3 Drug Quality and Safety Management

Chapter Highlights

NTD 2.22 billion	R&D spending increased by 56% and accounted for 43.5% of revenue
100%	Completion rate of drug safety monitoring training for new recruits
95%	First time to introduce a questionnaire survey on the recycling rate of supplier social/ environmental standards
89%	Proportion of local procurement amount
16 sessions	Global Drug Safety Surveillance Conference Tracker
25,000 hours	A total of 925 GMP/GDP quality education and training sessions were held
0	no post-marketing adverse drug recalls
100%	Completed the signing of supplier quality agreement and internal assessment for 5 consecutive years
Inspection Pass	Taichung factory successfully passed the Japan PDMA inspection

From drug research and development to the production phase, strict adherence to regulations and various quality requirements is essential; the drug supply chain must also be rigorously managed. This includes the sourcing of raw materials, manufacturing, filling, drug packaging, transportation, and ensuring safety up to the stage of patient use. All these aspects are critical issues that we prioritize.

3.1 New Drug Research and Development and Innovation Management

Materiality Assessment

GRI3-3

Materiality Assessment

New Drug Research and Development and Innovation Management

Impact Assessment

PharmaEssentia's PEGylation technology platform is a core of its R&D, prolonging time of the effective concentration of protein drugs in human blood. Besremi, a new generation long-acting PEGylated α-interferon, treats multiple indications and is under development for more to benefit additional patients.

Management Policies and Commitments

In addition to the breakthrough indication approval for MPN, PharmaEssentia focuses on addressing unmet mln addition to the breakthrough indication approval for MPN, edical needs, especially in hematological diseases and solid tumors, guided by the Access to Medicine Index. Commitment to animal welfare in preclinical testing during new drug research and development.

Responsible Departments

- New Drug R&D Division: Manages new drug discovery, with decisions made by the "Project Evaluation Team ," including cross-functional members and senior management, and "Project Review Meeting."
- Clinical Operations Department: Manages clinical trials.
- Sustainable Significant Theme: Managed by the Sustainability Development Center - Access To Health care Team.

Resource Allocation

- Global R&D Clinical Staff: 142 personnel, up 15.4% from last year.
- R&D Investment: NT$2.22 billion in 2023, a 56% increase from 2022.
- Key R&D Items: PEG-IL-2 technology for inflam- matory and immune diseases, clinical trials of other various drugs from Phase I to III, post-marketing research, and IIT.
- Collaboration: Development of TCR-T cell therapy through external partnerships.

Measures

- Number of drugs in development: 13
- The headquarters completed 2 IND applications and conducted 4 new clinical trials

Practices to ensure that actions are effective

- Through the combination of AI and machine learning, we will expand the capacity of R&D
- Continue to recruit scientific professionals with experience in drug development, and combine AI/ML technology to improve efficiency in the early stage of drug development, design and optimization

2023 Performance

- The PharmaEssentia Innovation Research Center Corporation (PIRC) was established to combine AI and machine learning to further expand the capacity of R&D innovation, effectively identify research objectives in the early research stage, reduce development time and cost, and accelerate the process from R&D to market.
- Clinical trials: In 2023, 4 new plans including CML, HDV, PMF, and HCC will be added, bringing the total number of 9 clinical trial plans currently underway. In 2023, there will be 453 new patients, bringing the total number of clinical trial patients to 1,332.
- In 2023, PharmaEssentia completed the application for the IND of the Phase 1 TFDA clinical trial in Taiwan for the treatment of solid tumors with anti-PD-1 antibody (P1801). and the multi-national and multi-center Phase III clinical trial of essential thrombocythemia (ET), which also received a government grant of NT$5,435K.

Continuous Growth Trend in R&D Costs Over the Past Five Years (2019-2023)

Year	2019	2020	2021	2022	2023
Global R&D Expenditure (NT$ '000)	639,575	922,380	1,272,944	1,425,964	2,224,054
Increase in Expenditure from Previous Period (NT$ '000)	-	282,805	350,564	153,020	798,090
Growth Rate of Expenditure	-	44.2%	38.0%	12.0%	56.0%
Global R&D Personnel (number)	56	74	83	123	142
Increase in Personnel from Previous Period (number)	-	18	9	40	19
Growth Rate of Personnel	-	**32.1%**	**12.2%**	**48.2%**	**15.4%**

Innovative R&D Focus

SASB HC-BP-000.B

Apart from continued investment in MPN (Myeloproliferative Neoplasms), PharmaEssentia is also investing in PEG-IL-2 technology for the treatment of inflammatory and immune diseases. Additionally, it is engaged in joint development of TCR-T cell therapy through external collaborations.

PharmaEssentia plans to initiate two IND (Investigational New Drug) research projects:

- This includes starting clinical trials for an anti-PD-1 antibody (P1801) and a long-acting G-CSF
- clinical trials for new indications of P1101 in early PMF (Primary Myelofibrosis) and low-risk PV (Polycythemia Vera).
- the company aims to complete
  - at least one project up to the development candidate stage
  - at least one project up to the preclinical candidate development stage
  - Additionally, 1-2 external technology platform assets will be introduced. The development of an AI/ML (Artificial Intelligence/Machine Learning) platform is also planned.

Key Development Focus for the Next Five Years (2024-2029):

Continuous Growth in Besremi Operations

- Market Expansion:
  Patient usage and numbers continue to increase in existing markets.
- PV Indication:
  Expected to obtain drug approvals in China and Singapore-Malaysia in 2024.
- ET Indication:
  Plans to apply for U.S. drug approval in 2025, with approval anticipated by early 2026.

Expansion of indications for P1101

- Early PMF Clinical Trials:
  A global Phase III pivotal clinical trial for Early PMF (Primary Myelofibrosis) is currently underway, with plans to submit an FDA drug application by the end of 2026.
- Research in Other Blood Disorders:
  Ongoing research into the application of P1101 for other hematologic diseases, including ATL (Adult T-cell Leukemia/Lymphoma) and CTCL (Cutaneous T-cell Lymphoma).

Global supply capacity expansion

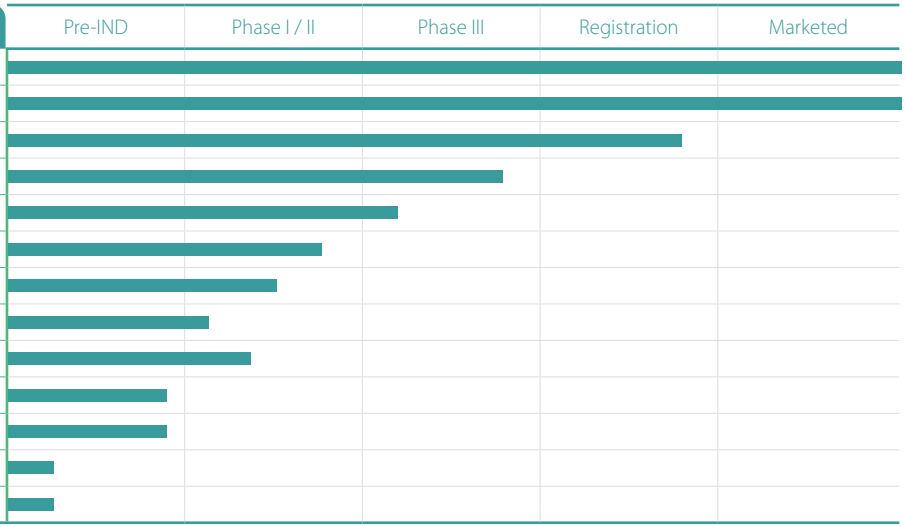
- Global Production Capacity :
  Expected to supply over 10,000 people
- Zhubei Plant Construction:
  In response to market demand, construction has begun on the Zhubei plant, with completion projected for 2026.

Top-tier R&D platform

- Innovative Immune Checkpoint Molecules and Cytokines:
  New types of immune checkpoint molecules and cytokines are being developed for the treatment of solid tumors, blood disorders, and immune diseases.
- Cell Therapy with TCR-T:
  This advanced therapy targets cancer antigens on the cell membrane for the treatment of solid tumors.

Source: March 2024 Analyst Presentation Documents

Therapeutic Area	Candidate	Indication	Market
Hematology	Ropeginterferon alfa 2b (P1101)	PV	EU
			US, TW, KR, JP
			CN, MY, HK, SG
		ET	Global
		Early myelofibrosis	Global
		Aduit T-cell Leukemia	JP, TW, CN
		CML	KR
Oncology	TCRT	Solid tumors	US, TW
	P1101 + anti PD-1	HCC	Global
	anti PD-1 (P1801)	Solid tumors	Global
	PEG-GCSF	Neutropenia	Global
	PEG-cytokine X, Y	Solid tumors	Global
	Novel checkpoint Abs	Solid tumors	Global



Note: For the latest updates on our R&D product line, please refer to the official PharmaEssentia website at https://hq.pharmaessentia.com/index.php?/en/pipeline

Commitment to Animal Welfare in Preclinical Animal Experiments

To ensure adherence to animal welfare, the company selects domestic and international contract research organizations (CROs) that are GLP-certified. These organizations are required to comply with the regulations of the Institutional Animal Care and Use Committee (IACUC) and adhere to the 3Rs principle (Refinement, Reduction, Replacement). This approach aligns with the directives of the Animal Welfare Committee to conduct experiments humanely. Currently, the company has entrusted three qualified domestic and international institutions to carry out preclinical animal experiments.

Participant Safety in Clinical Trials SASB HC-BP-210a.1

To ensure the safety of participants in clinical trials, PharmaEssentia has developed about 20 Standard for clinical operations management. Audit and verification mechanisms are implemented at each phase to maintain trial quality. All clinical trials, including Phases I, II, and III, are conducted in accordance with approved study protocols and comply with local national regulations. Currently, there are no clinical trials that have been terminated due to violations of Good Clinical Practice (GCP) standards.

Clinical Trial Quality Maintenance and Risk Management

Before Clinical Trials	Based on the characteristics of the drug and the differences in the trial design, the risks and extent that may be encountered during the trial process are evaluated.	
Risk Assessment	Develop "Monitoring Plan" and "Auditing Plan" through contracted CRO based on risk level to ensure QA and QC. Ensure participant rights and welfare protection and compliance with trial protocols, GCP, and regulations regarding trial execution and data generation、recording and reporting.	
Execution Process	**Quality Assurance (QA):** Independent auditing system, issue assessment and tracking, formulation of corrective and preventive actions (CAPA)	**Quality Control (QC):** Execute monitoring and co-monitoring activities.

Phase I Clinical Trial — Safety Exploration

Phase II Clinical Trial — Preliminary Efficacy Study

Phase III Clinical Trial — Large-Scale Confirmatory Efficacy Study

Trial Planning

Risk Assessment: Evaluate risks based on the services provided by the Contract Research Organization (CRO) and the characteristics of the clinical trial.
Monitoring and Auditing Plans: Develop monitoring and auditing plans based on the level of assessed risks.
Quality Management and Assurance: Establish plans for quality management and assurance to maintain high standards throughout the trial based on the level of assessed risks.

Before the Trial

Regulatory and Ethics Approval: The trial protocol and related documents must be reviewed and approved by health regulatory authorities and the Institutional Review Board Committee.
Investigator Meeting: Conduct training related to the trial.
Informed Consent from Participants: Participants must be fully informed and give written consent after careful consideration before screening can commence.
Participant Screening: Strictly screen participants based on the inclusion and exclusion criteria outlined in the trial protocol.

During the Trial

Co-Monitoring by Clinical Operations: The clinical operations department conducts co-monitoring with the CRO handling monitoring duties.
Auditing: Carry out audits according to the audit plan to ensure that the CRO's services meet quality standards.

After the Trial

Data Compilation and Review: Compile data on efficacy and safety for review and onsite verification by health regulatory authorities. Only after assessing benefits and risks can approval for marketing be granted.

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

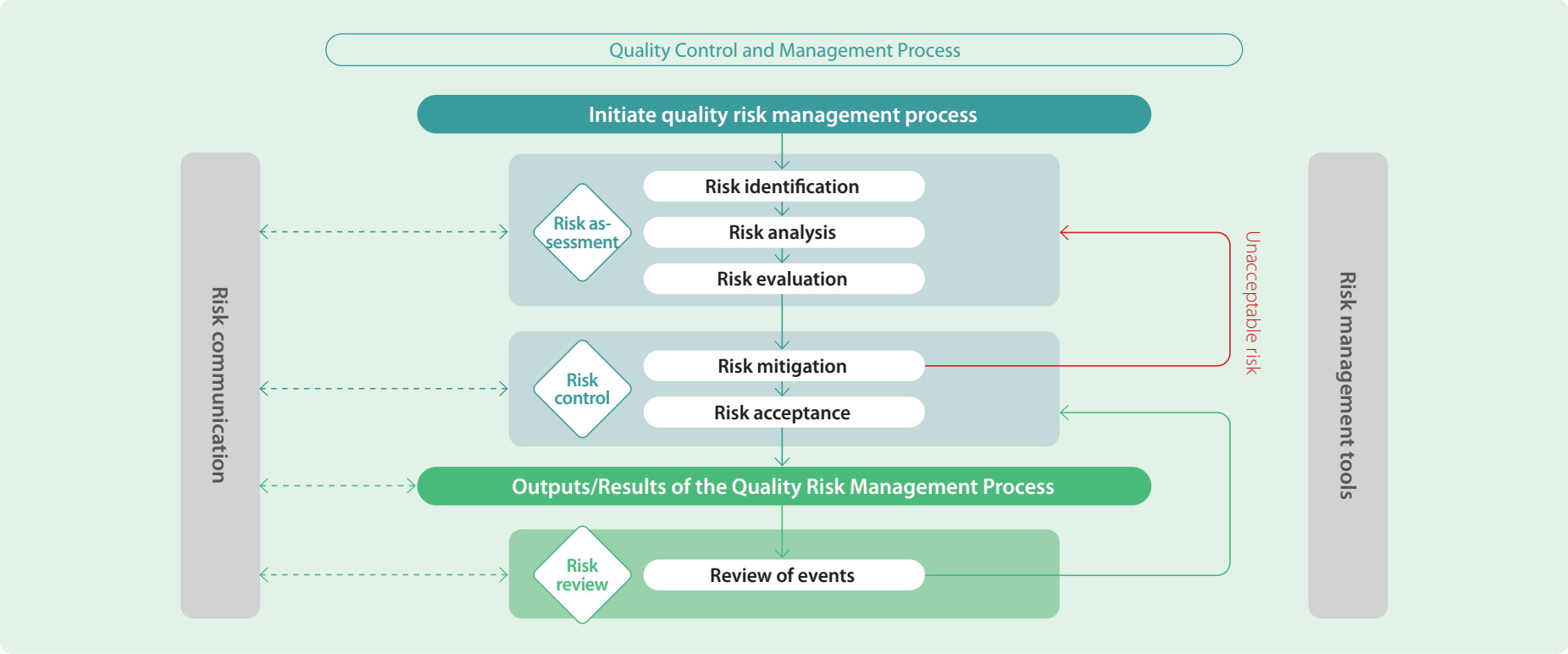
Every year, PharmaEssentia continually optimizes each stage of the manufacturing process. In recent years, in response to the demands of commercial-scale production, we have enhanced overall production capacity, mitigating risks in the production supply chain and ensuring stable supply.

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

3.3 Drug Safety Management and Patient Safety Monitoring

Materiality Assessment

GRI 417-1, 417-2 SASB HC-BP-250a.1~a.5

PharmaEssentia has established a comprehensive global pharmaceutical safety monitoring system, adhering to international drug safety monitoring regulations. The company continuously monitors the safety of newly marketed drugs post-launch. Additionally, PharmaEssentia persistently optimizes policies and internal standard operating procedures related to drug safety management to safeguard patient health and safety. In 2023, there were no incidents of non-compliance related to product service labeling or product recalls.

Materiality Assessment

Pharmaceutical Safety Management and Patient Safety Monitoring

Management Policies and Commitments

Patient Safety Monitoring: Diligently track adverse drug events and reporting channels, deeply embed the concept of "Quality First, Patient Safety" into the daily operations and lifestyle of all colleagues, and implement drug risk management to protect patient medication safety.

Responsible Team

- Product Safety & Risk Management (PSRM) Team composed of pharmacovigilance staff from PharmaEssentia headquarters and various international subsidiaries, along with pharmacovigilance quality assurance personnel, under supervision of Global Vice President of Pharmacovigilance and Executive Director.
- Quality of marketed drugs and clinical drugs is managed by the headquarters' Quality Assurance and Quality Control departments, in collaboration with the pharmacovigilance function team
- Sustainability Significant Themes: Managed by the Sustainability Development Center - Product Ethics and Safety team members.

Actions and Mythology

- Invested over 24 million New Taiwan Dollars in global pharmacovigilance activities.
- Since 2022, appointed a Global Vice President of Pharmacovigilance and a Global Executive Director of Pharmacovigilance, responsible for overseeing global pharmacovigilance efforts.
- Pharmacovigilance professionals are stationed at the Taiwan headquarters and each subsidiary or regional office.
- Contracted a pharmacovigilance CRO (Contract Research Organization) to form a project team that manages and maintains the BESREMi® drug safety data database, assisting in pharmacovigilance and the reporting/handling/exchange of information, as well as regulatory reporting in various countries.

Indicators and Objectives

- Implement all legal compliance requirements for the drug safety monitoring program, and report drug safety information within the timeframe set by regulations.
- Complete periodic safety reports for drugs post-marketing as required by regulations.
- Pharmacovigilance education and training.

2023 Performance

- According to requirements from the Taiwan Food and Drug Administration (TFDA), the pharmacovigilance plan was completed and submitted.
- PharmaEssentia headquarters and its subsidiaries achieved a 100% execution rate in reporting drug safety information within the regulatory timeframe.
- From February 2022 to February 2023, 92 serious adverse drug reactions were reported globally, with no violations of product and service health and safety regulations.
- As per regulations, completed and reported the fifth Drug Development Safety Report (DSUR) for BESREMi®, the fourth Periodic Safety Update Report (PSUR) for BESREMi® post marketing, and the first Periodic Safety Update Report for Tirbanibulin post marketing.
- Completed four quarterly safety signal monitoring reports and implemented ten Standard Operating Procedures (SOPs) related to pharmacovigilance.
- In 2023, conducted six pharmacovigilance training sessions for new employees, achieving a completion rate of 100%.
- In Taiwan, one pharmacovigilance training session was held, with a total of 311 participants and a total training time of 155.5 hours.

Management Review Mechanism

- Post-Marketing Safety Monitoring: According to the requirements of regulatory authorities in various countries, timely reports are issued and immediate reporting mechanisms are maintained in operational condition.
- Regular Safety Reports: Regularly submit "Drug Development Safety Reports" and periodic safety reports to regulatory authorities in different countries.
- Internal Auditing: Conducted by the Quality Assurance department or outsourced to an independent third party.
- External Audits: Inspections by international and domestic drug safety regulatory authorities.
- Evaluation of Immediate Reporting Mechanisms: Assess the functioning of the immediate reporting systems.
- Evaluation of Drug Safety Hotline Operations: Assess the operation of the drug safety hotline services in Taiwan, the USA, Korea, and Japan.

Our company's 'Pharmacovigilance Team' is part of the Medical Research Department, working in coordination with relevant responsible units according to the 'Pharmacovigilance Policy,' 'Drug Safety Functions and Training Standard Operating Procedures,' and 'Post-Marketing Safety Data Collection Standard Operating Procedures.' PharmaEssentia also complies with the 'Serious Adverse Drug Reaction Reporting Regulations' and 'Drug Safety Monitoring Management Regulations,' entrusting professional CRO companies to conduct drug safety monitoring.

Drug safety monitoring can be divided into passive and active monitoring:

1. Passive Monitoring

Legally required to periodically submit Periodic Safety Update Reports (PSUR) and collect spontaneous safety case reports from healthcare professionals and the public; safety information collected in reports is entered into the safety database system for further processing. In 2023, PharmaEssentia submitted the fourth post-marketing PSUR for BESREMi® to the Taiwan Food and Drug Administration without any incidents of non-compliance with product health and safety regulations or voluntary codes. Additionally, Tirbanibulin, licensed to PharmaEssentia by Athenex, was approved in 2022, and PharmaEssentia will continue to submit PSURs annually until 2028 as required.

2. Active Monitoring

Proactively conducts safety signal detection, monitors medical warnings and safety signals issued by advanced pharmaceutical countries, and performs literature reviews; additionally, it may actively gather information through clinical trial programs (Registration trial/IIT) and Patient Support Programs (PSP)

Pharmacovigilance Reporting Education and Training

According to our country's pharmacovigilance regulations, contracted research institutions are required to develop and implement drug safety management and regulatory reporting plans. Regular pharmacovigilance education and training sessions for employees are conducted, and all training records are preserved. In 2023, six training sessions for new employees on pharmacovigilance were held, as well as one company-wide pharmacovigilance training session. All new employees underwent pharmacovigilance reporting training within one month of their start date, achieving a 100% completion rate.

PharmaEssentia's headquarters and regional subsidiary leaders regularly meet with the contracted research institutions to ensure that the global drug safety information collection and reporting tasks are effectively carried out. In 2023, PharmaEssentia held 16 meetings to track and manage the pharmacovigilance mechanisms.

Taiwan's Adverse Drug Reaction Reporting Mechanism

After the marketing of drugs, adverse reactions occurring under general usage can be reported through the following channels:

- Medical professionals and the public can fill out the 'Post Marketing Adverse Drug Reaction Report Form,' report online after registering an account, or via email (adr@tdrf.org.tw).
- Pharmaceutical companies can report online through the system by selecting the 'Post Marketing Adverse Drug Reaction Report Form,' completing it, and submitting it.
- Upon receiving such reports, PharmaEssentia follows the 'Guidelines for Completing the Post Marketing Adverse Drug Reaction Report Form,' submits the reports through the online reporting system (https://adr.fda.gov.tw), or sends the completed form v ia email to the ADR Center at adr@tdrf.org.tw.

Safety Monitoring of BESREMi® in the United States

- The U.S. subsidiary, with the assistance of quality-certified third-party logistics, follows the Drug Supply Chain Security Act (DSCSA) regulations related to drug traceability. It submits Transaction History (TH), Transaction Information (TI), and Transaction Statements (TS) for auditing purposes.
- Additionally, there is a dedicated PEC U.S. Call Center serving the American market, managed by the U.S. subsidiary's medical affairs team. This center is responsible for handling all drug quality and safety needs and reporting messages. Regarding the product traceability mechanism, drug serialization was completed in 2020, and there have been no adverse drug recall incidents in 2023.

Pharmaceutical Risk Management Plan

PharmaEssentia implements the Drug Safety Risk Standard Operating Procedures formulated by contracted research organizations. Additionally, tailored 'Drug Risk Management Plans' are established according to the pharmaceutical safety monitoring regulations of each country to comply with local legal requirements.

According to regulatory requirements, after a drug is marketed, actual clinical data must be collected to assess whether long-term use by patients may result in chronic side effects. This serves as the basis for "Drug Risk-Benefit Assessment." The results of the 2023 Periodic Safety Report showed no new safety information that could affect the safety of BESREMi®. The company commits to continuously collect safety data from the countries where it is marketed, to update periodic safety reports and assess the risk-benefit of BESREMi®.

0

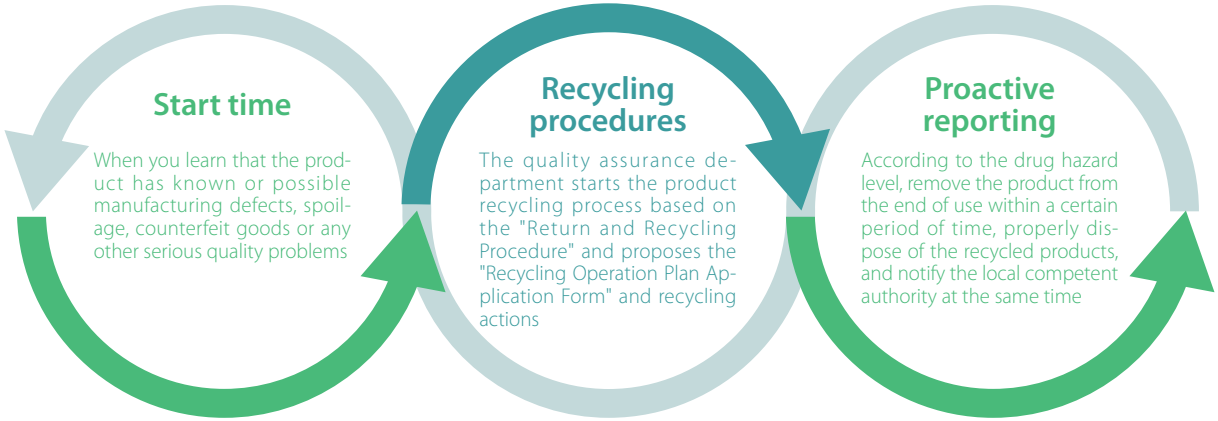
no post-marketing adverse drug recalls

Product Traceability Mechanism SASB HC-BP-260a.1

PharmaEssentia has established a product traceability mechanism across its global supply chain and has implemented drug serialization to standardize the packaging and serialization operations of contract manufacturers, achieving the goal of fully tracing individual product flows and usage records. BESREMi® sold in the United States has also fully implemented drug serialization. This is carried out by a qualified U.S. injectables filling contract manufacturer following the FDA's Drug Supply Chain Security Act (DSCSA) standards, ensuring drug quality and safety.

Drug Recall Mechanism SASB HC-BP-260a.2

PharmaEssentia's "Return and Recall Procedures" clearly specify a product traceability system to perfect the drug recall mechanism. This allows for the rapid and effective completion of drug recalls when product quality is in question, providing an additional layer of safety for patient medication. Annual mock recall drills are conducted to ensure the accuracy and proficiency of recall actions. In 2023, there were no incidents of adverse drug recalls.



3.4 Sustainable Supply Chain Management

PharmaEssentia constructs effective supply chain management through three major aspects, working collaboratively with suppliers and contractors to embody and practice sustainability principles, creating long-term and stable value for the pharmaceutical industry and patients.

Sustainability Declaration

- Mutual benefit and prosperity with supplier partners
- Communicating PharmaEssentia's sustainability principles and practices
- Advocating the "Supplier Code of Conduct" to all suppliers
- Inviting suppliers to sign the "Supplier Code of Conduct

Enhancement of Management Capabilities

- Facing a constantly changing world, the strategies to enhance management and response capabilities include:
- Information Mastery
- Strengthening Supply Chain Management Capabilities
- Enhancing Interaction with Suppliers

Establishment of Alternative Sources of Supply

- Identifying Critical Materials
- Screening Raw Material Candidates
- Quality Confirmation, Experimental Verification
- Trial Production
- QA Monitoring, Compliance with Regulations

1. Sustainability Declaration: Building a Sustainable Supply Chain

In 2023, we formulated the "Group Supplier Code of Conduct," which focuses on labor rights, workplace safety and health, environmental sustainability, and business ethics, aiming to set a positive example in the industry. This code was also signed by the chairman and published on our website. For the first time, we issued an ESG questionnaire to 20 suppliers in 2023; of these, 9 have published ESG reports, 7 are preparing ESG/CSR data collection, 3 do not yet have a corporate sustainability plan, and 1 lacks a clear understanding of ESG issues. PharmaEssentia hopes to continue conveying both formal and informal sustainability declarations to our supply partners to create a positive, long-term impact. In 2024, we plan to continue signing ESG agreements with suppliers, hoping to grow together, share benefits, and emphasize corporate sustainability responsibilities

Supplier/Contractor Management Process

GRI 2-6, 204-1 | SASB HC-BP-260a.1 | SASB HC-BP-430a.1

PharmaEssentia's Quality Assurance department has established the "Supplier Management Standards" and "Supplier Management Procedures" as the approval process and operational standards for suppliers and outsourced service contractors. This involves strict monitoring of the selection, evaluation, and approval of raw material, material, and equipment/instrument suppliers to ensure that the supplied raw materials and equipment meet our company's standards for quality, delivery schedules, and Good Manufacturing Practices (GMP). We also require suppliers to sign a "Quality Agreement" to ensure a mutual understanding of product and quality requirements. All vendors required to sign the quality agreement have done so 100%

New Suppliers/Contractors

GRI 308-1, 308-2, 414-1, 414-2

PharmaEssentia is committed to the environmental and social impacts of our supply chain. In addition to the indicators of quality systems, technical capabilities, and service and support, in 2023, we introduced environmental and social standards into our supplier selection process and conducted regular supplier performance evaluations. In 2023, 87 new suppliers/contractors were added, of which 73 were local, representing 83.91% of the total.

Environmental Standards

1. Compliance with Applicable Environmental Regulations: Adhere to all applicable environmental laws, follow relevant operational standards, and meet reporting requirements.
2. Waste Management: Ensure that the treatment, transportation, storage, recycling, reuse, and management of waste, exhaust gases, and wastewater comply with regulations.
3. Resource Use and Recycling: Minimize resource consumption by implementing resource use and recycling measures.
4. Biodiversity Conservation: Commit to no deforestation, land conservation, and the goal of Zero Net Deforestation.
5. Climate Commitment: Reduce greenhouse gas emissions and fulfill the commitment to achieve carbon neutrality.

Social Standards

1. Commitment to Providing an Acceptable Living (Working) Environment for Laborers.
2. Prohibition of Forced Labor: It is not permissible to deprive or restrict the personal freedom of laborers.
3. Freedom of Association and Collective Bargaining Rights.
4. Maintenance of Employee Health and Safety.
5. Guarantee of Minimum Wage, Overtime Hours, and Statutory Benefits.
6. Humane Treatment of Employees: Free from any form of sexual harassment, physical punishment, mental or emotional abuse, and verbal violence.
7. Anti-Discrimination.
8. Prohibition of Child Labor.

Management by Supplier Category

To improve supplier management efficiency, PharmaEssentia headquarters and Panco define suppliers who transact directly with PharmaEssentia as first-tier suppliers, based on risk and procurement amount. PharmaEssentia and Panco also define GMP suppliers that cannot be easily replaced as key suppliers. We manage suppliers according to these two dimensions. Our supplier classification is as follows:

Supplier Category	Tier 1 (Number of Suppliers)	Non-Tier 1 (Number of Suppliers)	Total
Key	107	61	168
Non-Key	221	40	261
Total	328	101	429

For PharmaEssentia's subsidiary in the United States, supplier qualification follows the American procedure SOP-QA-003 Supplier Qualification (GMP) and SOP-QA-009 External Audit Results. In 2023, there were a total of 8 Tier 1 suppliers in the United States, all qualified for critical first tier GMP supplier criteria. Suppliers have passed quality inspections in both the United States and Taiwan.

Supplier Category	Number of Supplier	%
All Tier 1 Suppliers	8	100%
Key Tier 1 Suppliers	8	100%

Supplier/Contractor Risk Assessment and Due Diligence

We conduct an annual assessment of our trading partners, which includes evaluating: product or service quality, capability in handling exceptions and improvements, completeness and timeliness of documentation, on-time delivery rate, emergency order responsiveness, service satisfaction, price stability, and ESG performance score, totaling 8 criteria. PharmaEssentia places particular emphasis on the delivery of raw materials, as shortages can significantly impact our manufacturing processes and research and development progress. Therefore, we strictly require suppliers to ensure supply and quality reliability.

In terms of supplier management at our Taiwan headquarters, criteria for assessing supplier risk include:

1. Whether they are critical suppliers, or provide materials or services directly related to patients or trial participants.
2. Whether the materials or services provided are used in pilot production, clinical trials, or commercial production stages.
3. High impact of the materials or services provided; changing suppliers could significantly impact research and development or manufacturing.
4. Low substitutability of the materials or services provided, including factors such as single sourcing or patented technology.
5. Large annual procurement volume or high monetary value.
6. High impact of environmental, governance, or social factors on the materials or services provided, which could affect supply continuity or regulatory compliance.

In 2023, among the evaluated 419 suppliers, 4% were classified as high risk, 74% as low risk, and 22% as medium risk.

Year	2022		2023	
Risk Leve	Number of Suppliers	%	Number of Supplier	%
Low Risk	148	49%	309	74%
Medium Risk	41	14%	94	22%
High Risk	12	4%	16	4%
Total	301	100%	419	100%

Note: Risk level assessment includes PharmaEssentia Taipei and Taichung. Risk levels are categorized as follows: The Taichung plant categorizes per GMP quality management standards (Minor, Major, critical). In Taipei headquarter, the risk levels are categorized into: High risk: meeting 3 or more of the above criteria; Medium risk: meeting 2 or 1 of the above criteria; Low risk: not meeting any of the above criteria.

Supplier Management Mechanism

PharmaEssentia's Management Strategies for Suppliers/Supplied Products with Different Risk Levels are as follows:

Risk Level	Management Mechanisms for Suppliers
High Risk	1. Strategic Alliances: Actively strengthen alliances with suppliers for mutual benefit and symbiosis. 2. Maintain good interaction with suppliers to establish strong cooperative relationships. 3. Evaluate Total Cost of Ownership (TCO): Assessing performance metrics such as service scope, quality, and timelines. 4. Signing contracts to ensure service quality, content, and sources. 5. In-house production (or reprocessing) 6. Ensure stability of the supply source 7. Maintain good interaction with suppliers and utilize service information provided by them. 8. Develop new suppliers and alternative sources (Second source) to mitigate risks of material shortages
Medium Risk	1. For materials used frequently, request suppliers to maintain inventory to facilitate timely delivery. 2. Integrate procurement items and departmental needs. 3. For materials with monopolistic competition, actively request and compare prices. 4. Analyze item prices and costs.
Low Risk	1. Implement routine procurement, following and maintaining the appropriate procurement procedures. 2. Centralize ordering quantities and frequencies

Annual Evaluation of Suppliers/Contractors

Our company conducts annual evaluations of suppliers/contractors according to the Supplier Audit Procedures, using a combination of internal review and on-site audits. In the case of high-risk suppliers, the re-evaluation frequency may be shortened, and improvement actions taken. If significant deficiencies are identified, procurement activities will be immediately suspended. In 2023, internal review assessments were completed 100% for all 188 suppliers, and the on-site audit plan included a total of 20 domestic and international suppliers (including 2 remote audits of foreign suppliers), all of which were completed 100%. During the supplier on-site audit, it was found that one supplier violated labor standards, and the supplier was requested to make improvements.

Remediation Procedures for Negative Impacts GRI 2-25, 2-26

PharmaEssentia regularly conducts environmental and social regulatory audits of suppliers. When deficiencies are found, relevant units conduct investigations and inquiries. In 2023, regarding the supplier violation of labor standards mentioned above, a supplier due diligence investigation was conducted, and follow-up actions to address the identified improvement areas were tracked. By the end of 2023, the tracking results showed that the supplier had been acquired and merged into another company.

100%

Completed the signing of supplier quality agreement and internal assessment for 5 consecutive years

2. Supply Chain Management and Resilience Enhancement

PharmaEssentia continues to enhance supply chain management and contingency capabilities, maintaining safety stock levels, establishing alternative material sources, and balancing cost considerations with long-term material reserves to rapidly respond and avoid disruptions to the supply chain from events such as the COVID-19 pandemic or other emergencies. Actively reducing the risk of material shortages that cannot be timely and stably supplied. The following are the internal supplier management tasks:

1. Monitor potential factors affecting the supply chain (diseases, climate change, natural disasters, etc.).
2. Strengthen supplier management adaptability and contingency capabilities.
3. Deepen communication with suppliers, monitor the status of material transportation in real-time, and obtain complete information on transportation logistics.
4. Update the time of arrival for supplier raw material purchases.
5. Increase safety stock levels, understanding changes in demand from frontline medical institutions and patients.
6. Pay attention to the situation in the countries where raw materials are produced, assess the risk of material shortages, and respond in advance.
7. Establish alternative material sources to reduce the risk of material shortages.

3. Establishing Alternative Material Sources

To prevent risks due to unforeseen events, we follow internal SOP and conduct comprehensive investigations into raw materials and determine importing priority of alternative sources.

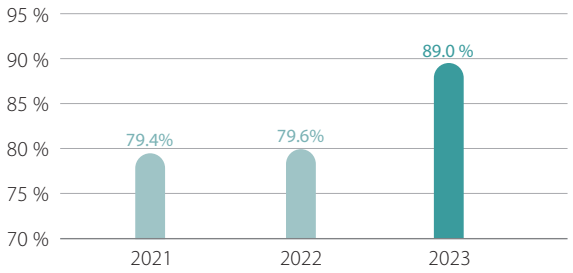
Inventory of Raw Materials Requiring the Establishment of Alternative Sources	Performing Quality Assurance Checks	Process Development Experimental Validation	Quality Assurance Continuous Monitoring
The following criteria are used for assessment: • Manufacturer notification of impending discontinuation. • Regulatory agency requirements. • Conducting material risk assessment based on the "Criticality Assessment of Materials" procedure.	Continuing Quality Assurance Checks for Materials at Immediate Risk of Supply Disruption	Upon successful trial production, raw materials passing the test enter the GMP control procedures (supplier assessment, specification inspection, method establishment, etc.). After completing the relevant procedures, they are added to the backup list	The Quality Assurance department continuously monitors testing data and documentation at all stages of material source development to ensure compliance with regulatory standards throughout the entire process.

Local Procurement

In 2023, the proportion of purchases from local suppliers in Taiwan increased to 89%, while the expenditure on purchases from non-local suppliers was 11%. This increase is primarily attributed to the capital expenditures associated with the expansion of the new manufacturing facility in Zhubei. PharmaEssentia, rooted in Taiwan but with a global perspective, prioritizes the development of local partnerships and continues to assess opportunities to increase the proportion of local procurement.

	Year	2021	2022	2023
Local Procurement	Taiwan (%)	79.4%	79.6%	89.0%
Non-local Procurement	Americas (%)	20.5%	20.4%	11.0%
	Other Asia (%)	0.1%	0	0
	Total	100%	100%	100%

Local Procurement Percentage



89%

Proportion of local procurement amount