# 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.

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| **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<br>• 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.