03

Drug Quality and Safety Management

Achievement Highlights

NT$25.9 billion
in R&D expenditures, an increase of 16% compared to 2023

14,797 hours
of Good Manufacturing Practice (GMP)/ Good Distribution Practice (GDP) training

12 global pharmacovigilance seminars

0 post-marketing recalls of defective drugs

+3 new second-source suppliers

+100% production capacity
completed establishment of second drug substance (DS) production line

4-8 times production capacity
completed establishment of scaled up PEG production line

Completed Ropeg Phase III
clinical trial for ET indication LPLV

Obtained Ropeg PV marketing authorizations
in China, Singapore, and Malaysia

Taichung Plant passed EMA & ANVISA factory inspections

3.1 Drug Quality and Safety Management GRI 3-3

PharmaEssentia is focused on independently developed R&D technologies which not only represent breakthroughs in the biomedical industry, but also improve patient wellbeing. All stages from new drug R&D, production, manufacturing, transportation, and launch rigorously and comprehensively adhere to complex regulatory and quality requirements. To maximize the life cycles of core products, PharmaEssentia conducts constant patent mining and enables comprehensive protection for innovative R&D technologies, and has established various intellectual property protection measures. We also manage post-marketing risks through continued monitoring and reporting of drug safety information as part of our responsibilities to protect patient interests.

Material Topics

- New Drug Research & Development and Innovation Management
- Drug Quality and Safety Management
- Business Integrity and Ethical Management

Main Stakeholders

- Patients
- Medical Personnel
- Commissioned Research/ Experiment Units
- Shareholders and Investors
- Suppliers and Business Partners
- Local Communities
- Government and Competent Authorities
- Media

Material Topics

PharmaEssentia MATERIALITY

New Drug Research & Development and Innovation Management

Description of Impacts

PharmaEssentia independently built a PEGylation technology platform. PEGylation is a type of technology that can maintain the stability of protein-based drugs in the human bloodstream, thereby prolonging the duration of therapeutic concentration. We used this technology to improve on existing protein-based drugs and successfully developed a new-generation long-acting interferon BESREMi (Ropeginterferon alfa-2b, Ropeg, P1101), which can be used for multiple indications. Apart from already obtained drug permits for PV, we are also working on multiple new indications to benefit more patients.

Policies and Commitments

PharmaEssentia is committed to solving unmet medical needs. After achieving breakthroughs in the MPN domain, we adhered to the spirit of the Access to Medicine Index and continued to invest in research on blood disorders and solid tumors. We are also working with external research institutes and biotechnology companies to jointly develop cell therapies. PharmaEssentia screens domestic and international research institutes with GLP, ISO 17025 (non-compulsory), and AAALAC certifications to ensure that research personnel rigorously adhere to all relevant regulations during R&D processes for new drugs and use humane procedures when conducting preclinical animal trials.

Responsible Unit

Research and Development of New Drugs center: Responsible for new drug discovery, and has established the "Project Evaluation Team" to serve as the research decision-making unit. Team members include colleagues and senior managers from different departments. Projects are initiated following approval at "Project Review Meetings," and project supervisors coordinate project progress and make regular progress reports.

Clinical operations department: Responsible for managing clinical trials

The Executive Center for Corporate Sustainability Access to Medicine Team: Responsible for compiling and managing material sustainability issues

Response Measures and Management Actions

Invested resources:

Manpower resources: A total of 165 R&D and clinical personnel around the globe, a reduction of 16.2% compared to the previous year

Financial resources: R&D investments: In 2024, PharmaEssentia invested a total of NT$2.59 billion to build R&D momentum, an increase of 16% compared to the previous year

R&D:

- Important R&D projects included use of PEG-IL-2 to treat inflammatory and immune diseases; many other products which are in Phase 1, Phase 2, Phase 3, or post-marketing Phase 4 clinical trials; and a number of IITs in collaboration with physicians
- Joint development of TCR-T cell therapies with external partners

Prospective projects:

- Combine AI (artificial intelligence) and ML (machine learning) to expand R&D capabilities
- Continue to recruit professional scientific talents with expertise in drug development, and utilize AI/ML technologies to enhance the efficiency of early drug development, design, and optimization stages

Evaluation Mechanisms

(Channels and Systems for Tracking Effectiveness of Response Measures and Management Actions)

- New drugs have to pass feasibility studies, preclinical animal trials, clinical trials, product manufacturing, and market authorization reviews before launch, and all R&D processes have product quality assurance, drug safety and efficacy, and regulatory compliance mechanisms that serve as a basis for determining whether development should be continued
- Our R&D department manages and reviews schedules for all R&D projects each month and makes quarterly reports to the Board
- Our R&D expenditures were approved by the Board in December 2023. The finance department tracks actual and budgeted expenditures of R&D projects every quarter, and reports on discrepancies to the Board
- Our auditing departments conducts audits on R&D cyclical management mechanisms each year in accordance with annual audit plans

Targets and Achievements in 2024

Number of drugs in development: 13

In 2024, our headquarters completed investigational new drug (IND) applications for PEG-GCSF and Anti PD-1, and conducted 5 new clinical trials for PEG-GCSF, Anti PD-1, TCRT-ESO-A2, HOPE PMF, and ATL.

- Submitted IND application for PEG-GCSF Phase 1 clinical trials and completed Phase 1 clinical trials
- Completed patient recruitment for EXCEED-ET and ECLIPSE-PV clinical trials in March and June of 2024
- Completed multinational, multicenter ET Phase 3 clinical trials, and completed Topline data analysis at the end of December
- Obtained government scientific subsidies of NT$10,428,000 for ET Phase 3 clinical trial
- Initiated patient recruitment for Japan ALT Phase 2 clinical trial

Targets

Short-Term Targets (1-2 Years):

- Expand into new indications and become a global leader in the MPN domain

Mid-Term Targets (3-5 Years):

- Develop PEG platform: Utilize independently developed PEC PEG platform to develop long-acting cytokines
- Develop other technologies such as BiC/FiC PEGylated cytokines (GCSF, IL-2, IFN-g, and others)
- Target solid tumors with low response rates such as renal cancer, pancreatic cancer, or immune-mediated diseases

Long-Term Goals (More Than 5 Years):

- Develop top-tier R&D platform: Develop best-in-class/first-in-class treatments
- Utilize novel BiC/FiC immune checkpoint molecules for treatment of solid tumors and hematologic diseases
- Cell therapies: TCR-T targets cancer antigens on the cell membrane as well as intracellular cancer antigens

R&D Focus

The global biopharmaceutical industry is flourishing due to advances in medical technologies and aging populations, and therefore continuous innovation and development is an important mission for pharmaceutical companies. PharmaEssentia is a new drug developer and biologics manufacturer that is actively developing drugs for MPN. The four main types of MPN are :

- Polycythemia Vera, PV
- Essential Thrombocythemia, ET
- Chronic Myeloid Leukemia, CML
- Primary Myelofibrosis, PMF

As MPN is a rare condition with many patients worldwide, there are many new drug developers working to develop associated drugs. We used our independently developed PEGylation technology platform to improve upon existing drugs, and successfully developed new-generation PEG long-acting α-interferon alfa-2b (Ropeg), a drug with multiple indications which breaks through limitations in traditional interferon drugs and treatments. We have currently obtained marketing authorizations for PV treatment and are working to obtain marketing authorizations for other indications. We have also extended use of the PEGylation technology platform to tumors, immune diseases, and cell therapies, expanding into other treatment indications and applications to provide innovative solutions for other diseases.

Even though development of new drugs requires large amounts of R&D technologies, time costs, and capital investments, we have spared no effort in utilizing our drug manufacturing and industry expertise to create innovations that enhance patient quality of life and contribute to society as we strive to become a benchmark enterprise in the biopharmaceutical industry.

Governance

New drugs have to pass rigorous quality, safety, efficacy, and regulatory controls over a long period of time that spans from drug discovery, feasibility studies, preclinical animal trials, clinical trials, product manufacturing, and market authorization reviews before launch. PharmaEssentia has established complete drug R&D governance organizations to ensure that all responsible units implement efficient management and progress at all stages of new drug development.

Our Research and Development of New Drugs Center reports directly to the chief executive officer and is responsible for R&D of drug technologies. We have also established the “Project Evaluation Team” to make decisions regarding R&D; team members mainly include R&D team members, personnel from intellectual property departments, and senior executives from our headquarters and US subsidiary. Personnel from other departments such as the corporate planning/market development department, finance department, and legal department attend meetings based on their respective functions and R&D needs. All stages from pre-initiation analyses on project feasibility and potential values; compilation of data associated with proofs of concept, literature, market potential, competitive environments, and experiment data; and fundamental research for project initiation adhere to internal controls. Associated meeting minutes are compiled and revised on a rolling basis as necessary.

Project achievements must be reported at "Project Review Meetings" during specific stages of progress. Review meeting attendees assess the competitive potential and infringement risks of projects based on their unique characteristics and associated experiment data, and project directions are ultimately determined by the "Project Evaluation Committee," which is composed of senior executives. After project launch, project supervisors coordinate project progress and ask internal patent lawyers to conduct assessments or provide recommendations as appropriate based on innovativeness, progressiveness, free operation, and other project characteristics to ensure the value of developed project technologies.

Apart from the Research and Development of New Drugs Center and intellectual property department, we have also established a medical research center to formulate medical strategies for products and clinical trial plans. Our Taichung Plant plans manufacturing processes and implements material management, and our global operations division is responsible for formulating global strategies and market development plans.

▶ PharmaEssentia drug R&D to marketing process

Strategy

▶ Innovation and R&D Focuses

SASB HC-BP-000.B

In 2024, PharmaEssentia completed Phase 3 ET clinical trials (LPLV) for Ropeg. We expect to apply for ET marketing authorizations in Taiwan, the US, Korea, and China in 2025 to bring more medical value to the MPN field and strengthen PharmaEssentia's leadership in this domain.

Preparations for ET marketing authorization applications and market launch

- Estimate drug permit application and acquisition schedules based on clinical trial report completion times
- Implement Good Clinical Practice (GCP) simulation inspections
- Formulate drug pricing and drug listing strategies and schedules
- Conduct national market surveys of ET in Taiwan, the US, Japan, Korea, and China to understand current drug treatments

Benefits of obtaining ET marketing authorization

- Our PV indication physician team has several years of experience in MPN market deployments; we therefore used the same team on the ET indication. PharmaEssentia was able to achieve global reach by surveying patient distributions, without the need to build a new team or spend excess marketing and preparation costs, achieving better depth and breadth with minimal effort
- At present, very few drugs have been approved for ET treatment, and these have severe side effects and poor patient adherence. These Phase 3 clinical trial results indicate that Ropeg has good efficacy, few side effects, and good patient adherence
- Enhance academic medical developments and patient well-being while strengthening Ropeg's leadership position in the MPN field

Apart from MPN, PharmaEssentia also used the patented PEGylation technology to develop the new drug PEG-IL-2 for treatment of inflammatory or immune diseases. We plan to submit Phase 1 clinical trial applications at the end of 2025. We are also working with external partners to jointly develop TCR-T cell therapies and will begin recruiting Phase 1 clinical trial patients in Taiwan at the end of 2025.

The following is a summary of R&D progress made on our drugs in 2024:

R&D Product Pipelines SASB HC-BP-210a.1

Therapeutic Area	Drug Candidate	Indication	Markets	Pre-IND	Phase I/II	Phase III	Registration	Marketed
Hematology	Ropeginterferon alfa 2b (P1101)	PV	Europe					
			US, Taiwan, Korea, Japan, China, Malaysia, Singapore					
			Hong Kong, Brazil, Argentina, Mexico, Columbia					
		ET	Global					
		Pre-PMF	Global					
		Adult T-cell leukemia/lymphoma	Japan, Taiwan, China					
		Chronic myeloid leukemia	Korea					
Oncology	TCRT	Solid tumors	US, Taiwan					
	P1101 + Anti PD-1	Hepatocellular carcinoma	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 information on our R&D product pipelines, please refer to our official website: https://hq.pharmaessentia.com/en/pipeline

PharmaEssentia Innovation Research Center (PIRC)

PharmaEssentia established the PharmaEssentia Innovation Research Center in 2023 to work with headquarters on breaking into new research fields. We hope to further expand our R&D and innovation capacity by combining AI (artificial intelligence) and ML (machine learning) to accelerate the process from new drug development to market launch. In 2024, we worked with Qiagen to utilize data analytics and AI in finding new indications for Ropeg, and presented the results at the ASH Annual Meeting. We also worked with DeepSeq.AI in using AI to design new-generation smart cytokines that could be used in cancer treatments. We continue to build AI platforms and introduce relevant tools to accelerate the development of new drugs, continue to recruit professional scientific talents with expertise in drug development, and utilize AI/ML technologies to enhance the efficiency of early drug development, design, and optimization stages.

Intellectual Property Strategies to Protect Innovative R&D Technologies

During the early stages, PharmaEssentia focused on increasing production and reducing costs, using blanket collection of R&D results combined with dedicated analysis by a team of medical patent lawyers to gradually develop patent strategies against potential future biosimilars. PharmaEssentia's core product BESREMi is listed in the US and other international markets. Our intellectual property department works with existing research achievements from the R&D department to actively respond to the US biosimilars patent dance process and to conduct in-depth considerations of technical research.

Apart from formulating innovative intellectual property strategies during the life cycles of core products, our internal patent lawyers also invite experienced research teams to conduct "invention mining" processes on R&D results to explore patent opportunities hidden within technical details, uncover and refine results previously missed by researchers, and transform these into new patents that bring greater value to technical innovations, thereby enhancing the value and life cycle of good products. For example, we inventoried, refined, and tested Ropeg, and uncovered detailed patent technologies and values in the technology which we used to apply for new patents, thereby continually extend our patent protection period through accumulation of Ropeg patents. In 2024, PharmaEssentia used this technology-mining approach to build upon and integrate multiple ongoing achievements from the R&D department. We spare no effort in exploring and protecting our innovative medical technologies. In the US, we secured provisional patents to provide protection for emerging technologies and several future product pipelines that are still in the R&D stage, using these as a foundation for strengthening future product patent landscapes in accordance with R&D progress.

Risk Management

Commitment to Animal Welfare in Preclinical Animal Experiments

We first determine whether institutes conducting trials adhere to our requirements and standards, such as whether they hold GLP (Good Laboratory Practice), ISO 17025 (Laboratory Quality Management System), and AAALAC (American Association for Accreditation of Laboratory Animal Care) certification, and then conduct online or on-site visits/audits to better understand the expertise of the CRO (Contract Research Organization) and expert team, trial schedule coordination, and market price rationales. We also review contracts and technical agreements with legal personnel, supervise trials and review data during trial periods, and compile reports for review once trials have concluded. We use this process to confirm that our CROs comply with regulatory requirements, and to ensure the reliability and compliance of data from animal trials. In 2024, we commissioned 5 domestic and overseas reputable and qualified institutes to conduct preclinical animal trials.

The pharmaceutical industry requires large amounts of horseshoe crabs for experimental use, so these crabs are now a borderline endangered species. The Pharmaceutical Supply Chain Initiative (PSCI), which was formed by multiple international pharmaceutical brands, has called on the biopharmaceutical industry and supply chain partners to cease capturing these crabs and use innovative alternative solutions such as microfluidic technologies and recombinant reagents to reduce reliance on limulus amebocyte lysate (LAL). Where there is still need to use LAL, initiative members are encouraged to actively enhance their understanding of raw material sources and associated animal welfare and biodiversity issues while also sharing information on horseshoe crab traceability, population numbers, and conservation conditions with other members.

PharmaEssentia only procures necessary amounts of reagents in LAL kits (the substances remaining after vendors have extracted horseshoe crab blood) to test whether drugs or medical equipment have been polluted by endotoxins. This significantly maintains survival rates of horseshoe crabs and prevents them from being endangered. Our collaborating vendors also adopt the 3R (Replacement, Reduction, Refinement) measures to protect horseshoe crabs by seeking out replacement reagents to test for endotoxins, using microfluidic technologies to reduce 95% of raw materials extracted from horseshoe crabs, and actively refining current LAL formulations. We have never used other endangered species during trial processes and we work to fulfill our responsibilities to protect endangered species.

Clinical Trial Quality Maintenance and Participant Safety in Clinical Trials

SASB HC-BP-210a.1

PharmaEssentia has developed a 20-step standard operating procedure for clinical operations to ensure the safety of clinical trial participants. We have established audit and inspection mechanisms at all stages to maintain trial quality, and conduct Phase 1, 2, and 3 clinical trials in accordance with approved trial protocols and local regulations. None of our clinical trials were suspended due to GCP violations in 2024.

Trial Planning

Evaluate potential risks of trial procedures based on preclinical data, drug characteristics, and clinical trial designs; require CROs to formulate a case-specific “Monitoring Plan” and “Audit Plan” based on risk levels to implement QC (quality control) and QA (quality assurance) items, ensuring that clinical trial processes, data records, and reports all adhere to trial protocols and GCP regulations, thereby protecting the rights and well-being of trial participants.

Phase 1 Clinical Trial: Safety Exploration

Quality Assurance (QA)	Quality Control (QC)
• Includes independent audit system and commissioning of alternate CROs or independent consultants to conduct audits during the later phases of clinical trials to ensure trial quality and consistency. Identified issues are assessed and tracked appropriately, and auditees must submit relevant corrective actions and preventive action (CAPA) to auditors for review • Data Safety Monitoring Committee (DSMC): Monitors patient safety and drug efficacy of clinical trials	Monitoring and co-monitoring

Before the Trial

Phase 2 Clinical Trial: Preliminary Efficacy Study

- The trial protocol and related documents must be reviewed and approved by health regulatory authorities and the trial institute Institutional Review Board Committee
- Investigator meeting: Conduct training related to the trial
- Informed consent from participants: Participants must be fully informed of and give written consent to join the clinical trial after careful consideration before trial screening can commence
- Participant screening: Rigorously screen participants based on the inclusion and exclusion criteria outlined in the trial protocol

During the Trial

Phase 3 Clinical Trial: Large-Scale Confirmatory Efficacy Study

- The clinical operations department conducts joint monitoring with CROs contracted for monitoring services
- Audits are carried out in accordance with audit plans to ensure that CRO services meet quality standards

After the Trial

- Compile data on efficacy and safety for review, on-site verification, and assessment of benefits and risks by health regulatory authorities to obtain marketing authorization

Metrics and Targets

R&D expenditures over past five years

Year	2020	2021	2022	2023	2024
Global R&D Expenditures (NT$ '000)	922,380	1,272,944	1,425,964	2,224,054	2,587,570
Expenditure Increases Compared to Previous Period (NT$ '000)	282,805	350,564	153,020	798,090	363,516
Expenditure Growth Rate	44%	38%	12%	56%	16%
Global R&D Personnel (Persons)	74	83	123	142	165
Personnel Increases Compared to Previous Period (Persons)	18	9	40	19	23
Personnel Growth Rate	32.1%	12.2%	48.2%	15.4%	16.2%

Continued increases in R&D expenditures brings four main benefits for PharmaEssentia:

Product innovation and technological breakthroughs

Increases in R&D expenditures indicate that PharmaEssentia is committed to development of new products and technological innovations, and is also actively seeking market breakthroughs to enhance competitiveness.

Increase future revenue potentials

Even though R&D expenditures increase costs in the short term, they also serve as a foundation for future corporate growth. Successful development of new drugs help to expand markets, increase revenues, and bring long-term returns and investment benefits.

Expand market share

PharmaEssentia is currently conducting in-depth research into specific therapeutic areas such as blood disorders and cancers, and we are also working to extend product patent protection periods to further maintain our market leadership so we can expand market shares in target markets.

Enhance corporate brand value and collaboration opportunities

We enhance our brand value through continued investment in breakthrough R&D technologies for new drugs to attract support from more collaborators and investors, and are working to become a leader in Taiwan's biopharmaceutical industry.

R&D Focuses in 2024

- Number of drugs in development: 13
- Submitting IND application for TCRT-ESO-A2-TW cell therapy
- Completed 2 IND applications (PEG-GCSF and Anti PD-1)
- Conducted 5 new clinical trials (PEG-GCSF, Anti PD-1, TCRT-ESO-A2, HOPE PMF, and ATL)
- Obtained PV marketing authorizations in China, Singapore, and Malaysia
- Future expectations:

☆ Submit IND application for PEG-IL-2 in 2025
☆ Advance at least 1 project to development candidate stage
☆ Advance at least 1 project to preclinical candidate development stage
☆ Introduce 1-2 external technology platform asset projects
☆ Build AI (artificial intelligence)/ML (machine learning) platform

Development Focuses for Next Five Years (2025-2030)

Continued growth in Ropeg operations
- Continue to increase patient numbers in existing markets
- ET indication: Apply for US marketing authorization in 2025 and obtain marketing authorization in 2026

Expansion of Ropeg indications
- Currently conducting global Phase 3 pivotal clinical trials for early PMF and plan to submit applications for FDA approval at the end of 2027
- Other blood disorders: Research into ATL, CTCL, and other application areas

Expand global production capacity
- Aim to fulfill demand for more than 100,000 patients around the world
- Initiated construction of Zhubei Plant in 2023 in response to market demand, with completion projected for year-end 2025

Top-tier platform
- Utilize novel immune checkpoint molecules and cytokines for treatment of solid tumors, blood disorders, and immune diseases
- Cell therapies: TCR-T targets cancer cell antigens and can be used for treatment of solid tumors

Source: February 2025 Analyst Presentation Documents and information from Zhubei Plant

3.2 Drug Quality and Product Safety GRI 3-3

Material Topics

Drug Quality and Safety Management

Description of Impacts

PharmaEssentia implements risk management on manufacturing processes, environmental controls, and material supplies. We have formulated case-specific "Monitoring Plans" and "Audit Plans" as part of our quality assurance and quality management procedures, and established the "Quality Risk Management Procedure" in accordance with the Taiwan ICH Q9 Quality Risk Management guidelines to serve as a risk management strategy for production and manufacturing. We also use the risk aspects recommended by ICH Q9 (probability, severity, and detectability) to assess risk levels. We established the Equipment Risk Assessment Procedure in accordance with the United States Pharmacopeia, and manage risk categories based on "GMP impacts" and "systemic complexities," thereby reducing quality hazards and risks from equipment operators.

Policies and Commitments

PharmaEssentia's Taichung Plant rigorously adheres to the Quality Risk Management Procedure, Equipment Risk Assessment Procedure, and Change Control Procedure; has incorporated risk management procedures into production processes, environmental controls, and material supplies; and conducts annual quality reviews to minimize quality hazards.

Production: We comply with quality management regulations for all manufacturing stages set by local competent authorities, and continue to maintain GMP qualification

Transportation: We rigorously adhere to GDP regulations, meet local standards for marketing authorization, and strictly control all packaging and transportation processes

Responsible Unit

- Production, transportation, quality management, and auditing departments at headquarters
- Quality control department, quality assurance department, clinical trial quality assurance and drug safety monitoring teams at headquarters: Maintain and monitor the quality of marketed and clinical drugs
- Executive Center for Corporate Sustainability Product Ethics and Safety Team: Responsible for compiling and managing material sustainability issues

Response Measures and Management Actions

- Introduced Trackwise electronic system to perform deviation management, corrective actions and preventive actions, supplier management, laboratory surveys, and other procedures under our quality system
- Production and manufacturing quality management and risk management: Hosted global interdepartmental risk assessment team meetings to jointly review risk issues and correction measures in factory areas
- Invested more than NT$33 million in global pharmacovigilance tasks

Evaluation Mechanisms

- Official periodic GMP inspections (such as those conducted by the US FDA, EU EMA, and Taiwan TFDA)
- All departments need to undergo at least 1 internal quality audit every year
- Invite external experts to conduct quality audits as necessary
- External evaluation mechanisms for clinical trials adhere to inspections conducted by health authorities, and audits are conducted regularly by third parties (such as the institutional review boards at hospitals where trials are being conducted). Internal evaluations are conducted by the Clinical Trial Quality Assurance Unit (established in 2025)
- Established a Data and Safety Monitoring Board (DSMB) for human trials to perform reviews and assessments
- Regularly submit annual drug safety reports to the US FDA, EU EMA, and Taiwan TFDA each year as well as real-time drug safety notifications

Targets and Achievements in 2024

- Good Manufacturing Practice (GMP) plant certificates were updated or extended/maintained according to schedule
- Regularly implemented and passeed internal and external audits
- Completed GMP/GDP education and training
- Factory inspections conducted by EU and Brazilian supervisory authorities confirmed that there were no major deficiencies
- Completed incorporation of Blue Mountain electronic system for hardware management of GMP equipment, including calibrations, verifications, qualification determinations, and label generation
- Completed a total of 12 internal audits and 6 external audits on suppliers; all audited units completed corrections and passed re-inspections after being informed of deficiencies
- Organized a total of 750 GMP/GDP education and training sessions, with total training hours amounting to 14,797 hours
- Received a total of 208 customer complaints, none related to product safety, and achieved customer complaint rate of 0.12%
- PharmaEssentia hosted 32 global interdepartmental risk assessment team meetings for a total of 196 attendees to jointly review risk issues in factories

Targets

Short-Term Targets (1-2 Years):

- Obtain regulatory approval for second API production line at Taichung Plant and officially begin production of APIs that comply with the regulations of different countries
- Complete construction and validation processes of new Zhubei Plant and obtain GMP certifications from various countries
- Complete construction of Taipei Bioinnovation Park site and commence production of Phase 1 and Phase 2 clinical APIs
- Continue to maintain drug quality and zero recall record

Mid-Term Targets (3-5 Years):

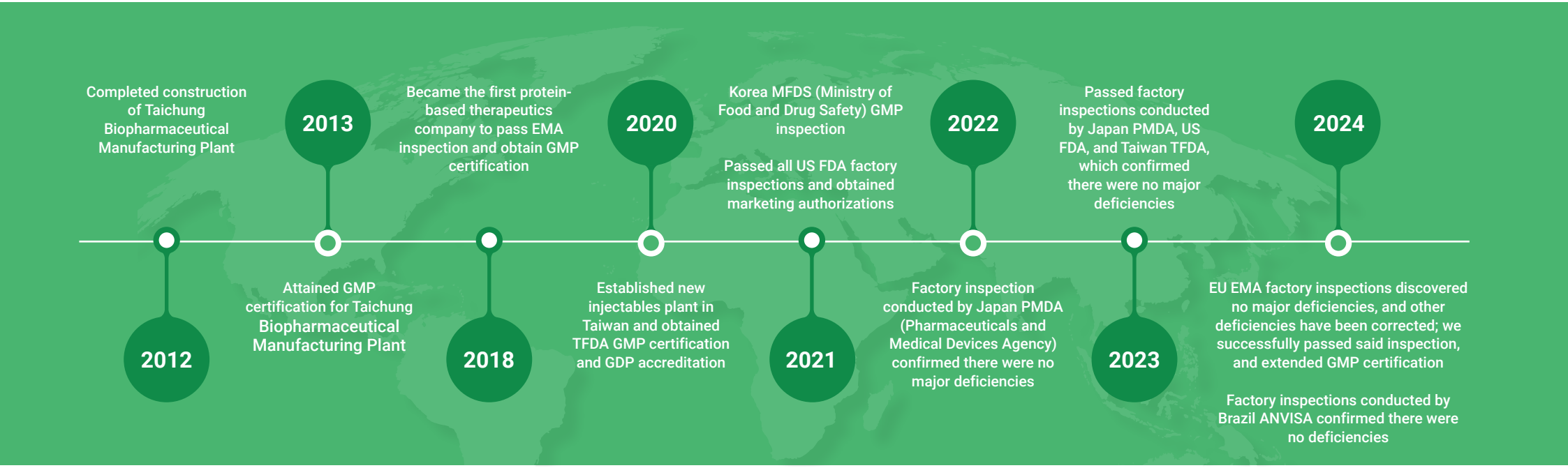
- Commence production of APIs that comply with the regulations of various countries at Zhubei Plant, and also begin production of GTP (Good Tissue Practice) cell therapies
- Support Houli Plant in passing international GMP inspections and commencing production of GMP-compliant PEG intermediates
- Continue to maintain drug quality and zero recall record

Long-Term Goals (More Than 5 Years):

- Establish production plants in Europe and the US to enable local production and make strides toward net zero targets
- Continue to maintain drug quality and zero recall record

PharmaEssentia Global Certification Landscape

We use practical actions to achieve vertical integration within our supply chain, gradually building our global market from production, quality control, filling, to delivery, actively demonstrating our vision to become a world-class pharmaceutical company.



International Standard Manufacturing Processes

PharmaEssentia's product Ropeg undergoes four critical stages in production: fermentation and cell processing, P1040 extraction and purification, PEGylation, and Ropeg DS purification. Sterile filling, labeling, and packaging processes all rigorously comply with GMP and international standards for quality management and standard operating procedures. In response to commercialization and mass production demands, we continue to enhance all production stages as well as overall production capacity, reduce supply chain risks, and improve supply stability.

Process Optimization

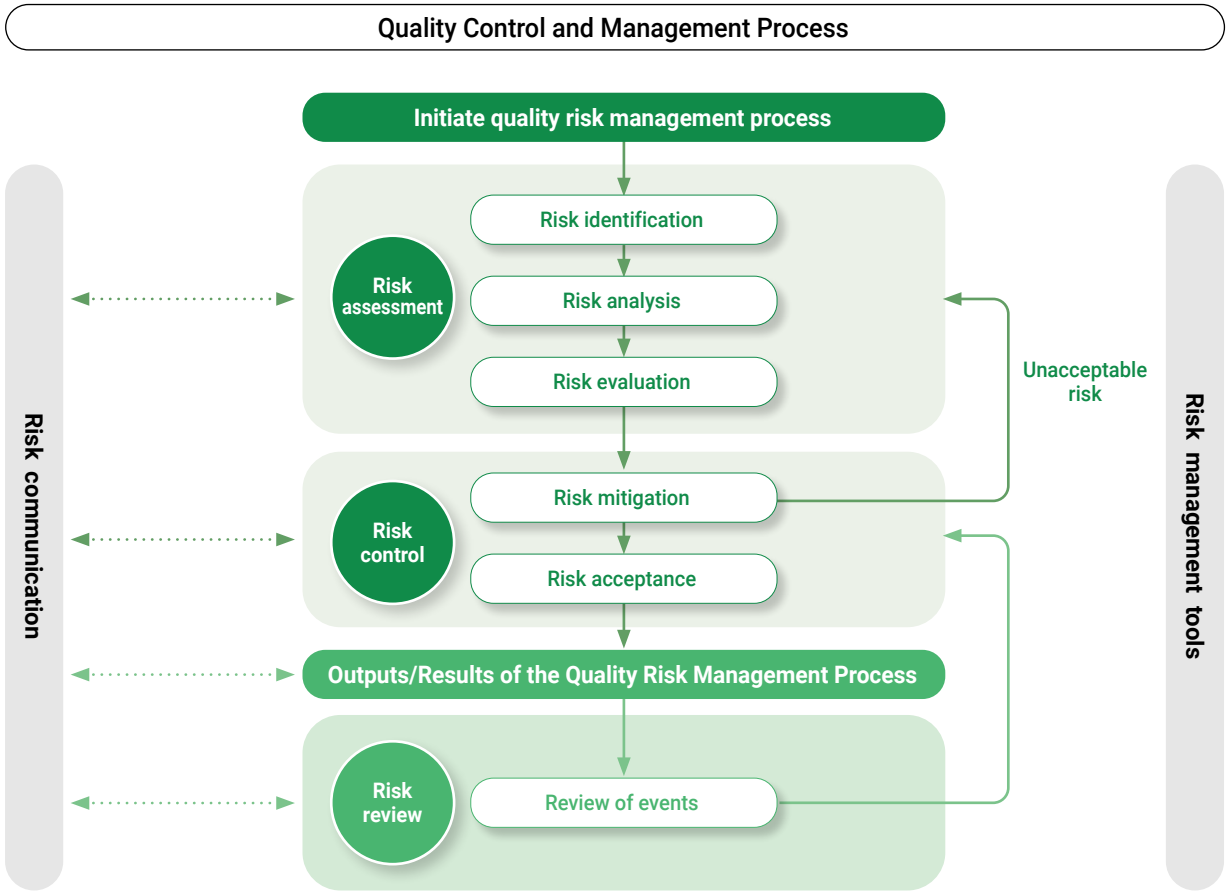
Enhancing Production Capacity

	Introduce second and third material sources	Establish second purification production line	Scale up PEG production line
Objective			
Goals and Results	To stabilize material supply, we completed 3 second-material source projects in 2024 and 3 more projects are in the testing phase. In response to major impacts on global supply chains caused by international situations, the pandemic, and extreme weather conditions, we introduced these projects to significantly reduce production risks and ensure stability of drug supplies.	Completed construction of second DS production line in 2024, increasing production capacity by 100%.	Completed scaling up of PEG production line in 2024, increasing production capacity by 4-8 times.

Quality Control and Risk Management in Manufacturing Processes

PharmaEssentia's Taichung Plant emphasizes product quality and safety management. Each year, our colleagues at the plant have to undergo education and training related to product safety and GMP regulations so they can update their knowledge and incorporate quality management concepts in daily tasks. The Taichung Plant has developed work procedures and organizational operational procedures for factories in different countries that produce GMP-compliant APIs and drug formulations, which are detailed below. In 2024, we continued to implement, monitor, and report trends associated with production environments (HVAC systems), water systems, compressed air systems, and biosafety cabinets, requiring all systems to comply with design specifications and legal regulations. The Taichung Plant has also formulated the "Plant and Facility Emergency Response Management Standard" to establish emergency response mechanisms for natural disasters, equipment abnormalities, and other emergency hazards, thereby ensuring that all equipment can operate normally and all personnel can work in safe environments.

The Ropeg product sold by our Japanese subsidiary is manufactured and produced at headquarters, where we ensure that production processes adhere to procedures that have been verified by the Japanese government. If there are any deviations during the manufacturing processes, the quality control department at our Japanese subsidiary will work with quality control personnel at headquarters to conduct appropriate assessments that guarantee product quality. Additionally, we also commissioned a Japanese testing agency to conduct relevant tests (such as product purity tests) on products imported from Taiwan and also outsourced product packaging to a Japanese pharmaceutical company to comply with Japanese regulatory requirements.



Education and Training	GMP/GDP regulations	**750** sessions and **14,797** hours
Established relevant work procedures for factories in many countries that produce GMP-compliant APIs and drug formulations	Quality manual, quality policies, master validation plans	**29**
	SOP guidelines	**100**
	Operational SOPs	**>900**
	Record forms	**>1,000**

GMP Certification and Quality Audits

PharmaEssentia's Taichung Plant is the first biologics manufacturer in Taiwan to pass EU EMA inspections and obtain GMP certification. Starting in 2020, we underwent a series of external inspections conducted by Korea MFDS, US FDA, Japan PMDA, and Brazil ANVISA. These inspections found no major deficiencies involving violations of GMP regulations or health & safety regulations, and we submitted CAPA plans within specified time limits for all non-major deficiencies. The Panco Healthcare Logistics Center conducted internal quality audits in 2023 and found no major deficiencies that deviated from our quality system.

Frequency of internal audits

- At least 1 internal audit each month (each department undergoes at least 1 random audit each year)
- If audits identify deficiencies, CAPA plans should be submitted within specified time limits based on deficiency levels, and related procedures should be completed

Frequency of external audits

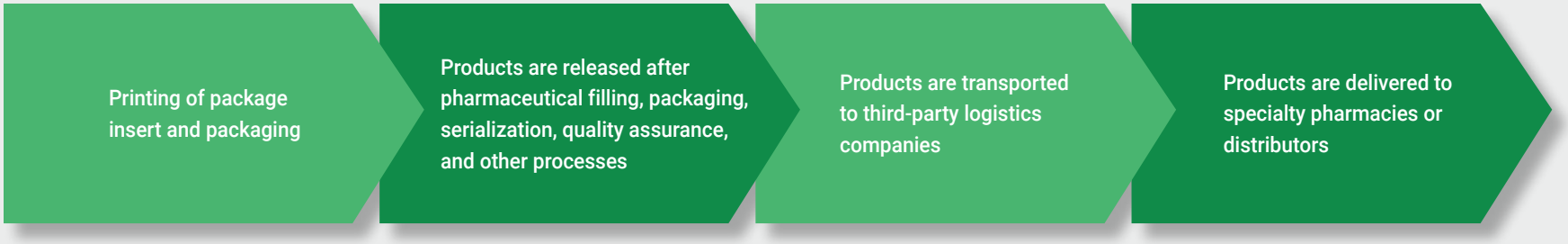
- Regular official GMP inspections every 2-3 years

CRO and CMO Management

In addition to filling and packaging operations conducted at our sterile formulation filling plant in Taichung, we also outsource filling and packaging processes to internationally GMP-certified CMO facilities in the US, Germany, and Japan to ensure proximity to local patients.

Secure Distribution Processes and Stable International Logistics & Transportation

Our secure distribution processes strictly adhere to GDP regulations and ensure proper management of pharmaceuticals throughout the transportation process. PharmaEssentia's GDP-compliant Panco Healthcare Logistics Center in Taichung supplies clinical drugs and marketed products, and also implements quality management regarding logistics management, warehousing management, and labeling processes.



PharmaEssentia has formulated the following strategies to maintain safe and stable international transportation:

1. "Storage and Distribution Policy" to regulate storage and distribution procedures that ensure appropriate storage conditions and management for raw materials, intermediates, and products
2. "Product Distribution Management Procedure," which stipulates that distribution procedures and tracking mechanisms at all operational sites around the globe must adhere to PIC/S Good Distribution Practice (GDP) requirements
3. "Import and Export Transportation Management Procedure" regulates import, export, and transportation procedures, and ensures regulation-compliant, fast, and safe delivery of all transported goods to designated destinations to effective safeguard patient medication safety
4. "Emergency Response and Handling Procedure" to prevent or mitigate negative impacts on distribution at Taichung Plant due to natural disasters
5. In 2024, we added a new air carrier to provide transportation services. PharmaEssentia verified transportation quality, ensured that appropriate temperatures were maintained during the transportation process, and confirmed there were no factors that could cause negative impacts on transported goods. This new transportation vendor helped to build another layer of transportation efficiency and additional protection for product transportation and logistics
6. We maintain at least 4 months of safety stock in the US in case of acute disaster risks within US borders caused by climate change to ensure that patients in the US can received their medications in a timely manner
7. Our Japanese subsidiary has formulated distribution procedures applicable for Japan and requires all Japanese logistics companies to comply with international and Japanese GDP regulations

Warehouse Management

PharmaEssentia has established the "Product Receipt and Storage Management Operation Standards" and "Storage and Distribution Policy" to prevent negative environmental and operational impacts on product quality. The Panco Logistics Center has established a "Storage Area Temperature Verification Plan" which stipulates that temperature verifications should be conducted twice every three years to ensure warehouse environment quality.

Product Entry 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 distribution processes for products manufactured at the Taichung Plant and by CMOs, as well as packaging and transportation processes at storage warehouses, are appropriately managed and all pharmaceuticals are transported under prescribed and suitable temperature conditions to uphold global drug transportation safety.

Packaging operations

- Confirm that transportation boxes are clean and temperatures meet appropriate product storage conditions; a temperature recorder is placed in each box to monitor temperatures.
- Ropeg, for example, must be stored between 2~8°C

Transportation process

- Comply with the "Storage and Distribution Policy" in executing appropriate storage and distribution procedures
- Conduct scenario simulations for pre-analysis to confirm that cooling statuses and equipment specifications meet specification needs
- Regularly check raw materials, intermediates, and products to ensure that they are stored and managed appropriately

3.3 Drug Safety Management and Marketing Ethics GRI 3-3

Material Topics

Business Integrity and Ethical Management

Description of Impacts

- Governments of all countries have established regulations on drug marketing. For example, the TFDA Pharmaceutical Affairs Act and Pharmaceutical Affairs Act Enforcement Rules have stipulations on drug advertising, and the US FDA has also established many Advertising and Promotion Guidances
- The WHO and other pharmaceutical NGOs in different countries, such as the International Research-Based Pharmaceutical Manufacturers Association (IRPMA), Pharmaceutical Research and Manufacturers of America (PhRMA), and National Council for Prescription Drug Programs (NCPDP) have also established relevant regulations

Policies and Commitments

PharmaEssentia prioritizes patient health and well-being, incorporates ethical management principles and medical ethics when marketing authorized drugs, and provides patients with professional and trustworthy products. In terms of drug safety management, we diligently track and report adverse drug events, and teach our colleagues to uphold "Quality First and Patient Safety" concepts to manage drug risks and protect patient safety. In terms of marketing ethics, we regulate the drug marketing behaviors of our colleagues, organize annual internal promotions of drug marketing ethics policies for employees who have business interactions with HCPs, and review processes for marketing promotions and business activities to avoid legal violations.

Responsible Unit

Drug Safety Management:

- Patients: The Product Safety & Risk Management (PSRM) Team (composed of pharmacovigilance personnel from PharmaEssentia headquarters and international subsidiaries) and pharmacovigilance quality assurance personnel; patient safety is managed by the global pharmacovigilance executive director, and is overseen by the chief medical officer
- Products: Quality control department, quality assurance department, clinical trial quality assurance, and pharmacovigilance teams at headquarters monitor the quality of marketed and clinical drugs
- Executive Center for Corporate Sustainability Product Ethics and Safety Team: Responsible for compiling and managing material sustainability issues

Marketing ethics:

- Marketing departments and medical affairs teams at Taiwan headquarters and all subsidiaries
- US MLR (Medical, Legal, and Regulatory) Affairs Review Committee: Conducts medical, legal, and regulatory reviews to ensure the appropriateness and regulatory compliance of advertising and promotion content
- Executive Center for Corporate Sustainability Product Ethics and Safety Team and Access to Medicine Team: Responsible for compiling and managing material sustainability issues

Response Measures and Management Actions

Drug Safety Management:

- In 2022, we hired a global pharmacovigilance executive director to conduct global pharmacovigilance tasks
- Dedicated pharmacovigilance personnel have been established at our headquarters and operational sites around the world
- Commissioned a pharmacovigilance CRO institute to form a project team responsible for managing the Ropeg pharmaceutical safety database and assisting with pharmacovigilance, reporting, handling, exchanges, and regular submission of safety reports to international regulatory authorities, as well as other notification matters

Marketing ethics:

- Related teams regularly conduct internal inspections to ensure effective execution

Evaluation Mechanisms

(Channels and Systems for Tracking Effectiveness of Response Measures and Management Actions)

Drug safety management:

- Post-marketing pharmacovigilance: Issue timely reports and maintain normal operations of real-time reporting mechanisms in accordance with the regulations set by competent authorities in each country
- Regular safety reports: Regularly submit DSURs and PSURs to the competent authorities in each country
- Internal audits: Conducted by the quality assurance department or a commissioned independent third party
- External inspections: Conducted by international and domestic drug safety authorities
- Assess operational status of real-time reporting mechanisms
- Assess operational status of drug safety reporting hotline (Taiwan, US, Korea, and Japan)
- No recalls for defective products

Marketing ethics:

- Marketing personnel regularly revise promotion content and submit said content to the MLR Committee for review

Targets in 2024

Drug safety management targets:

- Implement pharmacovigilance plans in accordance with regulatory requirements and report drug safety information within time periods specified by regulations
- Complete PSURs for marketed drugs in accordance with regulations
- Conduct regular pharmacovigilance education and training

Marketing ethics targets:

- Zero violation incidents
- Recruit medical and legal personnel with digital and extensive experience to join the US MLR Committee to reduce violation risks

Achievements in 2024

Drug safety management achievements:

- Drug safety management achievements:
- PharmaEssentia headquarters and all subsidiaries 100% achieved reporting of drug safety information within time periods stipulated by regulations
- In terms of post-marketing safety, a total of 132 serious adverse events were reported from February 2023 to February 2024, and there were no incidents that violated health and safety regulations for products and services
- Completed and submitted sixth Ropeg Development Safety Update Report (DSUR), fifth Ropeg Periodic Safety Update Report (PSUR), and second Tirbanibulin PSUR in accordance with regulations
- Completed 4 quarterly safety signal monitoring reports
- Established 8 pharmacovigilance process quality SOPs and 1 pharmacovigilance SOP
- Revised 8 pharmacovigilance SOPs and 1 pharmacovigilance plan
- In 2024, employees at PharmaEssentia headquarters completed annual pharmacovigilance education and training, and passed related assessments. New employees were required to complete employee pharmacovigilance education and training within one month of reporting for work, and we achieved a training completion rate of 100%

Marketing ethics achievements:

- PharmaEssentia headquarters and all subsidiaries around the world compiled with drug marketing ethics in 2024, and there were no violations of marketing or communication related regulations

Targets

Short-Term Targets (1-2 Years):

- Continue to maintain pharmacovigilance management
- Incorporate pharmacovigilance training into LMS system to effectively track employee training completion rates

Mid-Term Targets (3-5 Years):

- Maintain record of zero product recalls due to drug safety incidents
- Continue to pass pharmacovigilance inspections

Long-Term Goals (More Than 5 Years):

- Maintain 100% drug safety compliance to ensure patient safety

Pharmaceutical Risk Management Plan

PharmaEssentia implements drug safety risk standard operating procedures formulated by collaborating CROs and has established "Drug Risk Management Plans" in accordance with the pharmacovigilance regulations of each country. Our headquarters established pharmacovigilance plans in accordance with the "Regulations for Pharmacovigilance Management" in Taiwan, and completed amendments in 2024 to include pharmacovigilance organizational charts, operational processes and responsibilities at each stage, pharmacovigilance quality systems, pharmacovigilance personnel education and training processes, pharmacovigilance document management, and addition of document numbers, formats, effective dates, and other information in accordance with our pharmacovigilance quality documentation SOP. Our subsidiaries in the US, Japan, and other locations have also established "Drug Risk Management Plans" in accordance with local regulatory requirements. Regulations require collection of post-marketing clinical data to determine whether long-term use by patients result in chronic side effects, and also to serve as a basis for "Drug Risk-Benefit Assessments." Even though we have not yet been required by regulatory authorities to submit drug risk management plans, we still commit to collecting safety data in countries where our drugs have been authorized, and regularly update our safety reports and assess Ropeg risks.

Pharmacovigilance Management

Our Pharmacovigilance Team was established under the Medical Research Department and works in coordination with relevant units to carry out their duties according to our "Pharmacovigilance Policy," "Drug Safety Functions and Training Standard Operating Procedures," "Post-Marketing Safety Data Collection Standard Operating Procedures," as well as Taiwan's "Regulations for Reporting Serious Adverse Reactions of Medicaments" and "Regulations for the Management of Drug Safety Surveillance." We also commission professional CROs to conduct pharmacovigilance tasks. Our pharmacovigilance procedures include both passive monitoring and active monitoring:

Passive monitoring

We are legally required to submit PSURs and collect spontaneous safety case reports from healthcare professionals and the public. Safety information is registered in the safety database system for further processing. In 2024, PharmaEssentia headquarters submitted the fifth Ropeg PSUR to the TFDA and our Japanese subsidiary submitted the second and third PSURs to PMDA. All adverse events were reported in a timely and accurate manner, and there were no delayed reports or violations of product health and safety regulations or voluntary codes. Our reports found no new safety information that affects Ropeg safety. Additionally, we obtained marketing authorization for Tirbanibulin (a drug licensed to PharmaEssentia by US pharmaceutical company Athenex) in 2022 and are required to submit annual PSURs until 2028.

Active monitoring

We proactively implement safety signal detection, conduct monitoring and literature reviews of medical warnings and safety signals issued by medically advanced countries, and also actively gather information through clinical trial programs (registration trials/IITs) and patient support programs (PSP).

PharmaEssentia headquarters and all subsidiaries and regional heads convene regular meetings with CROs to ensure that collection and reporting of global drug safety information is thoroughly implemented. In 2024, we conducted a total of 12 meetings to track and manage pharmacovigilance mechanisms.

Pharmacovigilance Reporting Education & Training and Reporting Program

Taiwan's pharmacovigilance regulations require CROs to formulate and implement drug safety management and regulatory authority reporting plans, organize regular employee pharmacovigilance education and training, and preserve all training records.

Course Title	Course Content	Number of Participants	Sessions	Total Training Hours
New employee pharmacovigilance training	Pharmacovigilance regulations and reporting procedures	36	New employees are required to complete the course and assessments on the IT Portal within one month of commencing work	30
Company-wide pharmacovigilance training	Pharmacovigilance regulations and reporting procedures	327 (including Panco employees)	1	272.5
CMO pharmacovigilance training	Pharmacovigilance regulations and reporting procedures	11	2	9.2

All employees at our Japanese subsidiary are required to undergo 1 safety training session each year encompassing definitions of adverse events and side effects, procedures for reporting safety information, and safety management systems. Our sales department undergoes annual training in accordance with our SOP. Local safety information is collected and submitted to the safety department for formulation of supporting measures, including collection methods for safety information, reporting procedures, and penalties for delayed reports. Employees who serve as heads of safety departments or supervisors of marketing authorization holders are required to participate in lectures and learning groups organized by pharmaceutical industry associations to enhance their knowledge and stay up to date with the latest regulatory developments.

US Pharmacovigilance Reporting Education and Training

PharmaEssentia US conducts education and training for new employees associated with collection of post-marketing safety data and reporting of severe adverse drug reactions; if amendments are made to related regulations or operating standards, training is also carried out for amended content. Additionally, we are planning to conduct annual advanced courses for reporting severe adverse drug reactions in the second half of 2025 for continued strengthening of professional pharmacovigilance knowledge.

Drug Safety Reporting Mechanism

Taiwan

Severe adverse reactions that occur during general usage conditions for marketed drugs can be reported through the following channels:

- Medical personnel and members of the public can register for an account on the TFDA online reporting system (https://adr.fda.gov.tw) and fill out the "Post-Marketing Adverse Drug Reaction Reporting Form" or send an email to adr@tdrf.org.tw
- Pharmaceutical companies can select, fill out, and submit the "Post-Marketing Adverse Drug Reaction Reporting Form" on the online reporting system
- After receiving relevant reports, PharmaEssentia will submit reports via the online reporting system (https://adr.fda.gov.tw) or email (adr@tdrf.org.tw) in accordance with the "Post-Marketing Adverse Drug Reaction Reporting Form Guidelines
- In 2024, none of our drugs in Taiwan were recalled due to adverse events

US

- Our US subsidiary is assisted by qualified third-party logistics vendors which adhere to the Drug Supply Chain Security Act (DSCSA) and drug tracking regulations, and who submit transaction histories (TH), transaction information (TI), and transaction spreadsheets (TS) for review
- We have established the PEC US Call Center reporting management center exclusively for the US market. The Center is managed by the medical affairs team at our US subsidiary, and is responsible for handling reports and information related to drug quality and safety needs. In terms of production traceability mechanisms, we completed drug serialization procedures in 2020, and none of our drugs were recalled due to adverse events in 2024

Japan

- Medical reps collect information on drug hazards and side effects when meeting with doctors and pharmacists, and report these to the safety management department through the hazardous event reporting system
- The medical information and patient support program departments are responsible for handling calls from doctors, pharmacists, and patients reporting adverse drug reactions or drug hazards, and reports these to the safety management department through the hazardous event reporting system
- After receiving reports of severe or unreported adverse events, we confirm relevant potential risks, and, if necessary, conduct detailed investigations on report providers, and submit reports via email or the online reporting system within specified time limits
- Since Ropeg was launched in Japan (including in 2024), there have been no recalls of our drugs sold in Japan or overseas

The TFDA "Regulations for Reporting Serious Adverse Reactions of Medicaments" requires reporting of adverse drug reactions and collection of safety data within specified time limits. A total of 132 adverse reactions were reported worldwide for PharmaEssentia drugs from February 2023 to February 2024, and there were no violations of health and safety regulations for products and services. We pledge to continue compliance with the "Regulations for Reporting Serious Adverse Reactions of Medicaments" and track drug safety conditions in a timely manner to reduce potential risks to patients as we fulfill our drug safety and management responsibilities.

Product Traceability Mechanisms

SASB HC-BP-260a.1

PharmaEssentia has established a global product traceability mechanism and incorporated drug serialization. We regulate packaging and serialization processes at our Taichung injectables plant and CMOs to achieve our goal of full traceability for all individual product flows and usage records. Drug serialization has also been fully implemented for Ropeg sold in the US, Taiwan, Korea, and China, and a qualified injectables facility packages and serializes drugs in accordance with the Drug Supply Chain Security Act (DSCSA) to maintain drug quality and safety.

Product Recall Mechanisms

SASB HC-BP-260a.2 GRI 416-2

PharmaEssentia's "Return and Recall Procedures" clearly stipulates the use of a product traceability system to complete drug recall mechanisms, which allows for rapid and effective drug recalls if product quality concerns emerge, providing an additional safety mechanism for patients when using medications. Recall simulation drills are conducted every year to ensure accuracy and familiarity with recall actions. None of our drugs were recalled in 2024 due to adverse events.

Initiation time

When learning that a product has known or possible manufacturing defects, spoilage, counterfeits, or any other serious quality issues.

Recall procedures

The quality assurance department initiates product recall procedures in accordance with our "Return and Recall Procedures," submits the "Recall Operational Plan Application Form," and proposes recall actions.

Proactive reporting

Remove products from usage channels within certain time limits based on drug hazard levels, appropriately handle recalled products, and simultaneously notify local competent authorities.

Product Marketing Ethics

PharmaEssentia product marketing ethics adhere to the following 7 principles:

1. Prioritize patient medical care and well-being
2. Meet high quality, safety, and efficacy standards required by regulatory authorities
3. When interacting with related units or personnel, all behaviors should be ethical, appropriate, and professional. Provision or supply of any materials or labor that directly or indirectly result in negative impacts are prohibited
4. Be responsible for providing accurate, balanced, and scientifically valid product information
5. Product marketing activities should be ethical, accurate, and balanced, and should not be misleading. Product marketing information should include accurate product risks, risk-benefit assessments, and appropriate usage methods
6. Respect patient privacy and personal information
7. Sponsor/support clinical trials and scientific research aimed at pursuing new knowledge to enhance patient interests, promote advances in medical technologies, and maintain transparency of human clinical trials sponsored by the industry

Product Labeling

SASB HC-BP-270a.2

PharmaEssentia's product labels all comply with the regulatory requirements of each country. Label information includes permit number, Chinese name of drug, product lot number, prescribing information, batch number, validity period, and manufacturer/importer information. No incidents involving violations of product and service information and labeling regulations or voluntary codes occurred at PharmaEssentia in 2024.

To ensure the inviolability and authenticity of our products, we implement special packaging and labels for our serialized products:	• A unique identifier is applied to each package • Each package is marked with a holographic seal and assigned a unique and traceable serial number to prevent counterfeiting

Previous toxicology studies found that fetal toxicity occurred in cynomolgus monkeys treated with Ropeg during experiments. As a result, our US subsidiary updated Section 8.1 of the United States Prescribing Information (USPI) for Ropeg and the Instructions for Use (IFU) submitted to the US FDA to include clinical research data related to pregnancy and fetal development, and discussed possible adverse drug effects on maternal and fetal outcomes to ensure that HCPs and the public clearly understood the product's safety information.