# 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®.

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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.