3.2 Drug Quality and Product Safety

Materiality Assessment

GRI 3-3, 416-2, SASB HC-BP-250a.1~a.5

PharmaEssentia utilizes the highest standard operating procedures, quality management systems, and product traceability systems in its drug production processes. The company adheres to the PIC/S Good Distribution Practice (GDP) guidelines and has established over 4,000 documents related to quality safety management, standard operating procedures, and various plans and reports. These measures ensure compliance with operational processes as well as accuracy and completeness of record-keeping, thereby guaranteeing the quality and safety of the medications. This comprehensive approach safeguards medication safety for patients worldwide.

Materiality Assessment

Drug Quality and Product Safety

Management Policies and Commitments

PharmaEssentia Taichung plant strictly adheres to protocols such as the Quality Risk Management Procedure, Equipment Risk Assessment Procedure, and Change Control Procedure. It implements risk management for production processes, environmental control, material supply, and annual quality reviews to minimize quality hazards.

Responsible Team

- Headquarters Production, Transportation, Quality Management, and Auditing Departments
- Product Safety & Risk Management (PSRM) Team and Drug Safety Monitoring Quality Assurance Personnel in the headquarters and subsidiaries
- Quality Management of Marketed and Clinical Drugs is managed by the headquarters' Quality Assurance and Quality Control departments, in cooperation with Clinical Trial Quality Assurance and Drug Safety Monitoring teams.
- Sustainability Significant Themes: Managed by the Sustainability Development Center - Product Ethics and Safety team members.

Actions and Mythology

- Implementation of TrackWise Electronic System: PharmaEssentia has adopted the TrackWise electronic system to manage deviations, corrective and preventive actions, supplier management, and laboratory investigations within their quality system.
- Production Quality and Risk Management: The company conducts global cross-departmental risk assessment meetings to collaboratively review and address risk issues within the manufacturing facilities.

Indicators and Objectives

- Good Manufacturing Practice (GMP) certification is updated or extended as planned/maintain qualifications.
- Regularly perform internal and external audits, and successfully pass them.
- Complete GMP/Good Distribution Practice (GDP) training.

2023 Performance

- Passed routine inspections by Japan's PMDA, the U.S. FDA, Taiwan's TFDA, and Korea's MFDS with no significant deficiencies.
- Implemented the TrackWise digital quality management system for managing deviations, corrective and preventive actions, supplier management, and laboratory operations. Expected to complete the integration of equipment management and laboratory data systems by early 2024.
- Completed 12 internal audits and passed 20 external official inspections.
- Conducted 925 GMP/GDP training sessions, totaling 25,000 hours.
- Handled 143 customer complaints (unrelated to product safety), achieving a complaint rate of 0.15%, lower than the 0.86% in 2022.
- No recalls due to defective products.
- Held 15 global cross-departmental risk assessment team meetings to review risk issues within the manufacturing sites, with 92 participants involved.

Expanding Certification and Market Reach Year by Year

We are actively vertically integrating our supply chain, from production, quality control, and filling to shipping, as we expand into global markets, step by step implementing the development blueprint of an international pharmaceutical company.

2012	2013	2018	2020	2021	2022	2023
Completion of Taichung Biopharmaceutical Manufacturing Plant construction.	Attainment of GMP certification for the plant.	First Taiwanese protein pharmaceutical plant to pass EMA inspection and obtain GMP certification.	Establishment of new injectables plant receives TFDA's GMP certification and GDP accreditation.	Passes MFDS GMP audit in South Korea and FDA facility inspection in the United States, acquiring pharmaceutical licenses.	PMDA inspection in Japan reveals no significant deficiencies.	Successfully passes inspections by PMDA (Japan), FDA (United States), TFDA (Taiwan), and MFDS (South Korea), confirming absence of significant deficiencies

International Standard Manufacturing Processes

Our company's product, Ropeginterferon alfa-2b (P1101), undergoes four critical stages in production: fermentation and cell processing, P1040 extraction and purification, PEGylation and P1101 protein purification. Additionally, sterile filling and labeling packaging are conducted, with each phase strictly adhering to Good Manufacturing Practice (GMP) standards. These processes comply with international standards for quality management and standardized operating procedures.

2023 Next-Generation Process Optimization

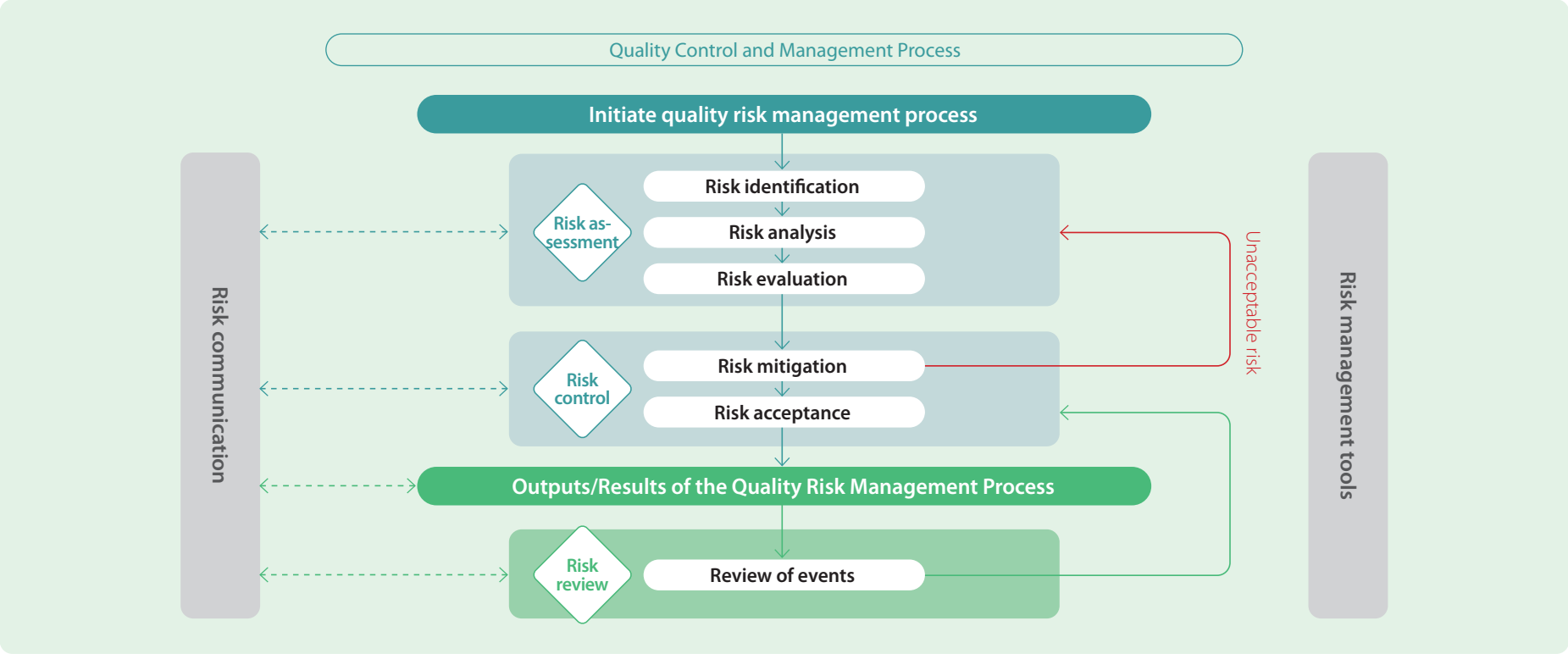
Every year, PharmaEssentia continually optimizes each stage of the manufacturing process. In recent years, in response to the demands of commercial-scale production, we have enhanced overall production capacity, mitigating risks in the production supply chain and ensuring stable supply.

Objective	Enhancing Production Capacity		
Improvement	Introducing Second and Third Material Sources	Establishing a Second Purification Production Line	Scaling Up the PEG Production Process Line
Goals and Results	In 2023, two new secondary material sources were established, while three others remained under testing. The introduction of this project serves to notably mitigate production risks and ensure pharmaceutical supply amidst significant global supply chain disruptions caused by international situations, pandemics, and extreme weather conditions.	Equipment and documentation setup is completed. Once the second production line is finalized, production capacity is expected to double.	Production testing is currently underway at an appropriate scale. Following the completion of the scaled-up PEG production process, production capacity is anticipated to increase by 4 to 8 times

Quality Control and Risk Management in Manufacturing Processes

PharmaEssentia's Taichung facility places significant emphasis on product quality and safety management. In 2023, a total of 925 GMP/GDP-related educational sessions were conducted, totaling 25,000 training hours. The facility is approved by multiple countries for GMP active pharmaceutical ingredients and formulation production, with 24 quality manuals, quality policies, and validation master plans established. There are 100 guiding SOPs and over 900 operational SOPs, along with more than 1,000 record forms. The organizational operational process is meticulously outlined, with Quality Assurance and Quality Control departments jointly responsible for managing and supervising the processes.

The 2023 monitoring trend report for the production environment (air conditioning), water systems, compressed air and biosafety operating cabinets shows that each system meets design requirements and regulatory specifications. Every year, through continuous education and training, employees can integrate the spirit of quality management into their daily operations, including training and updating the knowledge of GMP-related laws and regulations for colleagues in the factory, as well as comprehensive personnel training to ensure product safety. In consideration of emergencies, the Taichung plant has formulated the "Plant and Facility Emergency Response Management Standard" to implement the emergency response mechanism, so as to ensure the normal operation of the equipment and all personnel in a safe and secure environment when natural disasters and abnormal equipment hazards occur.



High-Quality Production Certification

Our Taichung facility is the first in Taiwan to pass the European Medicines Agency (EMA) inspection and receive Good Manufacturing Practice (GMP) certification for biopharmaceutical manufacturing. Since 2020, it has also undergone inspections by Taiwan's TFDA, South Korea's MFDS, the United States FDA, and Japan's PMDA, with no serious violations of relevant GMP regulations or health and safety laws found. Any non-serious deficiencies were promptly addressed within the specified timeframe through improvement preventive plans. In 2023, internal quality audits conducted at the Panco Logistics Center revealed quality system deviations, all of which were deemed non-significant and promptly addressed and closed

Internal Audit Frequency

- Conduct internal audits at least once a month (each department undergoes at least one random check per year).
- If any non-compliance issues are found during audits, corrective and preventive action (CAPA) plans must be submitted and completed within specified deadlines according to the severity of the deficiency.

External Audit Frequency

- Undergo and pass official periodic GMP inspections every 2 to 3 years.

Outsourced Manufacturing Management

In addition to filling and packaging operations at our sterile formulation filling plant in Taichung, our company also outsources filling and packaging to internationally certified contract manufacturing facilities in the United States, Germany, and Japan. This allows us to ensure proximity and supply locally to patients in the market and region. All contract manufacturing facilities are reputable partners that comply with and have official GMP certification.

Secure Distribution Process

Our secure distribution process strictly adheres to Good Distribution Practice (GDP) for pharmaceuticals, ensuring proper management of pharmaceuticals throughout the transportation process.

Package Insert and Packaging Printing → **Pharmaceutical filling, packaging, serialization, quality assurance, and other processes, the products are released.** → **Transporting Products to Third-Party Logistics** → **Delivering Products to Specialty Pharmacies or Distributors**

Secure and Stable International Logistics and Transportation

Inventory Distribution Operations System

To assure the safe and stable international transport, PharmaEssentia has established

1. "Storage and Distribution Policy" to create storage and distribution procedures, ensuring excellent storage conditions and management for raw materials, intermediates, and products.
2. "Product Distribution Management Procedure" adhering to PIC/S Good Distribution Practice (GDP) requirements has been implemented to establish distribution procedures and tracking mechanisms.
3. "Import and Export Transportation Management Procedure" has been set up to ensure compliant, fast, and safe delivery of all transported goods to designated destinations, effectively safeguarding patient medication safety.

- To address immediate disaster risks due to climate change in the United States, a safety stock level is maintained for over four months to ensure timely access to medication for patients in the country.
- The PharmaEssentia Logistics Center also complies with Taiwan's Good Distribution Practice (GDP) for pharmaceuticals. It assists in the supply of marketed and clinical products, with quality management throughout logistics, warehousing, labeling, and various operational processes. An "Emergency Response Handling Procedure" is in place to prevent or mitigate the negative impact of natural disasters on the facility's distribution operations.

Warehouse Management

PharmaEssentia has established "Product Receipt and Storage Management Operation Standards" and a "Storage and Distribution Policy" to ensure that neither the environment nor the operations have adverse effects on product quality. The Panco Logistics Center has a "Storage Area Temperature Verification Plan," conducting temperature verification twice every three years to ensure warehouse environmental quality.

Product receiving and storage process

Storage Application	Physical Verification	Conformity Confirmation	Confirmation of Storage	Medicine Storage
Storage of products requires submission of a "Product Storage Application" to warehouse management personnel.	Warehouse management personnel, along with quality assurance personnel, confirm and verify the physical product based on the information provided in the application.	The product labeling, including product name, code, batch number, required temperature, quantity, and container information, must match the details on the application form.	Ensure the product is properly sealed and packaged. Once the storage conditions are met, the product is stored accordingly.	During the storage period, the storage environment is monitored to ensure optimal conditions for medicine storage.

Quality Control in Shipping and Transportation

PharmaEssentia has established the "Product Shipping Operations Standards" to ensure that products manufactured at the Taichung production plant are fully prepared for shipment to contract manufacturers and storage facilities. This includes comprehensive pre-transport packaging operations to ensure effective transportation. The standards guarantee that pharmaceuticals are transported under prescribed temperature conditions to uphold global drug transport safety. This initiative reflects PharmaEssentia's commitment to operational excellence and risk management in its supply chain, aligning with ESG principles of environmental care and product responsibility.

Packing operation

- Confirm that the transportation box is clean and the temperature meets the product storage conditions, and place a temperature recorder in the box to monitor the temperature.
- Taking Ropeginterferon alfa-2b (P1101) as an example, it is necessary to ensure that the product is stored between 2℃~8℃

Quality control

transport process

- Based on the "Storage and Distribution Policy", establish appropriate storage and distribution procedures as quality goals
- Scenario simulation for pre-analysis: Confirm that the cooling status and equipment specifications meet the needs
- Regular verification: ensure that raw materials, intermediates and products can be stored well