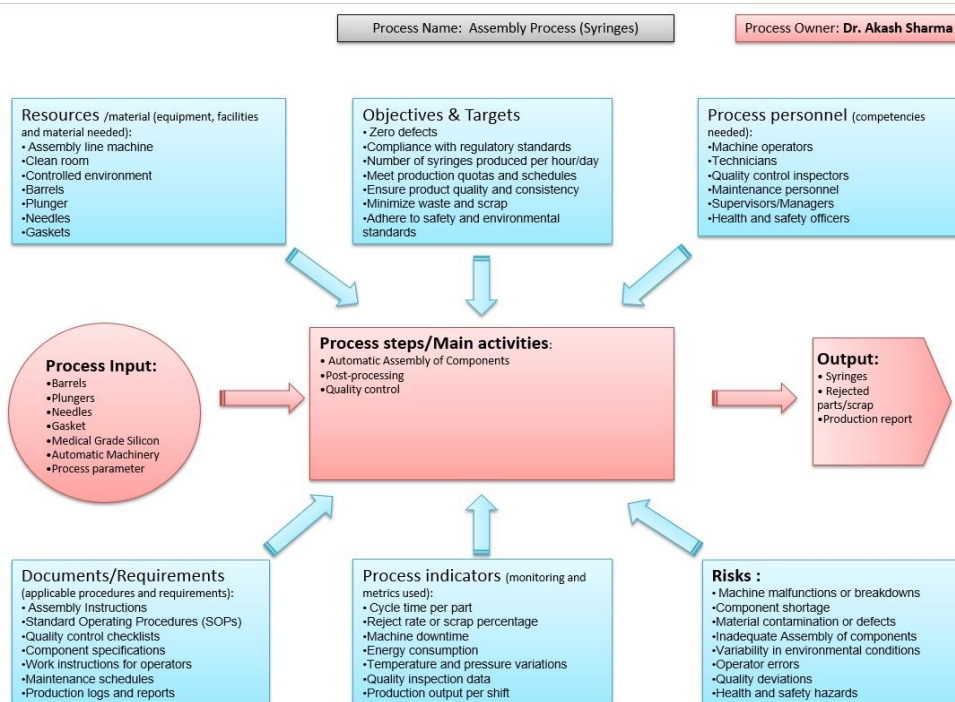
➤ **Risk Assessment in Assembly and Packaging**

Risk assessment in ethylene oxide (EO) sterilization processes is crucial due to the potential hazards associated with EO, including

its flammability, toxicity, and environmental impact. Here's how risk assessment is typically conducted in EO sterilization processes: Turtle diagram for EO Sterilization Process Risks is demonstrated in Fig. 6.



**Fig. 3. Turtle diagram for injection molding process risks**



**Fig. 4. Turtle diagram for assembly process risks**

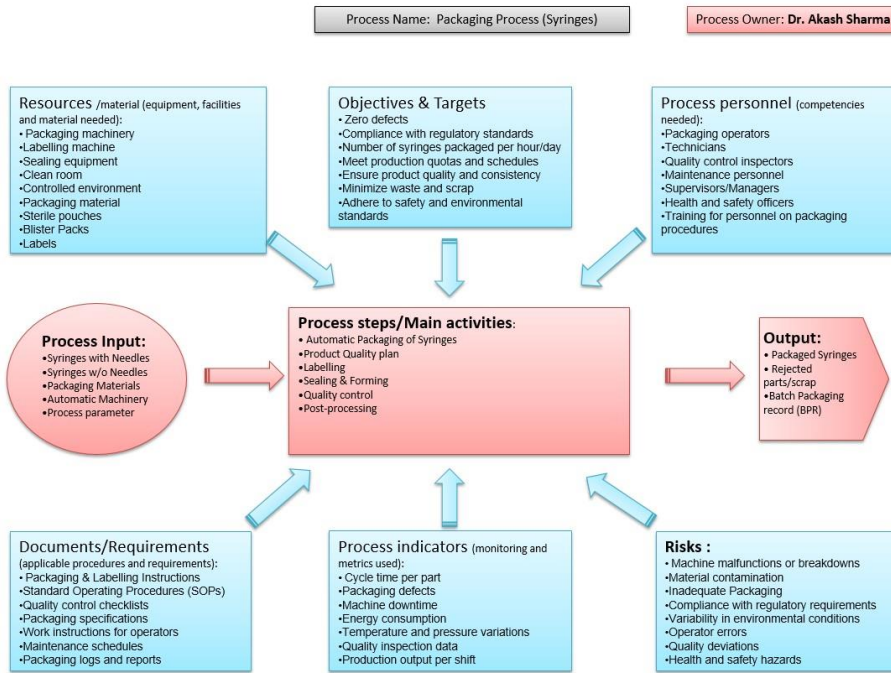


Fig. 5. Turtle diagram for packaging process risks

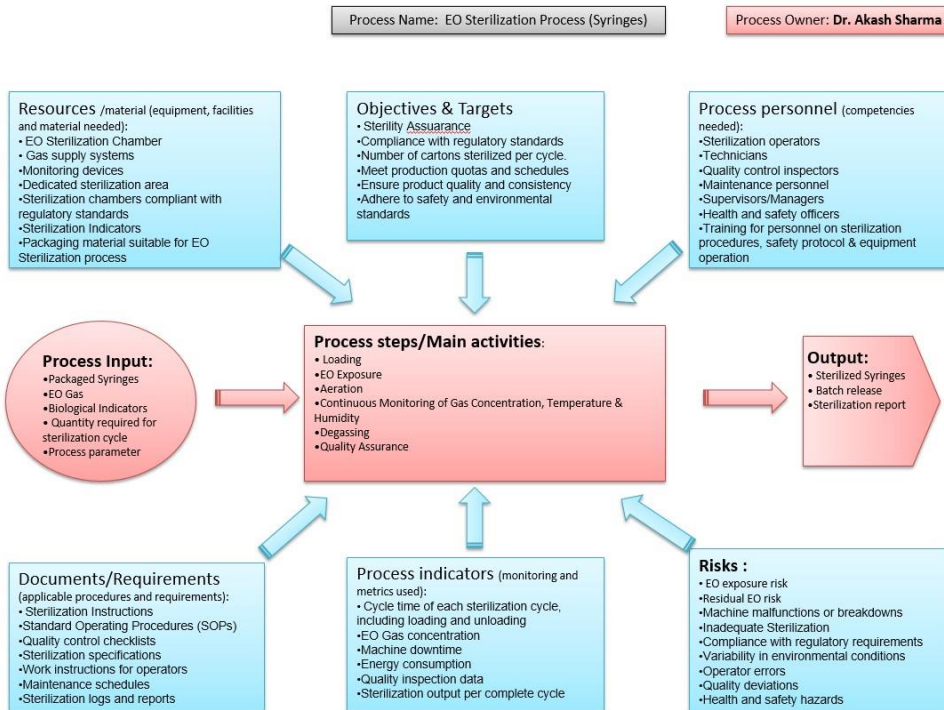


Fig. 6. Turtle diagram for EO sterilization process risks

- **Hazard Identification:**
  - **EO Exposure:** Identify potential exposure routes (inhalation, dermal contact) for personnel handling EO.
  - **Flammability:** Recognize the risk of fire or explosion due to EO's flammable properties.
  - **Environmental Impact:** Consider EO emissions and their impact on the environment.



- **Risk Analysis:**

- Assess the likelihood of EO exposure or release occurring during the sterilization process.
- Evaluate the severity of potential consequences such as health effects (acute or chronic toxicity), fire/explosion, or environmental contamination.
- Analyze factors contributing to EO emissions, such as process parameters, equipment design, and operational practices.

- **Risk Evaluation:**

- Determine the significance of identified risks based on their severity and likelihood.
- Establish acceptable risk levels for EO exposure, flammability, and environmental impact based on regulatory requirements (e.g., OSHA, EPA) and industry standards.
- Prioritize risks for mitigation based on their potential impact on personnel safety, facility integrity, and environmental compliance.

- **Risk Control Measures:**

- **Engineering Controls:** Implement engineering controls such as ventilation systems, gas detection alarms, and automated process controls to minimize EO exposure and emissions.
- **Administrative Controls:** Develop standard operating procedures (SOPs) for EO handling, including training for personnel on safe practices and emergency response procedures.
- **Personal Protective Equipment (PPE):** Provide appropriate PPE, including respirators, gloves, and protective clothing, to minimize exposure to EO.
- **Process Optimization:** Optimize sterilization parameters (temperature, humidity, cycle time) to reduce EO usage and emissions while ensuring effective sterilization.
- **Monitoring and Auditing:** Establish monitoring programs to regularly assess EO levels in air and wastewater, as well as conduct audits to verify compliance with safety and environmental standards.

- **Documentation and Training:**

- Maintain comprehensive documentation of risk assessments, control measures implemented, monitoring results, and corrective actions taken.

- Provide training to personnel involved in EO sterilization processes regarding the hazards of EO, safe handling practices, emergency procedures, and use of PPE.

- **Continuous Improvement:**

- Continuously review and update risk assessments based on new information, technological advancements, regulatory changes, and feedback from incident investigations or audits.
- Implement lessons learned from incidents or near-misses to improve safety and environmental performance in EO sterilization processes.

- **Safety and Regulatory Considerations:** EO sterilization requires adherence to stringent safety protocols and regulatory standards to mitigate potential risks associated with EO exposure, such as residual EO levels and product compatibility.

### 3.2 Compliance and Regulatory Requirements

- Compliance with regulatory requirements in risk management is essential for ensuring the safety, efficacy, and quality of medical devices. Here's how regulatory requirements influence risk management in the medical device industry [12,13]:

- **International Standards:**

- **ISO 14971:** This standard specifies requirements for risk management processes throughout the lifecycle of medical devices. It outlines principles and methods for risk analysis, evaluation, control, and documentation.
- **ISO 13485:** Quality management systems for medical devices require risk management to be integrated into all aspects of the quality management system.
- **FDA QSR (Quality System Regulation):** The FDA requires manufacturers to establish and maintain a risk-based quality management system that includes risk analysis, control, and management processes.

- **Risk Management File:**

- Manufacturers are required to maintain a Risk Management File (RMF) that

documents all risk management activities. This file includes risk assessments, risk control measures implemented, verification and validation activities, and updates based on post-market surveillance.

- **Regulatory Submissions:**
  - Regulatory submissions, such as premarket notifications (510(k)), premarket approval applications (PMA), or CE Marking applications, require evidence of compliance with risk management standards and regulations [14].
  - Manufacturers must demonstrate that risks associated with the device have been identified, evaluated, and adequately controlled to ensure patient safety and device effectiveness.
- **Post-Market Surveillance:**
  - Regulatory authorities require manufacturers to implement post-market surveillance systems to monitor the performance of devices once they are on the market.
  - This includes monitoring complaints, adverse events, and other sources of feedback to identify any new risks or changes in existing risks associated with the device [10].
- **Labeling and Instructions for Use:**
  - Risk management information, including identified hazards, residual risks, and instructions for mitigating risks, must be communicated effectively through labeling and instructions for use provided with the device.
  - Clear information helps healthcare providers and users understand the risks associated with the device and how to use it safely and effectively.
- **Audits and Inspections:**
  - Regulatory authorities conduct audits and inspections to assess compliance with risk management requirements.
  - Manufacturers must be prepared to demonstrate adherence to risk management standards, provide documentation of risk assessments and

controls, and show evidence of continuous improvement in risk management practices.

- **Global Harmonization:**

- Many countries and regions have harmonized their regulatory requirements with international standards (e.g., MDR in Europe, CMDR in Canada) to streamline compliance for manufacturers operating in multiple markets.
- Manufacturers must stay informed about regulatory updates and changes to ensure ongoing compliance with risk management requirements in all markets where their devices are sold [15].

#### 4. METHODOLOGY

##### Step-by-Step FMEA Methodology for a Syringe:

1. **Define the Scope and Objectives:**
  - The objective is to evaluate potential failure modes of a syringe to enhance its reliability and safety in medical applications.
2. **Assemble a Cross-Functional Team:**
  - Include experts such as design engineers, manufacturing specialists, quality assurance personnel, and healthcare professionals.
3. **Create a Process Flow Diagram:**
  - Diagram the lifecycle stages of the 5ml syringe: design, raw material procurement, manufacturing, quality testing, packaging, distribution, use by medical professionals, and disposal.
4. **Identify Potential Failure Modes:**
  - Potential failure modes are identified by examining each component or process step to determine possible failures. Each mode is evaluated for its causes, effects, and severity, enabling teams to prioritize risks and implement corrective actions to enhance reliability and safety.

**Table 1. Identification of Failure Mode**

Potential Failure Mode	Description
Cannula detachment	Cannula separates from the hub/syringe body during use.
Plunger sticking	Plunger does not move smoothly, affecting dosage accuracy.
Leakage	Fluid leaks from the syringe, compromising medication delivery.
Material defect	Structural weakness or impurities in syringe components.
Incorrect scale markings	Incorrect or unclear volume markings on the syringe barrel.

**5. Determine Failure Effects:**

- Determining failure effects involves assessing the consequences of each failure mode on system performance and safety. This prioritization helps teams focus on the most critical issues for effective mitigation.

**6. Assign Severity Ratings:**

- Assigning severity ratings involves evaluating the potential impact of each failure effect on system performance and safety, typically on a scale from 1 to 10. This rating helps prioritize failure modes based on their seriousness, guiding teams to address the most critical risks first.

**7. Identify Causes and Occurrence Ratings:**

- Root cause analysis identifies the underlying causes of failure modes, while occurrence ratings quantify the probability of these causes leading to failures on a scale from 1 to 10. This approach prioritizes mitigation efforts based on frequency and severity.

**8. Assign Detection Ratings**

- Detection ratings evaluate the likelihood of identifying a failure mode before it impacts the system, typically on a scale from 1 to 10. Lower scores indicate higher detection chances, guiding teams to enhance monitoring and diagnostics.

**9. Calculate Risk Priority Number (RPN):**

- RPN (Risk Priority Number) is a quantitative assessment used in Failure Modes and Effects Analysis (FMEA) to prioritize potential failure modes based on their severity, occurrence probability, and detectability. It helps teams focus on addressing the most critical issues first.

Calculation of RPN:

RPN is calculated using the formula:  $RPN = Severity \times Occurrence \times Detection$

Where:

**Severity:** A numerical value assigned to the potential impact of a failure mode (typically on a scale of 1 to 10, where 10 is the highest severity).

**Occurrence:** A numerical value representing the likelihood or frequency of the failure mode occurring (on a scale of 1 to 10, where 10 is the highest occurrence).

**Detection:** A numerical value indicating the effectiveness of current controls or processes in detecting the failure mode before it reaches the customer or causes harm (on a scale of 1 to 10, where 10 indicates the highest detection effectiveness).

**Interpretation of RPN:** Once you have calculated the RPN for each identified failure mode, you can interpret its significance as follows:

**High RPN (Critical Issues):** Failure modes with a high RPN indicate critical risks that require immediate attention. These are typically prioritized for corrective actions to reduce their impact and likelihood of occurrence.

**Moderate RPN (Important Issues):** Failure modes with moderate RPN values may require actions to mitigate their risks, although they are not as urgent as those with higher RPNs.

**Low RPN (Lower Priority Issues):** Failure modes with low RPN values may still warrant attention, but they are generally less critical and can be addressed after higher priority issues.

**Example:** Let's consider an example with a syringe and calculate RPN for one of the failure modes identified earlier (e.g., Needle detachment):



RPN is a valuable tool within the FMEA framework for assessing and prioritizing potential failure modes. It provides a quantitative basis for decision-making, ensuring that efforts are directed towards mitigating the most critical risks associated with products like syringes, thereby enhancing safety and reliability in medical applications.

$$\text{RPN} = \text{Severity} \times \text{Occurrence} \times \text{Detection}$$

**10. Develop Action Plans:**

- Prioritize actions based on highest RPN values. For instance, for needle detachment (RPN 252), actions might include improving adhesive quality control and enhancing visual inspection processes.

**11. Monitor and Review:**

- Implement changes, monitor effectiveness, and update FMEA documentation as necessary to continuously improve syringe quality and safety.

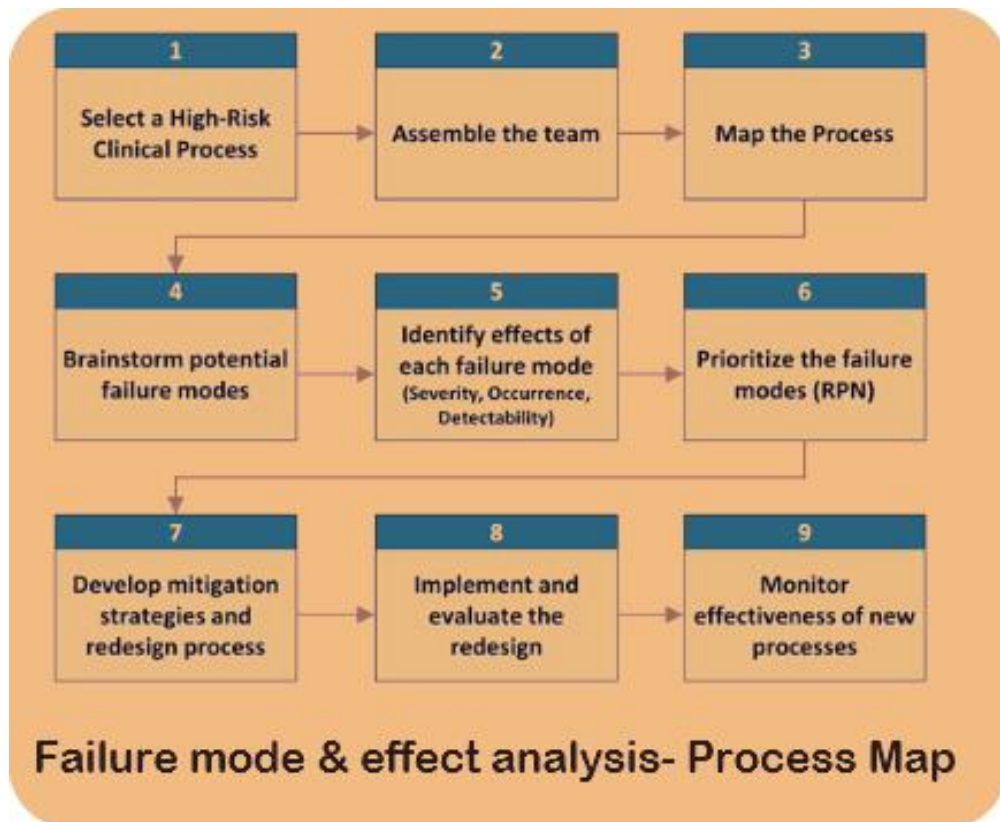
**12. Document and Communicate:**

- Maintain clear documentation of FMEA findings, actions taken, and outcomes to ensure all stakeholders are informed and aligned.

By systematically applying FMEA to a syringe, manufacturers can identify and mitigate potential risks before they impact patients or healthcare providers. This structured approach ensures that quality and safety standards are met, enhancing the overall reliability and performance of medical devices like syringes.

**4.1 Risk Management Strategies Based on ISO 14971**

Risk management is a critical component of ensuring the safety, efficacy, and compliance of medical devices such as syringes. ISO 14971 provides a systematic framework for identifying, evaluating, and controlling risks throughout the lifecycle of a medical device. This section explores the key risk management strategies based on ISO 14971 principles, specifically tailored for syringe manufacturing. Risk management cycle is shown in the Fig. 8 [1,4].



**Fig. 7. FMEA Process Map**



Fig. 8. Risk management process

1. **Risk Management Process:**

- **Risk Assessment:** Utilize methods such as hazard identification, risk estimation, and risk evaluation to systematically identify and prioritize potential hazards associated with syringe manufacturing. Consider factors such as materials, design, manufacturing processes, and intended use.
- **Risk Control:** Implement measures to mitigate identified risks to an acceptable level. This may include design modifications, process improvements, use of protective barriers, and implementing safety features in syringe design.
- **Risk Evaluation:** Assess the effectiveness of risk control measures and verify risk reduction achieved. Ensure alignment with regulatory requirements and standards applicable to syringe manufacturing.

2. **Integration into Manufacturing Processes:**

- **Design Control:** Integrate risk management activities into the design phase of syringe development. Conduct risk assessments early in the design process to proactively address potential hazards and incorporate safety features.
- **Manufacturing and Quality Control:** Implement stringent quality control measures to monitor and verify the

effectiveness of risk controls during manufacturing. Ensure consistency in production processes to minimize variability and maintain product quality.

3. **Documentation and Traceability:**

- **Risk Management File:** Maintain a comprehensive risk management file documenting all stages of the risk management process. Include hazard analyses, risk assessments, risk control measures, verification and validation activities, and periodic reviews.
- **Traceability:** Establish traceability of risk management activities to ensure accountability and facilitate regulatory audits. Document changes and updates to risk management strategies over the product lifecycle.

4. **Post-Market Surveillance:**

- **Monitoring and Feedback:** Implement post-market surveillance procedures to monitor the performance of syringes in clinical use. Collect and analyze feedback from healthcare professionals and end-users to identify potential risks or adverse events.
- **Risk Management Review:** Conduct periodic reviews of risk management strategies based on post-market data and emerging safety concerns. Update risk

assessments and risk controls as necessary to address new information and ensure ongoing product safety.

**5. Training and Awareness:**

- **Employee Training:** Provide comprehensive training programs to educate employees on the principles of ISO 14971 and their roles in implementing effective risk management strategies. Foster a culture of safety and quality throughout the organization.
- **Stakeholder Engagement:** Collaborate with stakeholders including regulatory authorities, healthcare providers, and industry associations to stay informed about evolving regulatory requirements and best practices in risk management.

**6. Continuous Improvement:**

- **Risk Management Plan:** Develop and maintain a risk management plan that

outlines proactive strategies for continuous improvement. Establish mechanisms for feedback, corrective actions, and preventive measures to enhance risk management effectiveness.

- **Benchmarking:** Benchmark against industry standards and best practices to identify opportunities for enhancing risk management processes and achieving excellence in syringe manufacturing.

**4.2 Ensuring Safety and Compliance of Syringes with Auto-Disable (AD) Feature**

Manufacturing syringes with an auto-disable (AD) feature according to ISO 7886-3 requires meticulous attention to safety and regulatory compliance throughout the product lifecycle, including robust processes during production. The AD mechanism must be designed, validated, and implemented to effectively prevent unauthorized reuse, ensuring the safety of users and patients.

**Table 7. Technical justification**

Aspect	Technical Justification
Regulatory Standards	Compliance with ISO 7886-3 ensures that AD mechanisms are designed and tested to reliably and irreversibly disable the syringe post-use, meeting regulatory requirements.
Design Requirements	Engineering robust AD mechanisms involves selecting and validating designs (e.g., breakable needles) that reliably prevent reuse without compromising safety or function.
Functionality Testing	Rigorous testing protocols ensure AD mechanisms consistently perform as intended, preventing reuse while maintaining accurate medication delivery.
Quality Management Systems	ISO 13485 certification ensures adherence to strict quality standards throughout production, verifying that AD mechanisms meet specified performance and safety criteria.
Risk Management	Implementing ISO 14971 involves conducting comprehensive risk assessments throughout the product lifecycle. This process identifies potential hazards associated with the AD feature and implements controls to mitigate risks effectively.
Supplier Management	Effective supplier oversight ensures components for AD mechanisms meet quality and regulatory requirements, maintaining reliability and traceability in production.
Usability and User Safety	Usability studies validate that AD mechanisms are intuitive and effective in preventing misuse or accidental needlestick injuries during medical procedures.
Lifecycle Monitoring	Continuous monitoring throughout production ensures AD mechanisms consistently meet standards, adapting to regulatory updates and technological advancements.
During Production	During production, adherence to ISO 14971 principles ensures that risk management practices are integrated into manufacturing processes. Manufacturers conduct risk assessments specific to AD mechanisms to identify and mitigate potential hazards such as mechanical failures or design flaws that could compromise safety or functionality. This approach includes:

### Mitigation of Risks:

1. **Design Optimization:** Implementing robust AD mechanism designs that are resistant to tampering or accidental activation post-use, ensuring reliable disablement.
2. **Validation Testing:** Conducting thorough functionality tests under various conditions to verify AD mechanisms reliably prevent reuse without impacting syringe performance.
3. **Supplier Qualification:** Establishing stringent criteria for supplier selection and monitoring to ensure components meet quality and regulatory standards, reducing variability in AD mechanism performance.
4. **Training and User Education:** Providing comprehensive training to healthcare professionals on the proper use and disposal of AD syringes to minimize misuse and enhance safety.
5. **Continuous Improvement:** Instituting ongoing monitoring and feedback mechanisms to identify and address emerging risks or performance issues throughout the syringe lifecycle.

### 4.3 Auto-Disable (AD) Mechanism Failures: Risks and Mitigation Strategies

Auto-disable mechanisms in syringes are critical features designed to prevent reuse and enhance safety in medical settings. However, like any mechanical system, AD mechanisms can fail, potentially compromising patient safety and regulatory compliance. Here's an exploration of common failure modes, associated risks, and effective mitigation strategies:

1. **Common Failure Modes of AD Mechanisms:**
  - **Mechanical Failure:** Breakage or malfunction of components like breakable needles or retractable mechanisms.
  - **Activation Failure:** Inability of the mechanism to activate or disable the syringe after use.
  - **Incomplete Disablement:** Partial or ineffective disablement of the syringe, allowing potential reuse.

### 2. Risks Associated with AD Mechanism Failures:

- **Patient Safety:** Reuse of syringes can lead to transmission of infections or inaccurate dosing, posing serious health risks to patients.
- **Regulatory Non-Compliance:** Failure to meet regulatory requirements (e.g., ISO 7886-3) for AD mechanism effectiveness and safety, resulting in legal and financial implications for manufacturers.

### 3. Mitigation Strategies using FMEA:

- **Failure Modes and Effects Analysis (FMEA):** Manufacturers conduct FMEA to systematically identify, prioritize, and mitigate potential failure modes of AD mechanisms:
  - **Identification:** Identify possible failure modes, such as mechanical breakage or insufficient activation.
  - **Assessment:** Assess the severity and probability of each failure mode's occurrence and its potential impact on patient safety and regulatory compliance.
  - **Mitigation:** Implement risk controls to mitigate identified risks, including:
    - **Design Improvements:** Enhance robustness and reliability of AD mechanism components through iterative design enhancements and material selection.
    - **Testing Protocols:** Develop comprehensive testing protocols to validate AD mechanism functionality under various conditions, including stress testing and usability assessments.
    - **Supplier Control:** Ensure suppliers adhere to stringent quality standards and provide components that meet regulatory requirements for AD mechanisms.
    - **User Training:** Provide thorough training and clear instructions for healthcare professionals on proper syringe use and disposal to minimize misuse and enhance safety.
- 4. **Ensuring Safety and Compliance:**
  - **Regulatory Adherence:** Continuously monitor and comply with ISO standards (e.g., ISO 13485, ISO 14971) and regional regulatory requirements to ensure AD



mechanisms meet safety and performance criteria.

- **Quality Assurance:** Implement robust quality management systems to maintain consistent product quality and traceability throughout the manufacturing process.
- **Usability and User Safety:** Conduct usability studies to ensure AD mechanisms are intuitive and effective in preventing misuse or accidental needlestick injuries during medical procedures.

#### 4.4 Ensuring Safety and Compliance in Plastic Syringe Manufacturing

##### 1. Decide on Risk Acceptability Levels (for each process):

For plastic syringe manufacturing, determining risk acceptability involves:

- **Identifying Hazards:** Identify potential hazards associated with plastic materials, such as chemical compatibility with medications, potential for breakage or leakage, and risks related to manufacturing processes.
- **Risk Evaluation:** Evaluate risks based on severity of harm (e.g., patient injury from breakage or contamination), probability of occurrence (e.g., likelihood of material failure), and usability factors (e.g., ease of handling).
- **Risk Control:** Implement controls such as:
  - **Material Selection:** Choose plastics that are biocompatible, chemically resistant, and suitable for medical applications.
  - **Design Controls:** Optimize syringe design to minimize risks of breakage, leakage, and user error.
  - **Process Controls:** Establish stringent manufacturing processes to ensure consistent quality and performance.
- **Risk Acceptance:** Assess residual risks after applying controls to ensure they are acceptable considering benefits to patients and healthcare providers.

##### 2. Effective Ways to Control Risk During Plastic Syringe Manufacture:

- **Material Selection:**
- Choose plastics (e.g., polypropylene, polycarbonate) known for their durability,

chemical resistance, and suitability for medical use.

- Ensure plastics meet regulatory standards for biocompatibility and compatibility with sterilization methods.

##### • Design Controls:

- Design syringes with features that enhance usability and safety, such as ergonomic grips and clear markings for accurate dosage.
- Ensure designs minimize risks of breakage or leakage during use.

##### • Process Controls:

- Implement robust manufacturing processes with strict quality controls to detect and prevent defects.
- Conduct validation tests to ensure materials and processes meet performance requirements under simulated or actual conditions of use.

##### • Supplier Controls:

- Maintain oversight of plastic suppliers to ensure materials consistently meet quality and safety standards.
- Verify compliance with regulatory requirements through supplier audits and ongoing monitoring.

##### 3. If Risk Cannot Be Completely Eliminated, Best Options in Each Process:

##### • Risk Mitigation:

- Use engineering controls to reduce risks associated with plastic syringe manufacturing, such as improving design features or material selection.
- Implement procedural controls (e.g., standardized operating procedures) to minimize variability and ensure consistent quality.

##### • Risk Management Documentation:

- Document residual risks and rationale for their acceptability in the risk management file.

- Clearly communicate residual risks to stakeholders and ensure transparency in risk management decisions.

#### 4. Risk Management Review Before Market Release and Addition to Risk Management File:

##### • Review Process:

- Conduct a comprehensive review of the risk management process before market release to verify compliance with regulatory requirements and internal quality standards.
- Ensure all documentation related to risk assessment, control measures, and risk acceptance is complete and up-to-date.

##### • Risk Management File:

- Compile a thorough risk management file that includes detailed documentation of risk analysis, mitigation strategies, and verification/validation activities specific to plastic syringe manufacturing.
- Maintain the file with updates throughout the product lifecycle to reflect any changes or improvements made.

#### 5. Local Regulations and Effects on Plastic Syringe Products:

##### • Regulatory Compliance:

- Adhere to local regulations (e.g., FDA in the US, EU MDR in Europe) governing the manufacture and sale of medical devices, including plastic syringes.
- Ensure compliance with standards for materials, design, manufacturing processes, and quality control.

##### • Impact on Product Development:

- Regulatory requirements influence the entire lifecycle of plastic syringe products, from initial design and development through manufacturing, testing, and commercialization.
- Manufacturers must demonstrate compliance through rigorous testing, documentation, and submission of regulatory filings.

##### • Market Access:

- Compliance with regulatory requirements facilitates market access by ensuring

products meet safety, efficacy, and quality standards.

- Non-compliance can lead to delays in market entry or restrictions on product distribution.

#### 4.5 Examining Hazards from Syringe Production in Healthcare

##### 1. Needlestick Injuries:

**Problem:** Needlestick injuries pose significant risks to healthcare workers, including exposure to bloodborne pathogens.

**Solution:** Corrosion-Free and Biocompatible Needles:

**Implement Corrosion-Resistant Materials:** Ensure needles are made from corrosion-resistant materials to prevent degradation over time.

- **Conduct Chemical Corrosion Tests:** Perform tests to assess the resistance of needle materials to chemical degradation in clinical settings.
- **Maintain ISO Standards:** Design needles according to ISO 7864 to ensure specifications such as bevel length, rotation angle, bevel angle, and outer diameter are consistently met.

##### • Biocompatibility Assurance:

- **Perform Biocompatibility Assessments:** Conduct tests to confirm that needle materials do not elicit adverse biological responses in patients.
- **Ensure Conformity to Biological Safety Standards:** Verify that needles comply with regulations and standards ensuring safe biological interactions.

##### Enhanced Patient Comfort and Safety:

- **Pain Minimization:** Design needles to minimize discomfort during use, enhancing patient compliance and comfort.
- **Environmental Sustainability:** Promote the use of materials that minimize environmental impact, supporting sustainability efforts in healthcare practices.

**Provide Comprehensive User Instructions:** Equip each syringe with clear instructions for

proper handling, emphasizing safety protocols to prevent accidents and ensure effective use.

This comprehensive approach ensures that needles not only meet stringent standards for corrosion resistance and biocompatibility but also prioritize patient comfort, environmental responsibility, and user safety through clear and thorough user instructions.

## 2. Material Compatibility and Contamination:

**Problem:** Materials used in syringes must be compatible with medications and withstand sterilization processes to prevent contamination.

### Solution:

- **Material Selection:** Choose biocompatible materials such as specific grades of plastics (e.g., polypropylene, polycarbonate) or stainless steel that meet regulatory standards.
- **Compatibility Testing:** Conduct comprehensive testing to ensure materials do not interact chemically with drugs and are resistant to degradation during sterilization.

### Implementation:

- Perform Biocompatibility/Chemical compatibility tests with various medications and solutions commonly administered via syringes.
- Validate sterilization processes to ensure materials maintain integrity and do not introduce contaminants.
- Implement strict supplier qualification processes and audits to maintain material quality and consistency.

## 3. Breakage or Leakage of Syringes:

**Problem:** Syringe breakage or leakage can lead to medication spillage, improper dosing, or potential harm to patients and healthcare workers.

### Solution:

- **Design for Durability:** Optimize syringe design to withstand mechanical stresses encountered during handling, injection, and storage.
- **Material Strength:** Select materials with appropriate strength and flexibility

properties to minimize the risk of breakage.

- **Quality Assurance:** Implement rigorous quality control measures throughout manufacturing to detect and mitigate defects that could lead to breakage or leakage.

### Implementation:

- Conduct mechanical stress tests and simulations to evaluate syringe durability under various conditions.
- Implement automated quality control checks during production to identify defects such as cracks, leaks, or irregularities.
- Validate designs through user feedback and clinical trials to ensure performance meets expectations under real-world conditions.

## 4. Dosage Accuracy and User Error:

**Problem:** Incorrect dosage administration due to unclear markings or user error can compromise patient safety and treatment efficacy.

### Solution:

- **Clear Markings and Ergonomic Design:** Enhance syringe design with prominently displayed volume markings, color-coded indicators, and ergonomic features for ease of use.
- **Training and Education:** Provide comprehensive training for healthcare staff on proper syringe handling, dosage calculation, and administration techniques.

### Implementation:

- Conduct human factors studies to optimize syringe design for intuitive use and minimize potential for user error.
- Develop standardized protocols and educational materials to reinforce best practices in dosage calculation and administration.
- Implement continuous training programs and refresher courses to ensure healthcare workers maintain proficiency in syringe usage.

## 5. Cross-Contamination and Infection Control:

**Problem:** Improper syringe handling and reuse can lead to cross-contamination and increase the risk of infection transmission.

### Solution:

- **Single-Use Designs:** Design syringes for single-use to prevent contamination between patients.
- **Backflow Prevention:** Incorporate features such as barriers or anti-reflux valves to prevent backflow of fluids and reduce contamination risks.

### Implementation:

- Validate single-use designs through microbiological testing and compliance with regulatory standards.
- Educate healthcare providers on the importance of proper syringe disposal and adherence to infection control protocols.
- Implement monitoring and surveillance systems to track and report incidents of cross-contamination or infection related to syringe use.

## 6. Regulatory Compliance and Documentation:

**Problem:** Non-compliance with regulatory requirements can lead to delays in market approval, product recalls, or legal liabilities.

### Solution:

- **Adherence to Standards:** Establish a robust risk management process aligned with ISO 14971 and relevant regulatory guidelines.
- **Documentation:** Maintain comprehensive risk management files documenting hazard analysis, risk assessments, mitigation strategies, and verification/validation activities.

### Implementation:

- Conduct regular reviews and updates of risk management documentation to reflect changes in regulations or product enhancements.
- Collaborate with regulatory authorities during product development to ensure

compliance with safety, efficacy, and quality standards.

- Implement a systematic approach to regulatory submissions and approvals to facilitate market access and maintain product integrity.

## 7. Patient Safety Monitoring:

**Problem:** Ensuring ongoing safety and effectiveness of syringe products throughout their lifecycle is critical for patient care.

### Solution:

- **Post-Market Surveillance:** Establish surveillance systems to monitor adverse events, complaints, and safety issues related to syringe use.
- **Feedback Mechanisms:** Gather feedback from healthcare providers, patients, and end-users to identify potential safety concerns and areas for improvement.

### Implementation:

- Implement post-market surveillance programs to promptly detect and respond to safety issues or emerging risks.
- Conduct periodic safety reviews and risk assessments to evaluate product performance and effectiveness in real-world settings.
- Use data analytics and trend analysis to proactively address safety issues and optimize product design and usage protocols.

## 5. CONCLUSION

In conclusion, this research has explored the critical intersection of risk management, safety enhancement, and regulatory compliance in syringe manufacturing, with a specific focus on the principles outlined in ISO 14971 and the role of EO sterilization. Through a comprehensive review of literature, case studies, and practical applications, several key insights have emerged [17,18]:

1. **Importance of ISO 14971:** ISO 14971 provides a structured framework for syringe manufacturers to systematically identify, assess, and mitigate risks associated with their products. By adhering to ISO 14971 principles, manufacturers

can enhance product safety, achieve regulatory compliance, and improve overall quality management practices.

2. **Integration of EO Sterilization:** Ethylene oxide (EO) sterilization plays a crucial role in maintaining the sterility of syringes, particularly those made from heat-sensitive materials. Compliance with stringent EO sterilization protocols ensures that syringes are free from harmful microorganisms, meeting essential safety standards for medical devices.
3. **Risk Management Strategies:** Effective risk management strategies based on ISO 14971 include rigorous risk assessment, implementation of appropriate risk controls, documentation of risk management processes, and continuous monitoring and improvement. These strategies are essential for identifying potential hazards in syringe manufacturing and implementing preventive measures to mitigate risks effectively.
4. **Challenges and Opportunities:** Syringe manufacturers face challenges such as navigating complex regulatory landscapes, adapting to technological advancements, and ensuring consistency in quality and safety standards across global markets. However, these challenges also present opportunities for innovation, collaboration with regulatory bodies, and adoption of best practices to enhance product quality and patient safety.
5. **Future Directions:** The future of syringe manufacturing lies in advancing risk management frameworks, integrating new technologies for sterilization and quality assurance, and enhancing collaboration among stakeholders to address emerging challenges. Continued research and development in these areas will drive improvements in syringe safety, compliance, and overall healthcare delivery.

In summary, by embracing ISO 14971 principles, leveraging EO sterilization processes, and continuously improving risk management practices, syringe manufacturers can uphold their commitment to delivering safe and effective medical devices. This research underscores the importance of proactive risk management in ensuring the reliability and safety of syringes, ultimately contributing to enhanced patient outcomes and public health globally.

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## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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*Peer-review history:*  
The peer review history for this paper can be accessed here:  
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