KEMENTERIAN KESIHATAN MALAYSIA
BAHAGIAN REGULATORI FARMASI NEGARA

2023
ANNUAL REPORT
NATIONAL CENTRE FOR ADVERSE DRUG REACTIONS MONITORING

National Pharmaceutical Regulatory Agency (NPRA)
Ministry of Health Malaysia

KEMENTERIAN KESIHATAN MALAYSIA
BAHAGIAN REGULATORI FARMASI NEGARA

NATIONAL CENTRE FOR ADVERSE DRUG REACTIONS MONITORING: ANNUAL REPORT 2023

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Our Purpose

Keeping medicines safe for the nation

This is what inspires and drives us as individuals and as a regulatory agency. This is how we contribute to the society by ensuring the safety of the products registered in Malaysia.

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Pharmacovigilance Capacity Building, Collaborations, Research, and Initiatives

The National Centre for Adverse Drug Reactions Monitoring

The National Centre for Adverse Drug Reactions Monitoring serves as a repository for all adverse drug reaction (ADR) reports and adverse events following immunisation (AEFI) reports received by the National Pharmaceutical Regulatory Agency (NPRA). The National Centre is housed within the Pharmacovigilance Section, Centre of Compliance & Quality Control, NPRA.

The National Centre plays an important role in managing and analysing information on suspected adverse reactions to medicines or vaccines. Based on the evaluation of a safety concern, NPRA may take regulatory action(s) to improve product safety and protect public health, such as updating product packaging information, restricting the use of the product, communicating new safety information to healthcare professionals and the public, or even removing a product from the market.

The Malaysian Adverse Drug Reactions Advisory Committee (MADRAC)

The Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) was established in 1987 under the Drug Control Authority (DCA) to perform the function of monitoring safety profiles of medicinal products registered for use in Malaysia.

Appointment of MADRAC members are made every three (3) years, and the Pharmacovigilance Section, Centre of Compliance & Quality Control, NPRA is the Secretariat to the Committee. During MADRAC meetings held once every three months, causality verification is done for all local reports of ADR/AEFI and all pertinent drug safety issues are discussed to provide DCA with information and recommendations if required.

A total of **four (4) MADRAC meetings** were held in 2023.

Table 1: Members of MADRAC Session 2023

Ex-officio	Chairperson **YBrs. Pn. Rosilawati Ahmad** Director of NPRA
	Secretary to the MADRAC **YBrs. Dr. Noraida Mohamad Zainoor** Deputy Director, Centre of Compliance & Quality Control
	Secretary of the Drug Control Authority **YBrs. Dr. Azuana Ramli** Deputy Director, Centre of Product & Cosmetic Evaluation
Commitee Members *(Alternate members)*	**YBhg. Datuk Dr. Noel Thomas Ross** Medical Consultant Hospital Kuala Lumpur *(YBrs. Dr. Marzilawati Abdul Rahman)*
	YBrs. Dr. Liza Mohd. Isa National Head of Rheumatology Services and Medical Consultant (Rheumatology), Hospital Putrajaya *(YBrs. Dr. Habibah Mohd Yusoof)*
	YBrs. Dr. Suganthi Thevarajah National Head of Dermatology Services and Consultant Dermatologist, Hospital Kuala Lumpur *(YBrs. Dr. Tang Min Moon)*

YBrs. Dr. Sunita Bavanandan
Head of Department and Consultant Nephrologist,
Hospital Kuala Lumpur
(YBrs. Dr. Suryati Yakob)

YBrs. Dr. Mazni Mat Junus
Head of Department and Consultant Psychiatrist
Hospital Selayang
(YBrs. Dr. Chin Loi Fei)

YBrs. Dr. Farah Inaz Syed Abdullah
Consultant Paediatrician and Neonatologist,
Hospital Tunku Azizah
(YBrs. Dr. Lim Poi Giok)

YBhg. Dato Dr. Mohd. Sapawi Mohamed
Consultant Cardiologist,
Hospital Raja Perempuan Zainab II
(YBrs. Dr. Siti Khairani Zainal Abidin)

YBrs. Dr. Voon Pei Jye
Medical Oncologist
Hospital Umum Sarawak
(YBrs. Dr. Ibtisam Muhamad Nor)

YBrs. Dr. Mohd Hanif Zailani
Vaccine Preventable Diseases and Food & Water Borne Diseases Sector
Disease Control Division
Ministry of Health
(YBrs. Dr. Jamiatul Aida Md. Sani)

YBrs. Prof. Madya Dr. Adyani Md Redzuan
Faculty of Pharmacy
National University of Malaysia
(YBrs. Dr. Norkasihan Ibrahim)

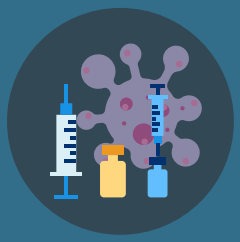
YBrs. Dr. Nur Sufiza Ahmad
Deputy Director
Formulary Management Branch
Pharmacy Practice & Development Division
(Dr. Aliza binti Alias)

YBrs. Dr. Sivanaesan Letchumanan
Malaysian Medical Association (MMA)
(YBrs. Dr. Balachandran Krishnan)

YBrs. Dr. G. Shanmuganathan
Federation of Private Medical Practitioners' Associations Malaysia (FPMPAM)
(YBrs. Dr. Pearl Leong Yuet Mae)

Pn. Ho Wan Dien, Jemima
Malaysian Pharmaceutical Society (MPS)
(YBrs. Dr. Syireen Alwi)

Pn. Eliza Basir
Association of Private Hospitals of Malaysia (APHM)
(Pn. Zarihasyum Wan Zein)



Highlights: Good Pharmacovigilance Practice (GVP) Inspections in Malaysia: Milestones Toward Safer Healthcare

Introduction

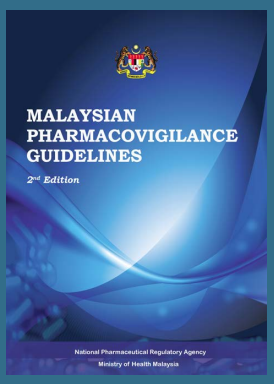
According to the World Health Organization (WHO), pharmacovigilance (PV) is the *science and activities related to the detection, assessment, understanding and prevention of adverse effects and other medicine- or vaccine-related problems.*[1] All countries and product registration holders (PRH) should establish a PV system to carry out pharmacovigilance duties and obligations, specifically to oversee the safety of authorized medicinal products and identify changes in their benefit-risk profile.

In Malaysia, the National Pharmaceutical Regulatory Agency (NPRA) has published a set of measures known as **Good Pharmacovigilance Practices (GVP)** which outlines the essential requirements for ensuring the ongoing safety monitoring of medicinal products.[2,3] The NPRA first introduced the concept of GVP inspections to PRHs in 2015 during a **pre-conference seminar for the National Regulatory Conference (NRC)**. Subsequently, the NPRA has continued to promote awareness and understanding of GVP Inspections among both regulators and PRHs through various activities.

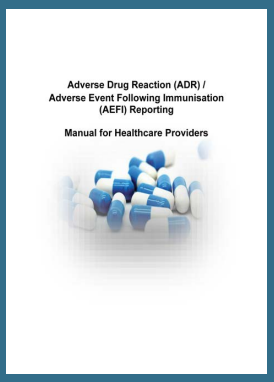
The PRH bears principal responsibility for the safety of their medicinal products registered in Malaysia. GVP inspections provide significant advantages to PRHs by identifying potential deficiencies or areas for improvement in their current PV practices.[4] This process aids PRHs in bolstering their PV systems comprehensively, thereby ensuring continual safety of registered medicinal products.

Legislation & Guidelines

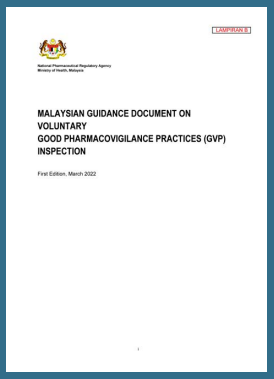
The NPRA's first pharmacovigilance guideline, the **Malaysia Guidelines for Reporting and Monitoring 1st Edition,** was issued in **2002**. In September 2016, the NPRA replaced this initial guideline with **the Malaysian Pharmacovigilance Guidelines, 2nd Edition, 2016.** However, this second edition did not include provisions for GVP Inspection.



In 2021, the NPRA made the decision to separate guidelines for PRHs and healthcare professionals (HCP). This decision was made to provide both PRHs and HCPs with easier access to the specific requirements relevant to them. The requirements for Pharmacovigilance System Master File (PSMF) and Pharmacovigilance System Summary (PVSS) have been included in the **Malaysian Guidelines on GVP for PRH, 1st Edition, Aug 2021.** Concurrently, the **ADR/AEFI Reporting Manual for HCP** was released in **September 2021**, replacing the 2016 guideline.



In preparation for the implementation of the GVP inpsection, a voluntary phase has been initiated. **The Malaysian Guidance Document on Voluntary GVP Inspection, published in March 2022**, aims to assist PRHs in understanding and aligning their expectations with the voluntary inspection process before they opt to participate in the program.



All the above guidelines were issued by the Director of Pharmaceutical Services under **Regulation 29, Control of Drugs and Cosmetics Regulations 1984.**

Milestones

Where are we now: Pharmacovigilance inspection journey in Malaysia (2015-2023)

2015

Introduction Phase

- Introduction of GVP Inspection concept to Product Registration Holders (PRHs)

2016

Foundation & Training

- Issuance of **Malaysian GVP Guideline, 2016**
- NPRA regulators received professional training on GVP Inspection by **UK MHRA**.
  (Ref: MADRAC Bulletin, Dec 2016)

2017

Observation & Exposure

- Two NPRA officers observed a PV inspection by **UK MHRA** in London
  (Ref: MADRAC Bulletin 02/2017)

2018-2019

Pilot Study Phase

- Conducted **PV Inspection Pilot Study** on four PRHs

2020

Guideline Revision

- **Malaysian PV Guidelines, 2016 revised** based on pilot findings
- Public consultation via **Unified Public Consultation (UPC)** for draft Malaysian Guidelines on GVP for PRH, 1st Edition

2021

Official Guideline Launch

- **Malaysian Guidelines on GVP for PRH (1st Edition)** officially launched

2022

Voluntary Inspection Initiatives

- Issuance of **Malaysian Guidance Document on Voluntary GVP Inspection**
- Announcement of voluntary inspection program to PRHs
- **13 PRHs expressed interest**
- Risk-based assessment to prioritise PRHs to be inspected and determine inspection methods.

2023

Commencement

- Commencement of voluntary GVP inspections in Malaysia
- **Four PRHs underwent voluntary inspections**
- No grading; focus on improvement and capability building

Abbreviations:
GVP: Good Pharmacovigilance Practices; **PRH**: Product Registration Holders; **PV:** pharmacovigilance;
UK MHRA: United Kingdom Medicines and Healthcare products Regulatory Agency

Training on GVP Inspection

Following the **initial introduction to GVP Inspections** during the **National Regulatory Conference (NRC) 2015 pre-conference seminar,** NPRA officers have delivered numerous presentations across various platforms to educate PRHs, including:

Date	Organiser	Event	Topic/Title Given	Venue
September 2017	PhAMA and EXTEDO	Introduction and Best Practices on PV and eCTD	Updates on NPRA's requirements on PSMF and PV Inspection	One World Hotel
August 2019	MOPI	MOPI Regulatory Conference	Developing a PV Framework within your company	One World Hotel
October 2020	PhAMA & MOPI	3rd Joint Industry PV Community Meeting	PV Requirements and GVP Inspection	Virtually
April 2021	MOPI	MOPI Regulatory Seminar	Updates on PV Requirements and GVP Inspection	Virtually at Eastin Hotel
May 2023	MOPI	Pharmacovigilance Workshop	Voluntary GVP Inspection	Eastin Hotel

Abbreviations:
eCTD: Electronic Common Technical Document;
GVP: Good Pharmacovigilance Practices;
MOPI: Malaysian Organisation of Pharmaceutical Industries;
PhAMA: Pharmaceutical Association of Malaysia;
PRH: Product Registration Holders;
PSMF: Pharmacovigilance System Master File;
PV: pharmacovigilance

Similarly, NPRA officers have also undergone training to enhance our expertise in GVP Inspection through the following channels

Date	Event	Speaker/Organiser	Venue
November 2016	Two-day course coordinated by World Health Organisation (WHO)	United Kingdom Medicines and Healthcare products Regulatory Agency (UK MHRA)'s Pharmacovigilance (PV) Information & Signal Management Unit	Armada Hotel, PJ
May 2017	May 2017 Join as an observer in PV Inspection	UK MHRA	London, UK
November 2017	PV Inspection Training Workshop	Indonesia National Agency of Drug & Food Control (NADFC)	IOI Resort
February 2020	MHRA Good Pharmacovigilance Practice Symposium	UK MHRA	Virtual
March 2021	Basic Pharmacovigilance Training	Saudi Food and Drug Authority (FDA)	Virtual
March 2021	Workshop on PV – Advanced PV Training	Saudi FDA	Virtual
September 2021	2021 KIDS-APEC PV Training	Korea Institute of Drug Safety & Risk Management (KIDS)–Asia-Pacific Economic Cooperation (APEC) PV Center of Excellence	Virtual
June 2022	PV Inspection Training Course	WHO	e-learning (virtual)
September 2022	Exchanging Experience in PV Inspection during Australia Therapeutic Goods Administration (TGA) & Malaysia NPRA Meeting	Sharing of GVP Inspection in Australia and Malaysia	Virtual
September 2023	2023 KIDS-APEC PV Training	KIDS–APEC PV Center of Excellence	Virtual

Accomplishment Gallery

2016 Professional training on GVP Inspection by inviting the United Kingdom Medicines & Healthcare products Regulatory Agency (UK MHRA)

2017

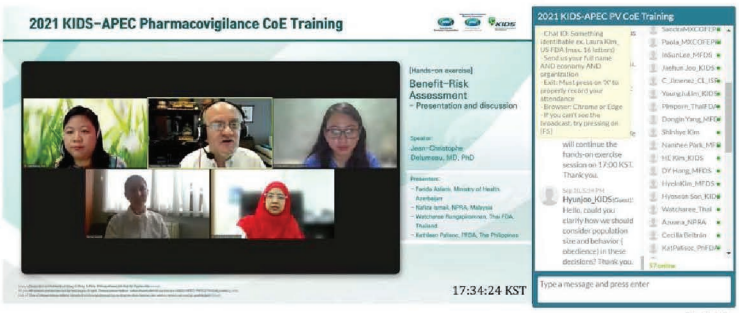
PV Inspection Training at the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA)

2017

PV Inspection Training Workshop 2017 at IOI Resort, with attending speaker from Indonesia National Agency of Drug & Food Control (BPOM, *Badan Pengawas Obat dan Makanan*)

2020 UK MHRA Good Pharmacovigilance Practice Symposium

2021 KIDS-APEC Pharmacovigilance Center of Excellence (CoE) Training 2023



KIDS: Korea Institute of Drug Safety and Risk Management (KIDS)
APEC: Asia-Pacific Economic Cooperation

2023 **MOPI Pharmacovigilance Workshop on Voluntary GVP inspection at Eastin Hotel**

References:

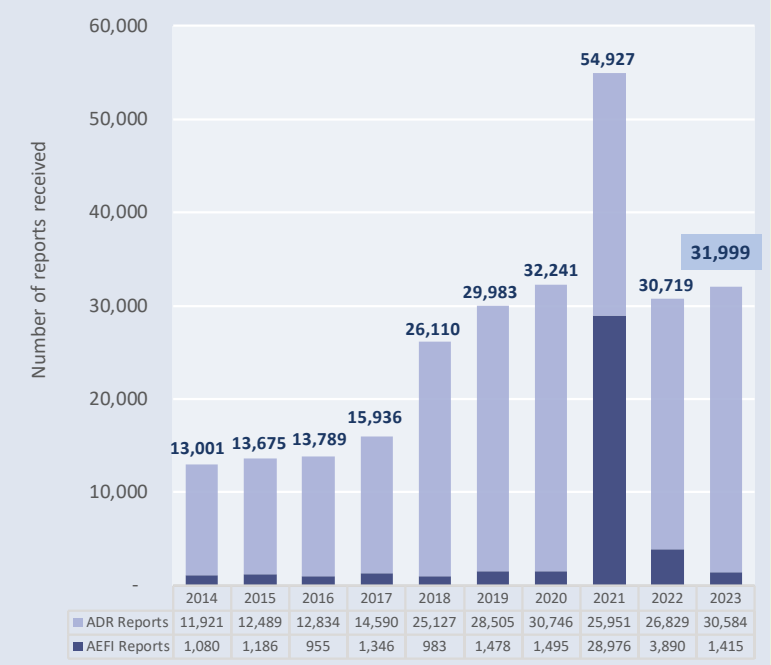
1. WHO, 2004. Pharmacovigilance: ensuring the safe use of medicines. WHO Policy Perspect. Med. 1–6.
2. https://npra.gov.my/index.php/en/guideline-for-pharmacovigilance/1729-malaysian-guidelines-on-good-pharmacovigilance-pratices-gvp-for-product-registration-holders-1st-edition-august-2021.html
3. https://www.gov.uk/guidance/good-pharmacovigilance-practice-gpvp
4. https://www.tga.gov.au/pharmacovigilance-inspection-program

Analysis of ADR/AEFI Reports

In 2023, the National Centre received **31,999 reports** of adverse events (ADR/AEFI), noting a slight increase of 4.2% compared to 30,719 reports in 2022. After filtering out duplicates, follow-up reports, rejected reports, or splitting reports as necessary, a total of **30,491 reports** were recorded in the Malaysian Pharmacovigilance Database (QUEST). Subsequent to causality assessments conducted during MADRAC meetings, in 2023, 19,740 viable new reports* (excluding unregistered/food products) were submitted to the World Health Organisation (WHO) Collaborating Centre for International Drug Monitoring in Uppsala, for inclusion into the VigiBase—the WHO global database of individual case safety reports (ICSRs). The collected data are being continuously monitored for not only changing patterns and trends in any adverse event but also for new safety signals that warrant further evaluation and confirmation.

**This includes reports received by the NPRA in the previous year and does not encompass all reports received in the current year. Due to the meticulous assessment and processing required, followed by causality assessment by MADRAC at quarterly intervals, reports received in a year may be submitted to VigiBase in the following year.*

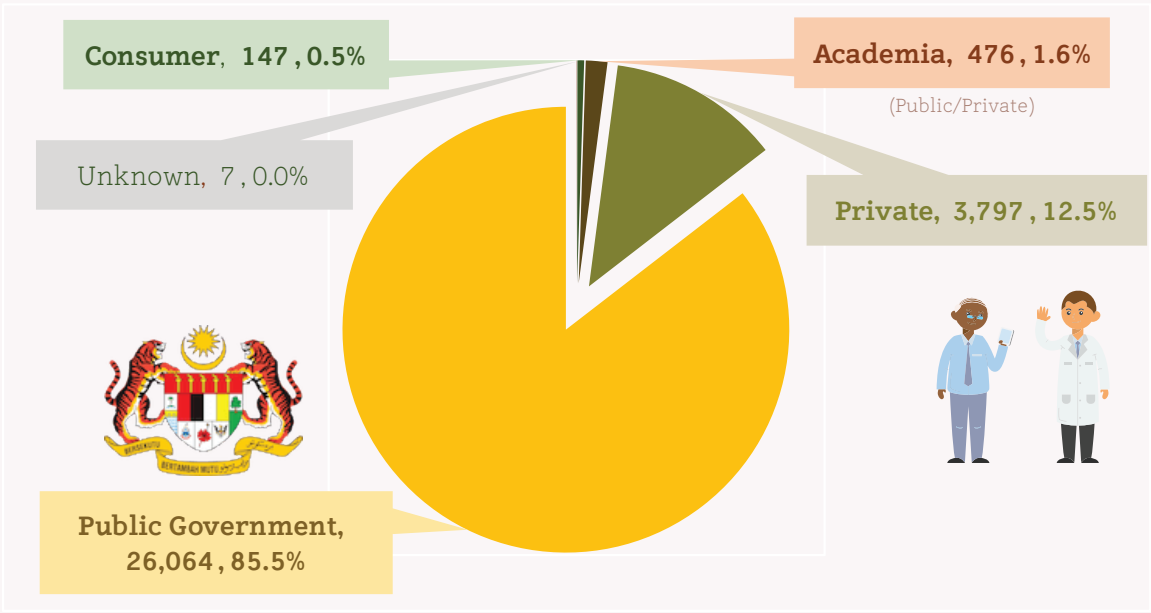
Total Number of ADR and AEFI Reports Received in Malaysia 2014-2023



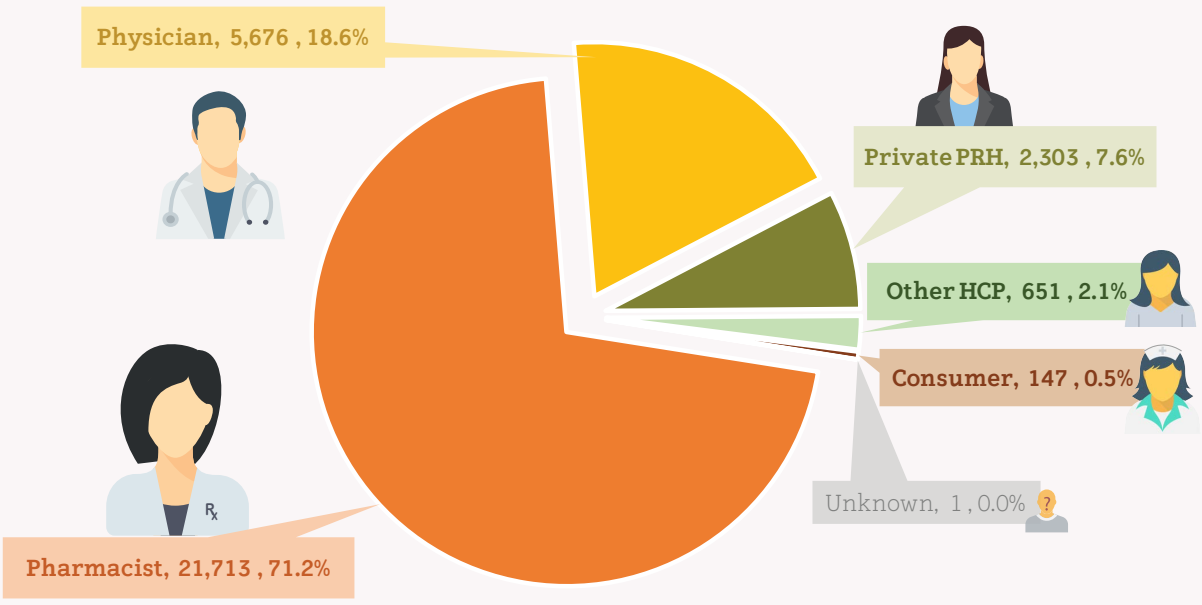
	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
ADR Reports	11,921	12,489	12,834	14,590	25,127	28,505	30,746	25,951	26,829	30,584
AEFI Reports	1,080	1,186	955	1,346	983	1,478	1,495	28,976	3,890	1,415

Note: The apparent surge in 2021 was attributable to the massive influx of AEFI reports following the mass vaccination roll-out under the National Immunisation Program for COVID-19 (PICK) in Malaysia since 24th February 2021.

Distribution of ADR/AEFI Reports Recorded by Sector, 2023*



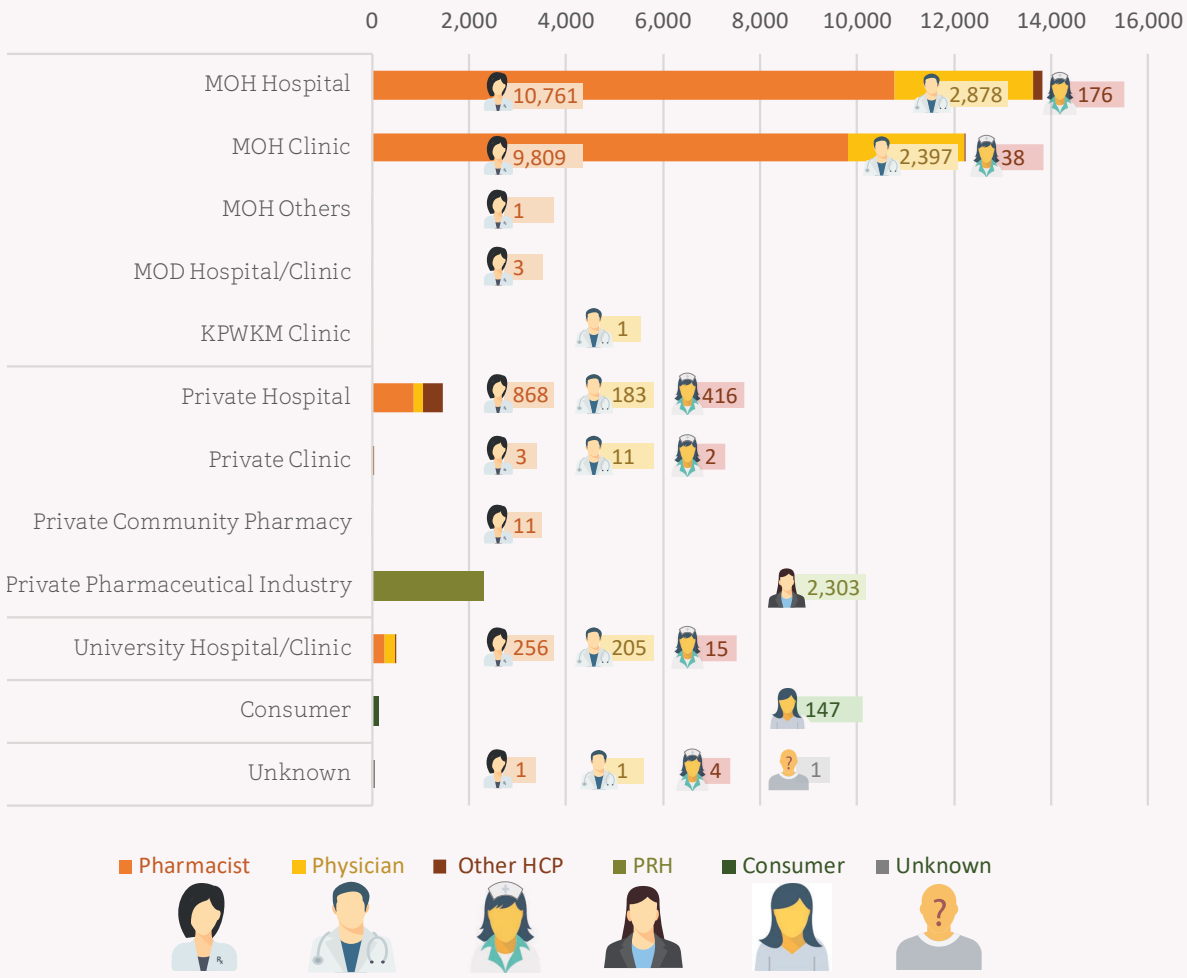
Distribution of ADR/AEFI Reports Recorded By Reporter Qualification, 2023*



HCP: Healthcare professionals; PRH: Product registration holders

*Based on total 30,491 processed ADR/AEFI reports

Distribution of ADR/AEFI Reports Recorded by Institution Type/Reporter Qualification, 2023*

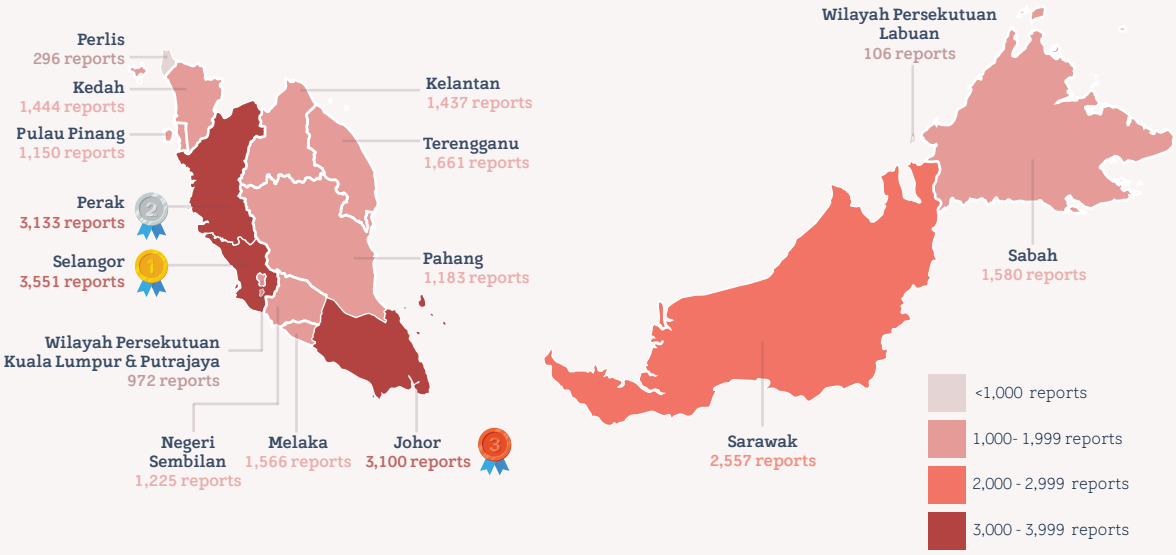


	Public / Government					Private				Academia			
	MOH Hospital	MOH Clinic	MOH Others	MOD Hospital/ Clinic	KPWKM Clinic	Pharmaceutical Industry	Hospital	Clinic	Community Pharmacy	University Hospital/ Clinic	Consumer	Unknown	Total
Pharmacist	10,761	9,809	1	3	-	-	868	3	11	256	-	1	21,713
Physician	2,878	2,397	-	-	1	-	183	11	-	205	-	1	5,676
Other HCP	176	38	-	-	-	-	416	2	-	15	-	4	651
PRH	-	-	-	-	-	2,303	-	-	-	-	-	-	2,303
Consumer	-	-	-	-	-	-	-	-	-	-	147	-	147
Unknown	-	-	-	-	-	-	-	-	-	-	-	1	1
Total	13,815	12,244	1	3	1	2,303	1,467	16	11	476	147	7	30,491

HCP: Healthcare professionals; KPWKM: Ministry of Women, Family and Community Development; MOD: Ministry of Defence; MOH: Ministry of Health; PRH: Product registration holders

*Based on total 30,491 processed ADR/AEFI reports

Distribution of ADR/AEFI Reports Recorded from Ministry of Health (MOH) Facilities, 2023*



Hospital Kuala Lumpur
597 reports

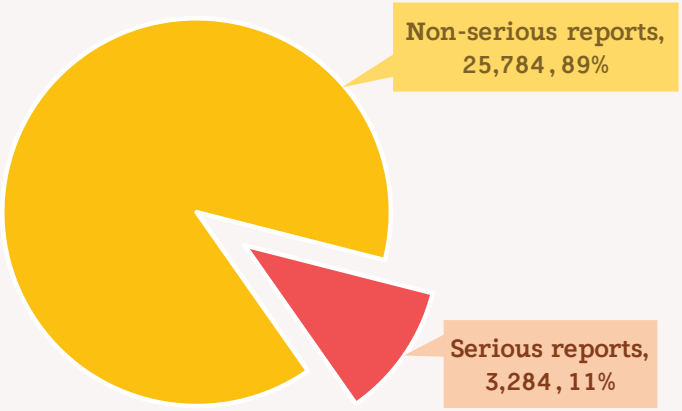
Respiratory Medicine Institute (IPR)
244 reports

National Heart Institute (IJN)
184 reports

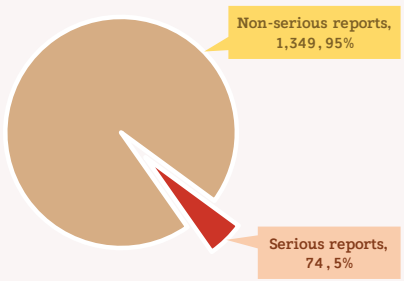
National Cancer Institute (IKN)
74 reports

Distribution of ADR/AEFI Reports Recorded by Case Seriousness, 2023*

ADR Reports



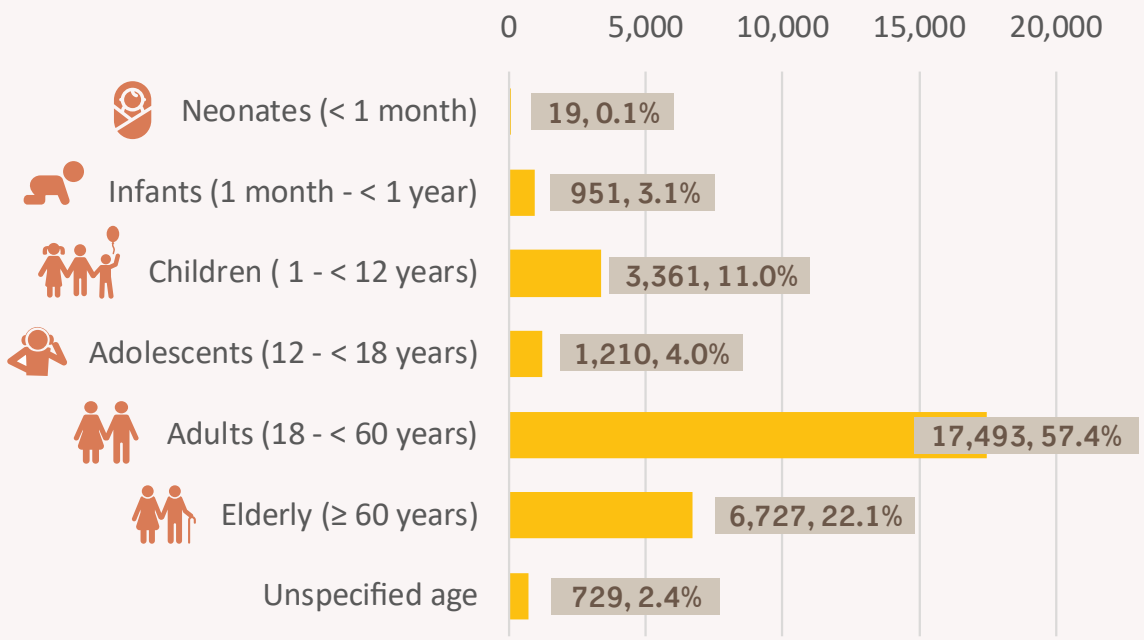
AEFI Reports



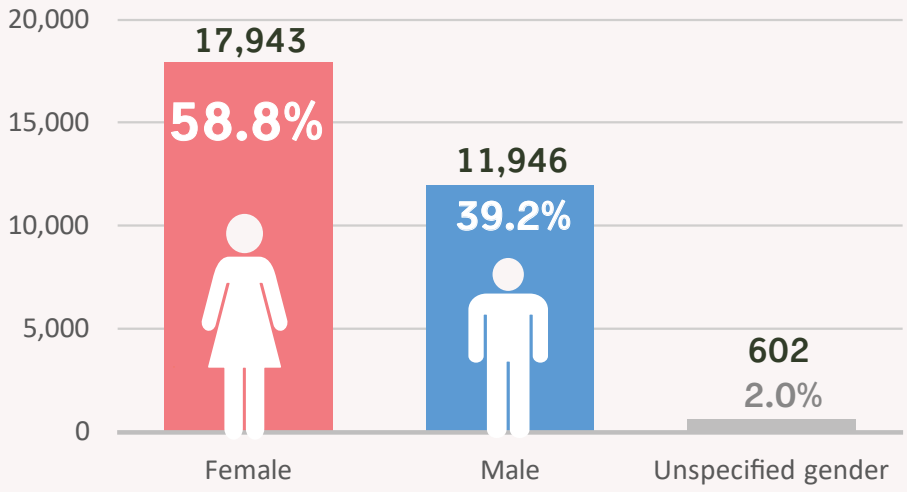
Serious cases include those that require hospitalisation, prolonged existing hospitalisation, are life-threatening, cause persistent or significant disability/incapacity, a congenital anomaly/birth defect, or suspected to cause death

*Based on total 30,491 processed ADR/AEFI reports

Distribution of ADR/AEFI Reports Recorded by Patient's Age Group, 2023*



Distribution of ADR/AEFI Reports Recorded by Patient's Gender, 2023*



*Based on total 30,491 processed ADR/AEFI reports

Number of Products Involved in ADR/AEFI Reports, 2023#

30,073 (93.0%)
Poisons & prescription items

2,120 (6.6%)
Non-poisons

28 (0.1%)
Natural products

125 (0.4%)
Unregistered/Food products

Top 10 Most Reported Route of Administration of the Products Involved, 2023#

Route of Administration	Number (%)
Oral	21,577 (66.7%)
Intravenous (not otherwise specified)	4,742 (14.7%)
Intramuscular	1,790 (5.5%)
Intravenous drip	912 (2.8%)
Subcutaneous	701 (2.2%)
Intravenous bolus	444 (1.4%)
Intraperitoneal	151 (0.5%)
Opthalmic	129 (0.4%)
Topical	128 (0.4%)
Inhalation	128 (0.4%)
Unknown	1,280 (4.0%)

#Based on total 32,346 products involved in 30,491 processed ADR/AEFI reports
Note: A report may involve one or more medicinal products

Top 10 Most Reported Pharmacological Group of the Products Involved, 2023#

1

Anti infectives

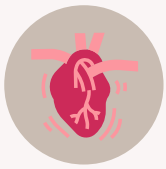
8,671 (26.8%)

2

Analgesics

4,908 (15.2%)

3



Cardiovascular

4,697 (14.5%)

4

Others

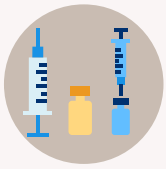
1,942 (6.0%)

5

Anti neoplastics

1,618 (5.0%)

6



Vaccines

1,448 (4.5%)

7

Anti diabetics

1,446 (4.5%)

8

Anti hyperlipidaemic

970 (3.0%)

9

Antiviral

861 (2.7%)

10

Anti tuberculosis

711 (2.2%)

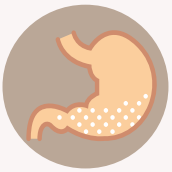
#Based on total 32,346 products involved in 30,491 processed ADR/AEFI reports
Note: A report may involve one or more medicinal products

Top 10 Most Reported MedDRA System Organ Class of the Adverse Drug Reactions (ADR) Recorded, 2023+

1

Skin and subcutaneous tissue disorders
18,145 (36.7%)

2



Gastrointestinal disorders
5,860 (11.8%)

3

General disorders and administration site conditions
5,809 (11.7%)

4

Eye disorders
4,924 (10.0%)

5

Respiratory, thoracic and mediastinal disorders
4,669 (9.4%)

6

Nervous system disorders
3,943 (8.0%)

7

Investigations
1,400 (2.8%)

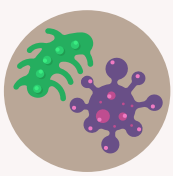
8

Musculoskeletal and connective tissue disorders
801 (1.6%)

9

Cardiac disorders
577 (1.2%)

10



Immune system disorders
541 (1.1%)

+Based on total 49,473 adverse events involved in 29,068 processed ADR reports.
Note: A report may involve one or more adverse events.

Top 10 Most Reported MedDRA System Organ Class of the Adverse Events Following Immunisation (AEFI) Recorded, 2023^

1

General disorders and administration site conditions

1,865 (62.7%)

2

Skin and subcutaneous tissue disorders

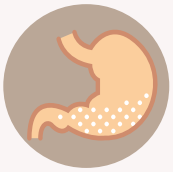
523 (17.6%)

3

Nervous system disorders

160 (5.4%)

4



Gastrointestinal disorders

125 (4.2%)

5

Respiratory, thoracic and mediastinal disorders

68 (2.3%)

6

Musculoskeletal and connective tissue disorders

58 (1.9%)

7

Eye disorders

47 (1.6%)

8

Infections and infestations

35 (1.2%)

9

Psychiatric disorders

32 (1.1%)

10

Metabolism and nutrition disorders

17 (0.6%)

^Based on total 2,976 adverse events involved in 1,423 processed AEFI reports.
Note: A report may involve one or more adverse events.

Safety Signal Detection and Risk Management

Detecting Local Safety Signals

*A **safety signal**, as defined by WHO-UMC, is information suggesting a possible link between a medicine and a new or known side effect, usually based on multiple reports. It does not confirm a causal relationship, but rather serves as a hypothesis that warrants further investigation.*

The process of detecting local safety signals consists of four main steps: signal triage, signal validation and prioritisation, signal assessment, as well as signal review and endorsement. In 2023, the MADRAC endorsed a total of **17 signals**, resulting in **updates of package inserts / consumer medication information leaflets (RiMUP)** for **3 signals** and **risk communication** via MADRAC Bulletin and NPRA website for **4 signals**. The remaining **10 signals** were **closed** as no regulatory actions required at the time of review.

7

Signals resulted in risk minimisation measures

3 **Updates of package inserts / RiMUPs required**

Lamotrigine - Erythema multiforme

Mefenamic acid - Generalised bullous fixed drug eruption (GBFDE)

Doxycycline - Fixed drug eruption (FDE)

4 **Risk communication issued**

Imatinib - Renal disorders

Colistin - Acute kidney injury

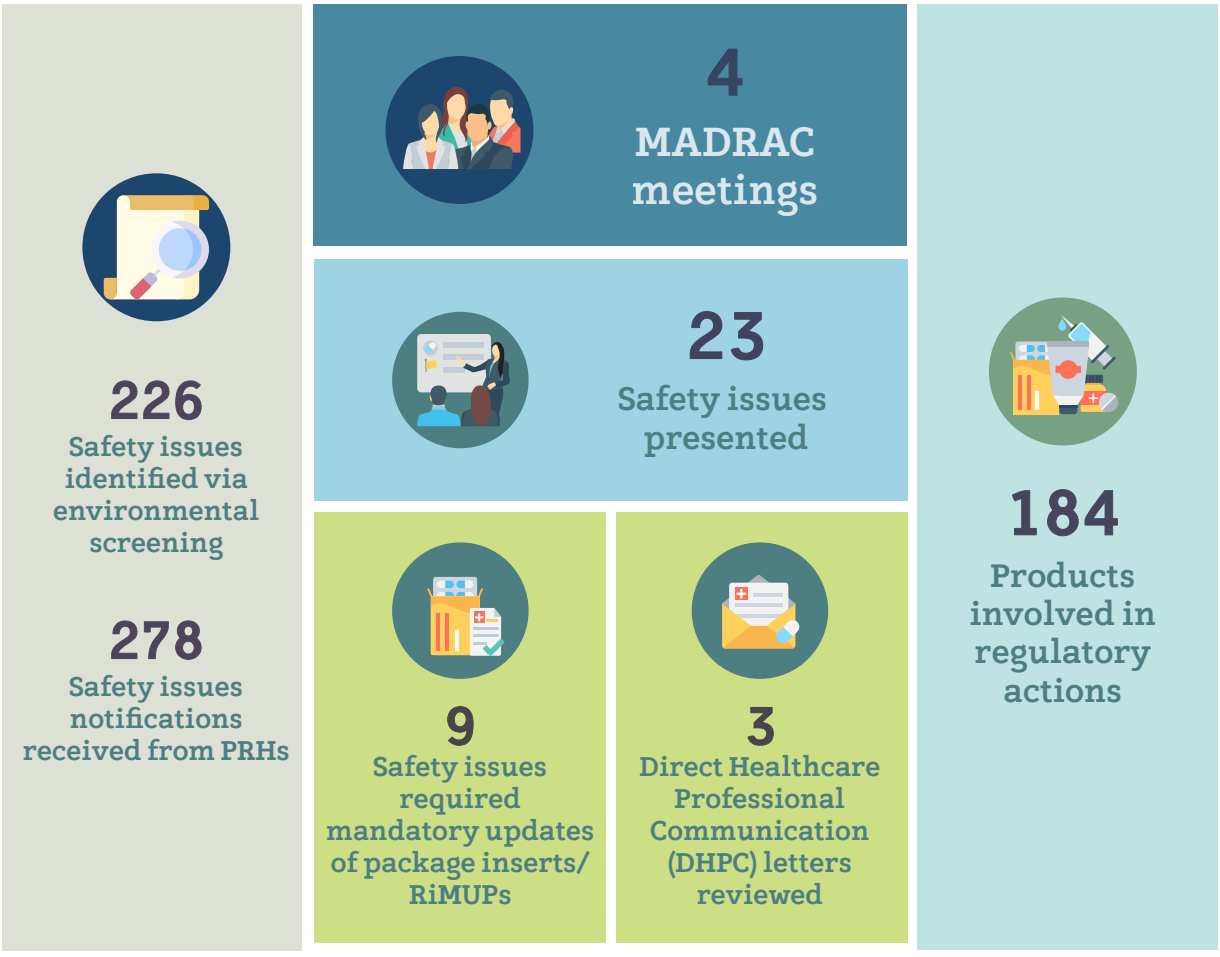
Efavirenz and Tenofovir/Emtricitabine - Drug reaction with eosinophilia and systemic symptoms (DRESS)

Atorvastatin - Photosensitivity

10 **Signals closed for monitoring**

Monitoring Drug Safety Issues

In 2023, a total of **226 drug safety issues** were proactively identified through the environmental screening of published information on reference agencies' websites. Additionally, **278 notifications of safety issues** were received from the product registration holders (PRHs). Following review, **23 safety issues were presented at 4 MADRAC meetings** to determine appropriate risk minimisation measures (refer to the following pages). The majority of these led to updates to the product safety information, including the addition of details related to newly identified safety concerns, harmonisation of product information across all products registered in Malaysia, or strengthening existing product information. **Nine recommendations for mandatory regulatory action** were proposed to the DCA, resulting in directives issued to ensure package inserts and consumer medication information leaflets (RiMUPs) of all products containing the affected active ingredients are updated with the crucial safety information.



MADRAC 185 23 February 2023	DCA Directive	Safety Alert	DHPC	Press statement	Product recall
Griseofulvin Risk of Severe Cutaenous Adverse Reactions (SCARs)	●	●			
Azacitidine Risk of Differentiation Syndrome	●	●			
Valaciclovir Risk of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome	●	●			
Topiramate Risk of Neurodevelopmental Disorder and Congenital Malformation		●			
Pholcodine Risk of Anaphylaxis with Neuromuscular Blocking Agent (NMBA) Use		●		●	●
Diclofenac Suppositories Risk of Acute Necrotising Encephalopathy of Childhood (ANEC)		●			
COMIRNATY (mRNA vaccine) Risk of Heavy Menstrual Bleeding		●			
MADRAC 186 25 May 2023					
Clindamycin (oral and injection) Risk of Acute Kidney Injury	●	●			
Terlipressin Risk of Serious or Fatal Respiratory Failure and Sepsis/Septic Shock in Patients with Type 1 Hepatorenal Syndrome (Type 1 HRS)		●	●		
Statins Risk of Myasthenia Gravis		●			
Third-Generation Aromatase Inhibitors (Anastrozole; Exemestane; Letrozole) Risk of Tendon Disorders		●			
Cephalosporins Risk of Seizures		●			

MADRAC 187 5 September 2023	DCA Directive	Safety Alert	DHPC	Press statement	Product recall
Loperamide Risk of Acute Pancreatitis	●	●			
Topiramate (TOPAMAX) [Updated] Risk of Neurodevelopmental Disorder and Congenital malformation	●	●	●		
Isotretinoin Risk of Psychiatric Disorders and Sexual Dysfunction		●			
Clomiphene Risk of Serious Visual Disturbances Potentially Leading to Blindness		●			
Ibrutinib Package Insert Updates to Dose Modifications for Adverse Reactions and to Special Warnings and Precautions for Use		●	●		
MADRAC 188 30 November 2023					
Metformin Risk of Acute Kidney Injury	●	●			
Imatinib Risk of Thrombotic Microangiopathy	●	●			
Rivastigmine Risk of QT prolongation and Torsade de Pointes	●	●			
Statins (Atorvastatin, Rosuvastatin, Simvastatin) Interaction with Ticagrelor Leading to Increased Risk of Rhabdomyolysis		●			
Domperidone Risk of Psychiatric Withdrawal Events When Used Off-Label for Lactation Stimulation		●			

Assessment of Drug Safety Documents

Periodic Benefit-Risk Evaluation Report (PBRER)/ Periodic Safety Update Report (PSUR)

For the first five years post-registration, product registration holders (PRHs) are required to submit Periodic Benefit-Risk Evaluation Reports/ Periodic Safety Update Reports (PBRERs/PSURs) on newly registered products, namely New Drug Products (NDPs) and Biologic products. PBRERs/PSURs contain information on the product safety profile in countries where it is registered, and any changes or new findings related to product safety. In addition, new COVID-19 vaccines and treatment were also required to submit Monthly Safety Summary Reports (MSSRs) as per their conditional registration requirement.

In 2023, assessment was conducted on **302 PBRERs** and **MSSRs** pertaining to **236 products**, including **141 new drug products** and **95 biologic products**. Thereafter, **19% (45/236) of these products underwent package insert updates** to incorporate the latest safety information.

Risk Management Plan (RMP)

A Risk Management Plan (RMP) is a detailed description of the risk management system for a product. After registration, an updated RMP for New Drug Products (NDPs) and Biologic products is required to be submitted by the product registration holder when there is a significant change in the safety specification.

In 2023, a total of **102 RMPs** were assessed. Additional risk minimisation measures mainly in the form of educational materials targeted for healthcare professionals and patients were also reviewed. The NPRA reviewed and approved **46 educational materials** involving **14 products** in 2023.

Drug Safety Communication

Publications

MADRAC Bulletin

Starting in 2023, the MADRAC Bulletin transitioned from a quarterly to a bi-monthly publication. It aims to provide a curated selection of local safety signals and articles discussing individual case safety reports (ICSRs), intended to raise awareness among healthcare professionals. The bulletin also features local pharmacovigilance-related activities and includes summaries of directives based on safety issues advised by the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) and endorsed by the Drug Control Authority (DCA), along with safety alerts published on the NPRA website.

In 2023, NPRA published and distributed **six issues** of the MADRAC Bulletin, all of which are available on the NPRA website under the MADRAC Bulletin section.

Safety Alerts

Safety Alerts are concise drug-related articles published in the NPRA website which are intended to alert healthcare professionals on new drug safety issues that arise as a result from drug safety reviews by NPRA and other international regulatory agencies. This communication is a form of risk minimisation measure taken to reduce the risk of adverse events of new and existing registered products in Malaysia.

In 2023, NPRA has published **19 safety alerts** to highlight drug safety issues. The full list of safety alerts is available on the NPRA website under the Safety Alerts Section.

Direct Healthcare Professional Communication (DHPC) Letters

In addition to the publications listed above, Direct Healthcare Professional Communication (DHPC) letters, previously known as “Dear Doctor letters”, are used to communicate recent safety information to healthcare professionals. Such instances include important new or emerging risks, important changes in prescribing information, new contraindications, suspension or withdrawal of product registrations, and product quality or availability issues that may possess potential detrimental effects on patient care. DHPC letters submitted by the product registration holders are carefully reviewed and approved by NPRA before being distributed.

In 2023, a total of **six DHPC letters** were reviewed and approved by NPRA.

Electronic Mailing List

The **NPRA Safety Information Mailing List**, an electronic mailing list, was established in 2014 for healthcare professionals in an effort to ensure wider and faster spread of information. This mailing list is managed by the Pharmacovigilance Section and currently consists of **more than 2,750 individuals**, including doctors, dentists, pharmacists, nurse, assistant medical officers, assistant pharmacists, regulatory affairs professionals, academicians, and journal editors.

Consumer Medication Information Leaflets

Consumer Medication Information Leaflets, otherwise known as ***Risalah Maklumat Ubat untuk Pengguna*** **(RiMUP)** are a source of information for consumers, containing advice on how to use the medicines as well as important warnings/precautions in more layman and easy-to-understand terms. RiMUPs are prepared in *Bahasa Melayu* and English by product registration holders, and are reviewed and approved by the NPRA.

In 2023, a total of **262 RiMUPs** were approved by the Pharmacovigilance Section in NPRA and are available on the NPRA website via Product Search.

Pharmacovigilance Capacity Building, Collaborations, Research, and Initiatives

Highlights of Training & Local Collaborations

Over the years, the NPRA has consistently provided training or sharing sessions on a wide range of pharmacovigilance topics to various stakeholders. These initiatives have reached healthcare providers in both the public and private sectors, pharmaceutical companies, authorities, and university students.

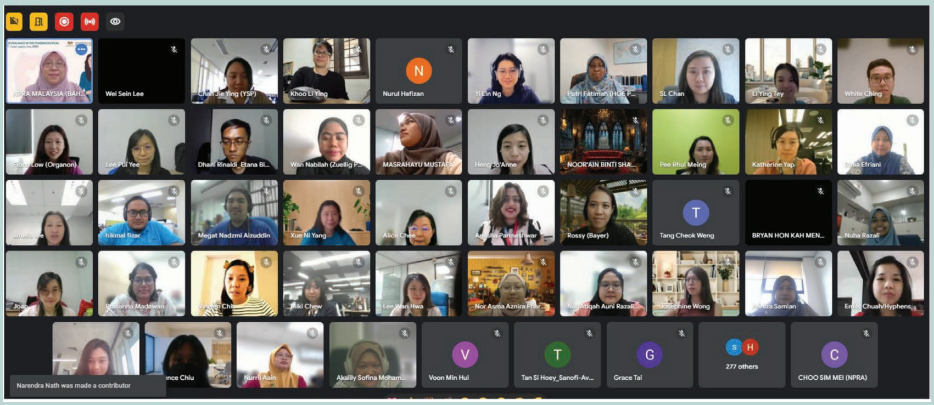
NPRA's National Training Workshops for Local Stakeholders

In 2023, the Pharmacovigilance Section of NPRA successfully hosted two significant virtual training workshops, engaging over 450 healthcare professionals and industry stakeholders across Malaysia. These sessions aimed to strengthen awareness and understanding of pharmacovigilance and regulatory practices to support the safer use of medicines nationwide.

The first seminar, "*Pharmacovigilance for Safer Use of Medicines*" (6 April 2023), was attended by over 250 private-sector pharmacists. It provided comprehensive insights into key pharmacovigilance activities—ADR/AEFI monitoring, safety signal detection, risk management, and risk communication—while guiding participants on constructing high-quality reports and understanding how safety signals are detected and managed.

Seminar 1: Pharmacovigilance for Safer Use of Medicines

The second seminar, "***Overview of Registration and Post-Marketing Activities of Registered Products in Malaysia***" (24 October 2023), attracted more than 200 public-sector healthcare professionals. The programme covered regulatory aspects such as fast-track registration, product quality monitoring, and pharmacovigilance processes, including the importance of ADR/AEFI reporting, signal detection, and the implementation of risk minimisation measures.



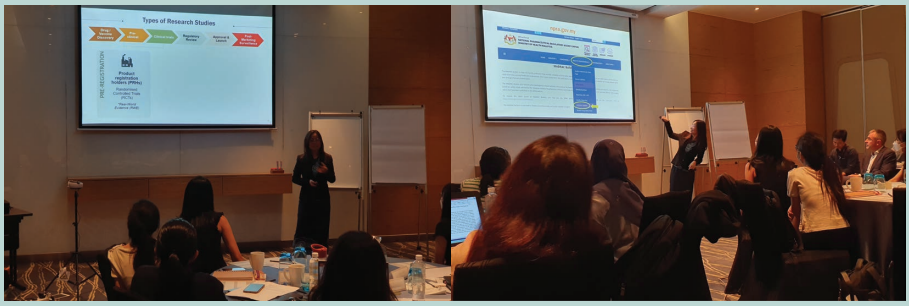
Seminar 2: Overview of Registration and Post-Marketing Activities of Registered Products in Malaysia

Both seminars received positive feedback and contributed to strengthening the culture of medicine safety in Malaysia.

Local Engagement and Collaborations

Throughout the year of 2023, NPRA pharmacovigilance officers received gracious invitations from numerous esteemed agencies to share our expertise through talks and presentations on subjects related to medication safety. A total of **18 presentations** were delivered over the course of the year, serving to enlighten and inform the target audiences on critical aspects of pharmacovigilance. Below are selected examples of the engaging talks delivered:

Monash Pharmacoepidemiology Workshop [11 May 2023]



NPRA pharmacovigilance officer delivered a talk on *Research Studies on Medication and Vaccine Safety in Malaysia: Regulatory Affairs Perspective* to the research community.

Malaysian Organisation of Pharmaceutical Industries (MOPI) Pharmacovigilance Workshop [16 May 2023]

NPRA pharmacovigilance officer delivered a presentation to industry stakeholders on Voluntary Good Pharmacovigilance Practices (GVP) Inspections.

MAHSA International Pharmacy Conference (Mi-PHARM) 2023

On 6–7 October 2023, officers from the NPRA participated as speakers at the MAHSA International Pharmacy Conference, held at MAHSA University, Bandar Saujana Putra.

The two officers delivered presentations titled “Safety Signal Detection in Pharmacovigilance” and “Risk Minimisation Measures to Enhance Drug Safety” respectively. Their sessions aimed to raise awareness and understanding of pharmacovigilance practices among future healthcare professionals.

The conference was attended by over 100 participants, comprising students and lecturers primarily from the Faculty of Pharmacy and Biomedical Sciences. Feedback from attendees indicated that the sessions were highly informative and eye-opening, offering valuable insights into the multifaceted roles of pharmacovigilance in ensuring medicine safety.

International Participation & Collaborations

Indo-Pacific Regulatory Strengthening Program (RSP) Regulatory Practice Workshop in Therapeutic Goods Administration (TGA) Canberra

From 20 to 23 February 2023, four officers from the NPRA participated in the Indo-Pacific Regulatory Strengthening Program (RSP) Regulatory Practice Workshop. Hosted by the Therapeutic Goods Administration (TGA) in Canberra, Australia, the event brought together approximately 60 participants across the region to foster knowledge exchange and strengthen collaborative regulatory practices.

During the workshop, NPRA's contribution was highlighted through a key presentation by Dr. Azuana Ramli from the Pharmacovigilance Section. Her session, titled *"Safety Signal Detection in Pharmacovigilance: The Malaysia Experience,"* provided a comprehensive overview of Malaysia's approach to signal detection. The presentation covered key methodologies, signal sources, operational workflows, and selected case studies, and specific case studies, offering valuable insights into our nation's robust pharmacovigilance system.

NPRA representatives pictured alongside TGA representatives in Canberra

Peiking University (PKU) -Asia-Pacific Economic Cooperation (APEC) Pharmacovigilance Seminar

An NPRA pharmacovigilance officer participated in the Peking University (PKU)–Asia-Pacific Economic Cooperation (APEC) Pharmacovigilance Seminar, held virtually from 15 to 19 May 2023. The seminar gathered international regulators from agencies including the U.S. Food and Drug Administration (US FDA), European Medicines Agency (EMA), Pharmaceuticals and Medical Devices Agency (PMDA, Japan), National Medical Products Administration (NMPA, China), and Korea Institute of Drug Safety & Risk Management (KIDS, South Korea), as well as experts from the International Society of Pharmacovigilance (ISoP).

The comprehensive programme covered key pharmacovigilance topics, including implementation of ICH guidelines, individual case safety report (ICSR) assessment, signal detection, benefit–risk evaluation, and risk communication. This engagement enhanced participants' capacity in global pharmacovigilance practices and supported regional regulatory collaboration.

The officer actively participated in seminar discussions and a practicum exercise on a hypothetical COVID-19 treatment, contributing to group work and presenting on key areas including risk identification, regulatory recommendations for various indications, and proposals for additional pharmacovigilance and risk minimisation strategies.

Work Visit from Department of Pharmaceutical Services, Ministry of Health, Brunei Darussalam

On 20 June 2023, the NPRA welcomed two officers from the Department of Pharmaceutical Services, Ministry of Health, Brunei Darussalam, for an official work visit. This significant engagement underscored NPRA commitment to strengthen collaborative ties and facilitate knowledge exchange on key regulatory functions, particularly in the areas of pharmaceutical quality, product registration, and Good Manufacturing Practice (GMP) in Malaysia.

The visit served as a valuable platform for NPRA to showcase its regulatory framework. NPRA representatives delivered comprehensive briefings on the agency's organisational structure, highlighting the core functions of its three main centres. The engagement also featured an overview of Malaysia's pharmacovigilance system, further enriching the visitors' understanding of NPRA's regulatory scope and operations.

KIDS-APEC Pharmacovigilance Center of Excellence (CoE) Training 2023

From 6 to 8 September 2023, five officers from the National Pharmaceutical Regulatory Agency (NPRA) participated in the virtual Korea Institute of Drug Safety and Risk Management (KIDS) – Asia-Pacific Economic Cooperation (APEC) Pharmacovigilance Centre of Excellence (CoE) Training Program. This professional training initiative aimed to enhance the capacity of regulators by promoting a shared understanding of current pharmacovigilance practices, facilitating the implementation of effective PV systems, and strengthening regulatory capabilities across the APEC region and beyond.

The program featured expert speakers from leading global regulatory authorities and organisations, including the United States Food and Drug Administration (US FDA), the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA), the European Medicines Agency (EMA), KIDS, IQVIA, the International Society of Pharmacovigilance (ISoP), and the Uppsala Monitoring Centre (UMC). The training included representatives from national regulatory agencies of several countries, including Malaysia, Azerbaijan, Mexico, Singapore, and Indonesia.

The training covered a broad range of key topics, beginning with an overview of Korea's pharmacovigilance system and PV for innovative biotherapeutics. Discussions included the US experience with COVID-19 vaccines, strategies to enhance adverse event reporting, and advancements in medication error detection and data mining. Sessions also addressed the use of routinely collected health data for signal validation, risk management planning for cell and gene therapies, and critical safety measures such as product recalls, revocations, and effective risk communication across healthcare systems.

The program concluded with a practical group exercise on risk communication, allowing participants to share and refine their approaches to effectively disseminating safety information.

WHO Regulatory Training Course at the Swiss Agency for Therapeutic Products (Swissmedic), Bern, Switzerland

From 23 to 27 October 2023, three officers from the National Pharmaceutical Regulatory Agency (NPRA) participated in a regulatory training course hosted by Swissmedic in Bern, Switzerland, in collaboration with the World Health Organization (WHO). The course aimed to strengthen the capacity of participating National Regulatory Authorities (NRAs) through knowledge exchange and practical insights in three key regulatory areas: Quality Management Systems (QMS), Registration and Marketing Authorisation (MA), and Vigilance (PVL), aligned with international standards and best practices.

NPRA's delegation included one officer for each focus areas. The five-day course fostered a rich environment for peer learning and cross-country collaboration, bringing together regulators from Bangladesh, Ghana, Indonesia, Malaysia, Nigeria, South Africa, Uganda, and Zambia.

The training comprised both joint and specialised sessions. Days 1 and 5 featured shared modules for all participants, while Days 2 to 4 were dedicated to targeted training in the respective focus areas. Swissmedic experts, together with WHO representatives, led the sessions and shared practical insights based on current regulatory practices.

The NPRA's pharmacovigilance officer attended the Vigilance track, covered core elements of post-marketing safety surveillance. Topics included an overview of the Swiss Adverse Event Reporting System, signal detection and management processes, oversight of Risk Management Plans (RMPs) and Periodic Benefit-Risk Evaluation Reports (PBRERs), as well as the conduct of pharmacovigilance inspections and post-market surveillance. The module also introduced specialised areas such as medical device vigilance and haemovigilance.

This comprehensive training enhanced NPRA's regulatory capacity and reinforced its commitment to aligning with global best practices in ensuring product quality, safety, and efficacy.

International Society of Pharmacovigilance (ISoP) 22nd Annual Meeting, Bali, Indonesia

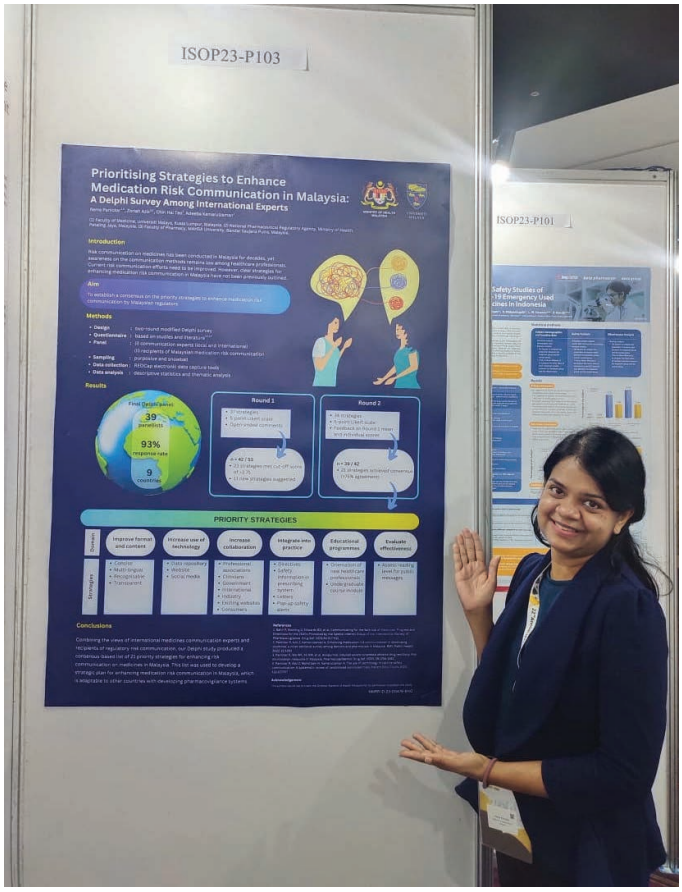
The 22nd Annual Meeting of the International Society of Pharmacovigilance (ISoP) was held from 6 to 9 November 2023 in Bali, Indonesia. One officer from the NPRA Pharmacovigilance Section represented Malaysia at the event.

ISoP is a global, non-profit professional society dedicated to promoting the safe and effective use of medicinal products. With over 1,000 members across 108 countries, the society serves as a platform for advancing pharmacovigilance science and practice worldwide.

Themed "*Putting Patients First in Pharmacovigilance: International Perspectives from the Global South*", the meeting featured a wide range of topics including patient engagement, vaccine pharmacovigilance, effective risk communication strategies, and professional development in the field.

With more than 400 participants from around the world, the event provided an invaluable platform for knowledge exchange, global collaboration, and networking among pharmacovigilance professionals, further strengthening NPRA's engagement with the international regulatory community.

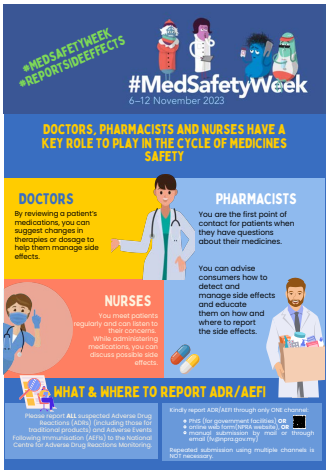
A representative from NPRA's Pharmacovigilance Section presented a research poster entitled "*Prioritising Strategies to Enhance Medication Risk Communication in Malaysia: A Delphi Survey Among International Experts.*" This poster described a Delphi study conducted in collaboration with NPRA, combining the views of medicines communication experts and recipients of Malaysian regulatory risk communication to develop a list of priority strategies for enhancing risk communication on medicines in Malaysia.

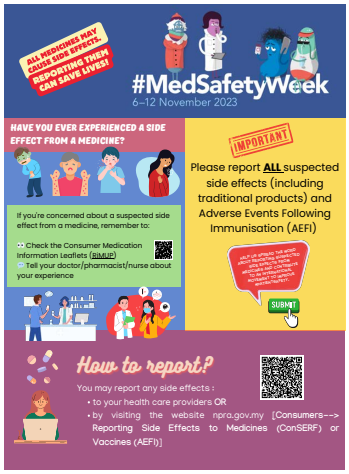


#MedSafetyWeek 2023: How Patients and Healthcare Professionals Make Safety Work

From 6 to 12 November 2023, NPRA representing Malaysia, actively engaged in the global #MedSafetyWeek campaign. Initiated by the World Health Organisation (WHO)-Uppsala Monitoring Centre (UMC), this year's campaign saw a remarkable collaboration of 100 organisations across 88 countries. Operating under the motto "*Who can report?*", the campaign aimed to further increase the safety of medicines by encouraging patients and calling upon healthcare professionals to report suspected adverse drug reactions.

Various communication materials in English and Malay languages, including infographics, animation videos, and posters, were collaboratively prepared and disseminated through diverse channels during the campaign week. This underscores Malaysia's commitment to strengthening pharmacovigilance and promoting a culture of medicine safety across the public, healthcare providers, and industry.

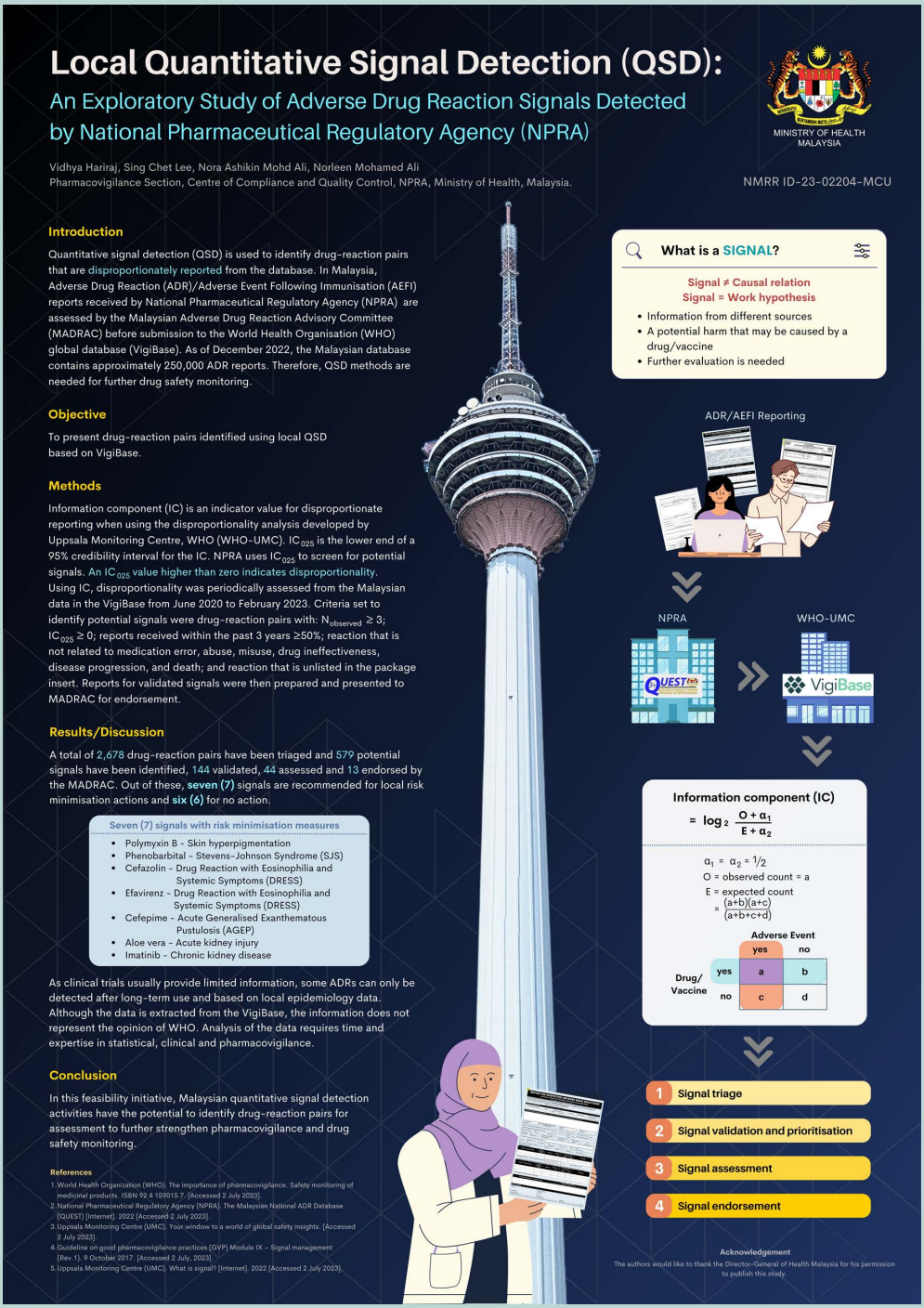




Research and Publications

Poster Presentation

National Regulatory Conference (NRC) 2023



A pharmacovigilance officer enthusiastically presenting a research poster to the Minister of Health, Director-General of Health, Deputy Director-General of Health (Pharmaceutical Services), and Director of NPRA at NRC 2023

Abstract for research titled "Local Quantitative Signal Detection (QSD): An Overview of Adverse Drug Reaction Signals Detected by National Pharmaceutical Regulatory Agency (NPRA)" can be assessed in ***Pharmacy Research Reports Volume 6 Supplement Issue November 2023***

Journal Publications

Thrombocytopenia and venous thromboembolic events after BNT162b2, CoronaVac, ChAdOx1 vaccines and SARS-CoV-2 infection: a self-controlled case series study

Scientific Reports 2023; 13, Article Number: 20471

Hearing loss and tinnitus associated with COVID-19 vaccines: An analysis from the national pharmacovigilance database in Malaysia.

Asian Pacific Journal of Tropical Medicine 2023; 16(7): 289-295

Carbamazepine-induced Severe Cutaneous Adverse Drug Reactions: A 21-year comparison between children and adults in Malaysia

The Journal of Clinical Pharmacology 2023; 63(10): 1126-1132

CPD Points for Adverse Event Reporting by pharmacists

As part of efforts to increase the quantity and quality of adverse event (AE) reports, in particular from private sector healthcare professionals, beginning January 2016, pharmacists are eligible to claim Continuing Professional Development (CPD) points for the submission of quality AE reports.

In 2023, a total of **169 reports received** from pharmacists in the private sector were evaluated and **133 reports** were approved for CPD points claim.

--- The End ---

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