2022

PHARMACOVIGILANCE ANNUAL REPORT

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG REGULATION AND RESEARCH

Food and Drug Administration PHILIPPINES

BAGONG PILIPINAS

CONTENTS

THE PHILIPPINE PHARMACOVIGILANCE SYSTEM

Mandated to ensure the safety, efficacy, and quality of health products, the Food and Drug Administration (FDA) is the regulatory authority under the Department of Health (DOH). Our mission is to guarantee the safety, quality, purity, and efficacy of health products in order to promote the right to health of the general public.

The FDA monitors the safety of medicines through a nationwide system of collecting suspected adverse drug reaction reports (pharmacovigilance). As a member of the World Health Organization (WHO) Programme for International Drug Monitoring (PIDM), the FDA has instituted the Pharmacovigilance (PV) Section under the Product Research and Standards Development Division (PRSDD) of the Center for Drug Regulation and Research (CDRR). The Section is in charge of monitoring the safety of medicines including vaccines authorized by the FDA.

The scope of PV includes but not limited to the following:

- suspected Adverse Drug Reactions (ADR) on the use of drug products, including Adverse Events Following Immunization (AEFI)
- lack of expected efficacy
- suspected ADR as a result of off-label use
- misuse and abuse
- medication error
- suspected ADR due to quality defects
- adverse outcome from use during pregnancy

ADR reports are collected and evaluated by the FDA and relevant Market Authorization Holders (MAHs). If there is an issue identified through the PV system, appropriate steps are taken to reduce the level of any associated risk.

For more information on pharmacovigilance, you may visit our website at https://www.fda.gov.ph/pharmacovigilance/.

PHARMACOVIGILANCE TOOLS

As a member of the PIDM, Uppsala Monitoring Centre (UMC), the WHO Collaborating Centre for PIDM, provides its member countries with tools, resources, and services to help translate data to better clinical practices and health outcomes.

VigiFlow

The national database for ADR reports. It is a system for recording, processing, and sharing reports of adverse events. WHODrug and Medical Dictionary for Regulatory Activities (MedDRA) are used in coding medical terminologies to allow international comparison of reports.

eReporting

A way of reporting ADR electronically for healthcare professionals, patients, consumers, programs, and industry.

- Primary eReporting - the online reporting system for healthcare professionals (HCPs), patients, and consumers.

- Industry eReporting - allows MAHs to submit Individual Case Safety Reports (ICSRs) directly and securely to the FDA via the VigiFlow.

- Vaccine eReporting - an additional online reporting tool for the DOH facilities to report AEFI from COVID-19 vaccines.

VigiBase

The WHO global database of ICSRs. It serves as the repository for millions of ICSRs shared by its member countries. It holds data on conventional medicines, traditional and herbal medicines, biologicals, and vaccines.

VigiLyze

The search and analysis tool used to retrieve global ICSR data from VigiBase. It supports the national centers' processes for signal detection and signal management through its analysis of PVdata.

VigiAccess

Provides public access to VigiBase statistics. You may visit it through this link: https://www.vigiaccess.org.

WHODrug

Maintained by UMC, WHODrug is a drug dictionary that contains standardized medicine information. This is used in coding medicine information in an ADR/AEFI reports.

MedDRA

Medical Dictionary for Regulatory Activities (MedDRA) is a standardized medical terminology, developed by the International Council for Harmonization (ICH), that is used internationally by regulators and stakeholders to code medical information.

ADVERSE DRUG REACTION DATA

A total of 29,637 Adverse Drug Reaction (ADR) reports, including adverse events following immunization (AEFI), were received, assessed, and processed by the FDA for the year 2022 with a reporting rate of 26.56 reports per 100,000 population. This number is almost 2x lower compared to the reports received in 2021. The decline on the number of reports is attributable to the decreasing COVID-19 vaccine coverage as a big portion of the population is already fully vaccinated. Suspected AEFI to COVID-19 vaccines account for 85.48% of the reports.

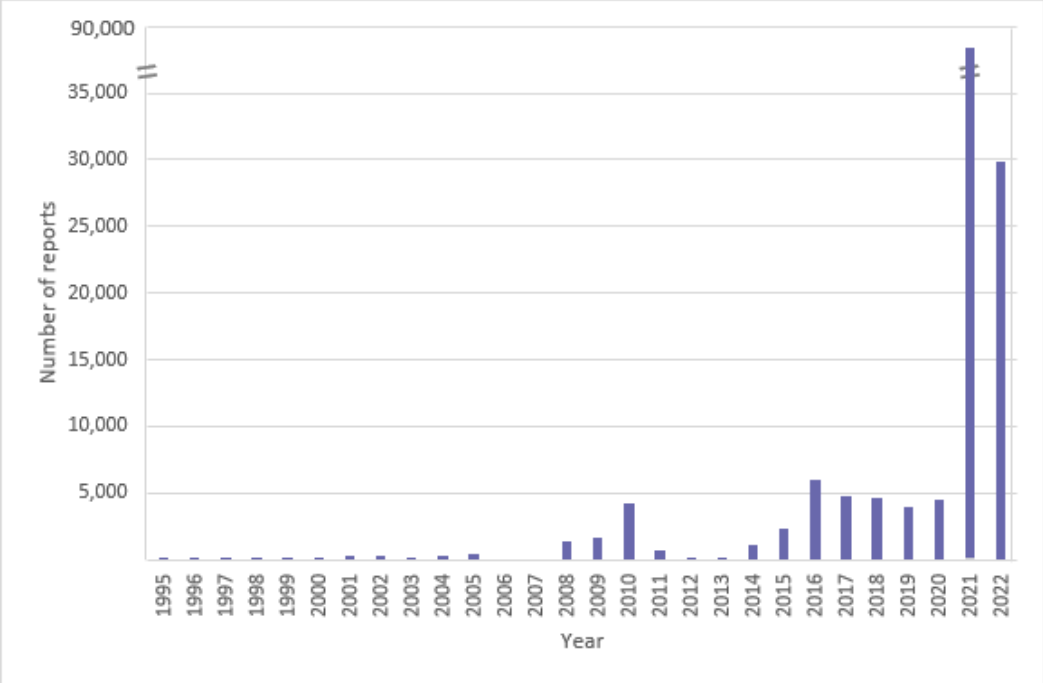


Figure 1. ADR reports over the years

Reports from different DOH programs make up for 82.65% of all reports submitted, 11.92% from pharmaceutical companies, 4.31% from healthcare professionals and hospitals, and 1.13% from patients/consumers.

Out of the total reports received, 28.23% were serious, 71.42% were non-serious, and 0.35% unknown seriousness criteria. A report is considered serious if it results to any of the following: in-patient hospitalization or prolongation of existing hospital stay, significant disability/incapacity, life threatening and death, birth defect or congenital

malformations, and those events that are considered to be medically important. The top reported reactions were:

- Pyrexia
- Vaccination site pain
- Cough
- Headache
- Dyspnea
- Dizziness
- Blood pressure increased
- COVID-19 (breakthrough)
- Nasopharyngitis
- Rash

Demographics

Below is the distribution of the reports by sex and age:

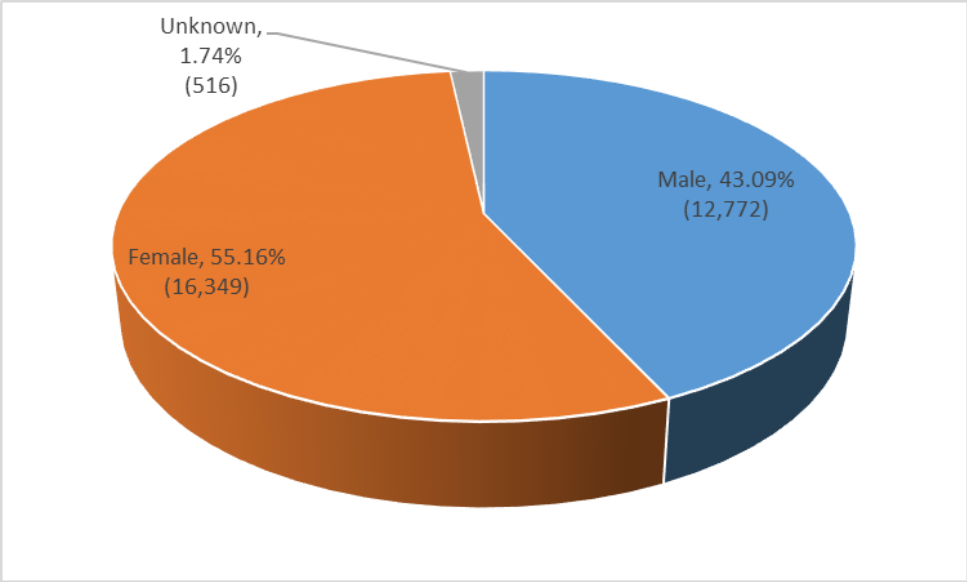


Figure 2. Report distribution by gender

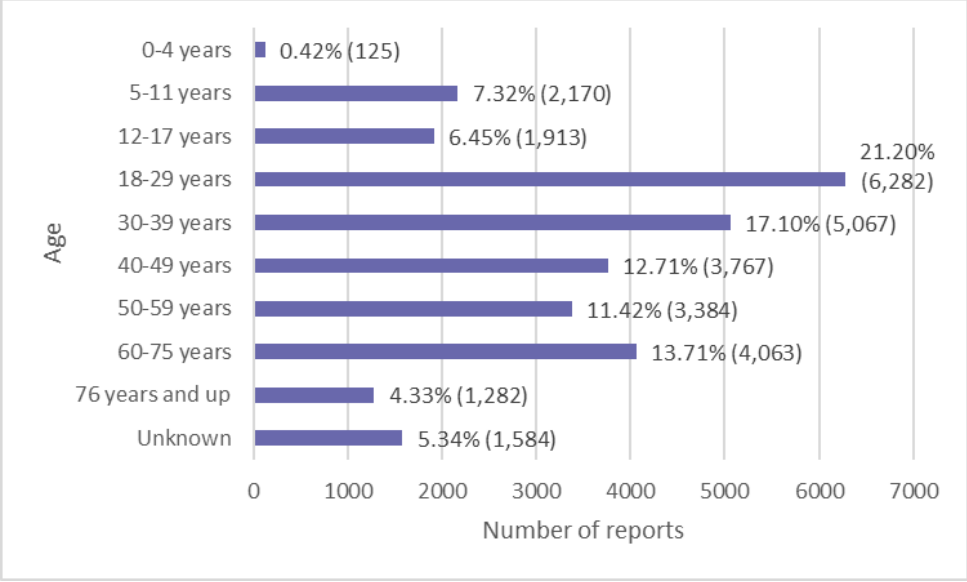


Figure 3. Report distribution by age

DOH Programs

National Tuberculosis Control Program (NTP)

There were 168 reports from NTP for 2022: 77 reports were tagged as serious, 55 reports were non-serious, and five (5) reports with unknown seriousness criteria. The top reported reactions include:

- Hemoglobin decreased
- Hepatic enzyme increased
- Hepatotoxicity
- Electrocardiogram QT prolonged
- Hypoesthesia, dizziness

Tuberculosis (TB) medicines reported as either suspect or concomitant drugs include a combination of the following.

- Bedaquiline (Bdq)
- Clofazimine (Cfz)
- Cycloserine (Cs)
- Delamanid (Dlm)
- Ethambutol (E)
- Isoniazid (Inh)
- Levofloxacin (Lfx)
- Linezolid (Lzd)
- Prothionamide (Pto)
- Pyrazinamide (Z)
- Rifampicin (R)

According to the NTP Manual of Procedures (6th edition), medical management for TB consists of the following:

1. Designation to an appropriate treatment plan,
2. Monitoring of response to treatment, and
3. Monitoring and management of adverse events.

Below are the treatment regimens for Multi-Drug Resistant (MDR)-TB and Drug Resistant (DR)-TB:

Table 1: Treatment regimen for MDR-TB and DR-TB

Regimen name	Type of DR-TB	Regimen
Standard Short All Oral Regimen (SSOR)	MDR-TB and Rifampicin Resistant (RR)-TB	4-6 months: Lfx-Bdq (6)-Cfz-Pto-E-Z-HdH* 5 months: Lfx-Cfz-Z-E
Standard Long All Oral Regimen for Fluoroquinolone (FQ) Susceptible (SLOR-FQ-S)	MDR-TB and RR-TB (No FQ resistance)	6 months: Lfx-Bdq-Lzd-Cfz 12-14 months: Lfx-Lzd-Cfz
Standard Long All Oral Regimen for FQ Resistance (SLOR FQ-R)	MDR-Tb and RR-TB eligible to SLOR (with FQ resistance)	6 months: Lzd-Bdq-Dlm-Cfz-CS 12-14 months: Lzd-Cfz-Cs
Individualized Treatment Regimen (ITR)	Retreatment MDR-TB and RR-TB cases (not legible to SSOR nor SLOR)	Construct to have at least 4-5 likely effective drugs

Source: NTP Manual of Procedures (6th edition)
*HdH: High dose isoniazid

National HIV, AIDS, and STI Prevention and Control Program (NASPCP)
A total of 94 reports were received from NASPCP for 2022: 28 reports were tagged as serious, 64 reports were non-serious, and 2 reports with unknown seriousness criteria. The top reported reactions include:

- Dizziness
- Blood creatinine increased
- Dyslipidemia, insomnia, depression
- Red blood cell count increased, nausea, blood cholesterol increased
- Abnormal dreams, blood triglycerides increased, anxiety, rash, headache, somnolence

Medicines under the program reported as either suspect or concomitant drugs include a combination of the following:

- Abacavir
- Dolutegravir
- Efavirenz
- Emtricitabine
- Lamivudine

- Lopinavir
- Ritonavir
- Tenofovir
- Zidovudine

The Research Institute for Tropical Medicine had the most submitted reports for 2022 and sends reports quarterly. While the following HIV facilities submit reports spontaneously:

- Antipolo Social Hygiene Clinic
- Imus Social Hygiene Clinic
- Lily by Loveyourself
- Makati Medical Center
- Our Lady of Lourdes Hospital
- Quezon Medical Center- Live Positive Wellness Hub
- Research Institute for Tropical Medicine
- SAIL Clinic (Makati and Calamba)
- Southern Philippines Medical Center
- The Green Clinic

National Family Planning Program

One (1) report was received from the Family Planning Program. The reaction was anaphylaxis which is considered a serious reaction. The suspect medicine was Medroxyprogesterone acetate.

Routine Immunization

The effectiveness of routine vaccinations is highly dependent on dose integrity and compliance with subsequent doses within the prescribed schedule/time of administration. The integration of routine catch-up immunizations was implemented by the DOH to accommodate those who missed a dose or has not received a vaccine, despite being eligible for vaccination.

Although immunizations are administered annually, monitoring for side effects continues to ensure the safety and effectiveness of the vaccines used in the program. In 2022, there were 61 reports from the routine immunization programs of DOH: 36 reports were serious and 25 reports were non-serious. The top reported reactions were:

- Pyrexia
- Seizure
- Vaccination site swelling
- Cyanosis, erythema, dyspnea, vomiting
- Rash, febrile convulsion, swelling, cough, musculoskeletal stiffness

Vaccines reported under routine immunization were single active ingredient or a combination of the following:

- BCG
- Diphtheria
- Hepatitis B
- Influenza
- Measles
- Mumps
- Meningococcal
- Pertussis
- Pneumococcal
- Polio
- Rabies
- Rubella
- Tetanus
- Varicella zoster

COVID-19 Vaccines

The roll-out of COVID-19 vaccine started last 01 March 2021 and it still continuously implemented. To ensure the safety and efficacy of COVID-19 vaccines, reports of suspected adverse reactions to the vaccines were closely monitored. In 2022, a total of 25,335 reports were reported from COVID-19 vaccines namely:

- CoronaVac (Sinovac)
- Vaxzevria (AstraZeneca)
- Sputnik V/Sputnik Light
- Comirnaty (Pfizer)
- Spikevax (Moderna)
- Janssen COVID-19 vaccine
- Sinopharm

Out of these reports, 5,767 were tagged as serious and 19,568 were non-serious. Top reported reactions were:

- Pyrexia
- Vaccination site pain
- Cough
- Headache
- Dyspnea

Most of the reported reactions were reported by Epidemiology Surveillance Units

(ESUs) of the Epidemiology Bureau of DOH. But a proportion of the reports came from the pharmaceutical companies. In 2021 a total of 464 reports were received from the industry. The distribution of received reports included AstraZeneca with 192 reports, Pfizer with 178 reports, and Janssen with 94 reports. While in 2022, the total number of reports received was 944 reports with the distribution of 477 reports from Pfizer, 355 reports from AstraZeneca, 112 reports from Janssen, and four (4) from Zuellig (Moderna).

For the complete report on COVID-19 vaccines, please refer to the Reports of Suspected Adverse Reaction to COVID-19 Vaccines posted in the FDA website.

Other aspects of pharmacovigilance

This includes medication error and lack of efficacy. However, only medication errors and reports of lack of efficacy that resulted in an adverse reaction are reportable. There were 325 reports of medication error and 285 reports of lack of efficacy.

Lack of efficacy is when a product failed to produce its expected pharmacologic or therapeutic benefit that results to an adverse outcome. Clinical judgement should be exercised when reporting for lack of efficacy. The medicines with most reports of lack of efficacy are antineoplastics and COVID-19 vaccines which can be attributed to disease progression and to development of new strains as a result of the virus' ability to undergo rapid genetic changes and wanning immunity over time, respectively.

Medication error in an unintended failure in the medicine treatment process that resulted in an adverse reaction. The commonly reported medication errors are:

- Product use issue
- Inappropriate schedule of product administration
- Wrong technique in product usage process
- Product dose omission issue
- Incorrect dose administered

Sharing of ADR data

In accordance with international data privacy laws including Philippines' Data Privacy Act of 2012, reports are shared with VigiBase, the WHO global database of ADR reports. These reports are shared with member countries of the WHO Programme for International Drug Monitoring and contribute to the safety profile of the products. To allow international comparison of reports, suspected ADRs are coded using the MedDRA terminology while suspect medicines are coded using WHODrug. The Philippines shared a total of 29,358 ICSRs equivalent to 99.06% of the reports received.

Pharmacovigilance indicators

PV indicators are a set measure of the pharmacovigilance system to identify, monitor, and foresee trends to implement corrective, preventive, and improvement action when necessary. Such indicators will provide analysis of data from the previous year (2022).

Table 2: PV indicators

Cumulative total number of reports in the national database	156,082
Total number of ADR reports received in 2022	29,637
Reporting rate per 100,000 population	26.56
Percentage of the total number of reports shared to the WHO global database	99.06% (29,358)
Percentage of reports of therapeutic failure	0.96% (285)
Percentage of reports on medication errors reported in the previous year	1.10% (325)
Percentage of reports received from:	
• Medical Doctors	2.17% (642)
• Pharmacists	4.04% (1,198)
• Nurses or midwives (other HCPs)	72.65% (21,531)
• General public	8.60 (2,549)
• Manufacturers	11.92% (3,532)
• Unknown	0.62% (185)

PV ADVOCACY

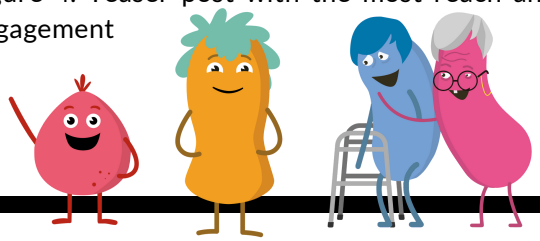
Continuous efforts are made by the PV Team to increase PV awareness and promote ADR reporting in the country. These advocacies include topics on understanding what to report, how to report, what happens to the report, and why do we need to report. An informed public will be empowered to report.

#MedSafetyWeek

#MedSafetyWeek is our annual social media campaign. Led by UMC and together with other regulatory authorities and stakeholders around the world, the campaign was held last 07-13 November 2022. With an aim to encourage reporting of side effects and increase awareness of national PV systems, the message of #MedSafetyWeek 2022 is "All medicines may cause side effects. That is why there are steps in place to monitor their safety. By reporting suspected side effects, you are actively participating in identifying emerging safety issues – so that we can take action when necessary and protect others from harm."

The campaign had 1-2 posts per day using our main platform – the FDA Facebook page. Posts are also published in the FDA website and shared in the DOH Facebook page and DOH Philippines Viber group. The campaign had a total Facebook reach of 850,839 and 2,535 engagements. Our teaser post had the most reach and engagement.

Figure 4. Teaser post with the most reach and engagement



Pharmacovigilance Page

Embedded in the FDA Website, the Pharmacovigilance Page had its major updates in 2022 to better educate PV stakeholders. The PV page now provides an overview of PV in the country, information for PV stakeholders, publications, and PV educational materials. The PV page is like a one-stop shop that contains all the needed information regarding pharmacovigilance.

The PV page is updated as needed.

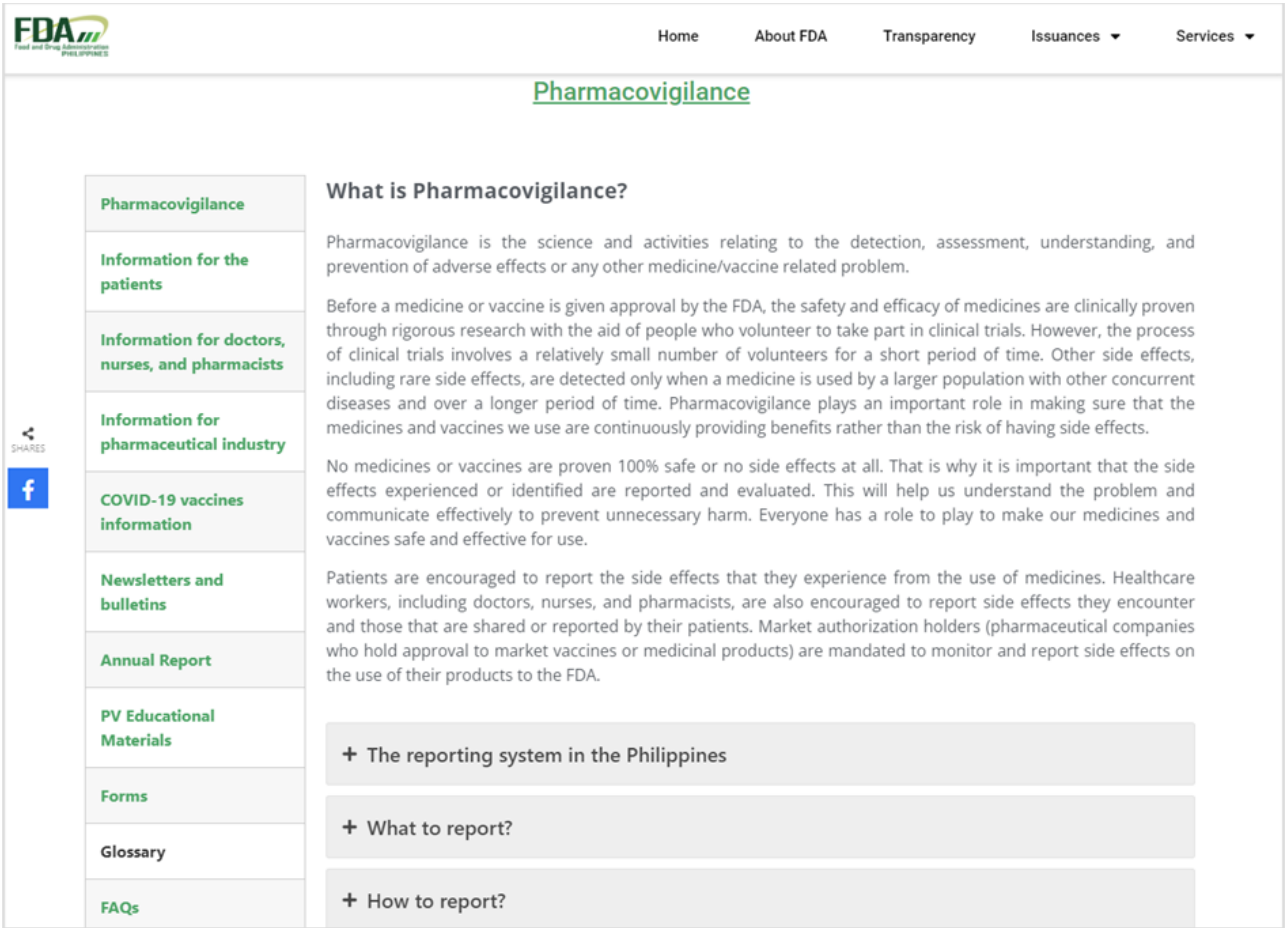


Figure 5. Preview of the PV page

Training Sessions Conducted on Pharmacovigilance

Several training sessions on PV were conducted and the PV Team served as resource speakers.

Pharmacovigilance 101 Webinar

PV 101 Webinar is a training offered by the FDA through its FDA Academy. This training aims to provide a discussion on how PV is done and its important role in ensuring the quality, safety, and efficacy of pharmaceutical products. Two (2) training sessions were conducted last 10 August 2022 and 08 November 2022 via Cisco Webex platform.

The topics discussed include the following:

- Introduction to Pharmacovigilance
- Pharmacovigilance Regulations
- The Philippine Pharmacovigilance System
- Pharmacovigilance in the Pandemic Situation
- Risk Management Plan
- Periodic Benefit-Risk Evaluation Report

The two (2) webinars had a total of 80 and 164 participants, respectively. All are healthcare professionals (doctors, medical technologists, nurses, pharmacists) and other allied health professionals (chemists, chemical engineers).

Training in Preparation for Vaccination Rollout in Pharmacies and Clinics
Conducted by National COVID-19 Vaccination Operations Center (NVOC) via Zoom, the PV Team took part in the training sessions offered to HCPs during the 1st quarter of 2022 in preparation to the vaccine rollout in pharmacies and clinics that started on 20 January 2022. The team provided a discussion on AEFI reporting and the use of Vaccine eReporting.

There were nine (9) sessions attended by hundreds of healthcare professionals in the country.

Other Training Session on PV
Other training sessions on PV were aimed to introduce PV, its basics, and reporting. These training were in collaboration with other DOH offices and professional organizations.

There were six (6) trainings conducted with health professionals as audience.

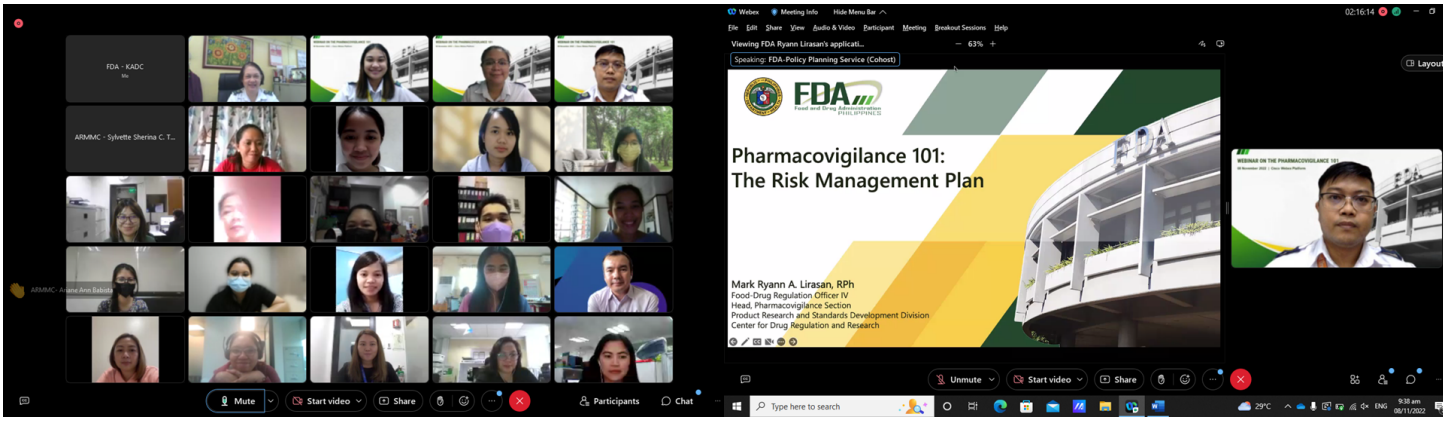


Figure 6. Pharmacovigilance 101 Webinar

RESEARCH INVOLVEMENT

The PV team partakes in several studies to better understand issues relating to PV and ensure the safety of our medicines.

Understanding underreporting of adverse drug reactions in the Philippines

To address underreporting, it is important to first understand the cause of the problem. The study aims to assess the knowledge, prevailing attitudes, and current practices (KAP) of HCPs in ADR reporting and assess the effectiveness of the eReporting – the online reporting system of the FDA. After which, interventions will be implemented, and a post evaluation analysis will be performed.

1st Philippine Pharmacovigilance Summit

The summit was utilized to invite participants to take part in the study. Phase 1 of our research methodology is to give a self-administered questionnaire to study participants to assess their KAP. This will be followed by focused groups discussions for phase 2.

The Philippine PV Summit is an interprofessional collaboration in strengthening PV in the country. Co-organized by Philippine Women's University (PWU), our partner organizations are Philippine Medical Association, Philippine Nurses Association, and the Philippine Pharmacists Association. It was held last 04 March 2022, 3-6 pm, via Facebook Live.

Hematologic Adverse Effects Reported after COVID-19 Vaccination in the Philippines: A study based on National Database – HAEVAx Study

In collaboration with the Philippine College of Hematology and Transfusion Medicine, the study aims to analyze hematologic adverse events after COVID-19 vaccination and their outcomes and to provide information on its benefit-risk to address vaccine hesitancy and provide recommendations on the management of hematologic AEs.

The scope of the study is the AE/ADRs reported to the FDA from 01 March 2020-30 April 2022.

Cohort Event Monitoring (CEM) of Molnupiravir

Molnupiravir is the first medicine given Conditional Marketing Authorization for the treatment of patients with mild to moderate COVID-19 disease who are at an increased risk of developing severe infection. It is generally well tolerated during clinical trials, however, there are still concerns about its safety profile. Thus, the aim of this research is to monitor the safety of molnupiravir through an observational study. This active pharmacovigilance surveillance is one of the mitigation measures recommended by the WHO before more safety data becomes available.

The FDA, in collaboration with the World Health Organization, together with other member countries including Egypt, Jordan and Egypt, the Philippines through the Philippine College of Physicians joined the cohort event monitoring of molnupiravir.

STRENGTHENING PHARMACOVIGILANCE

Several regulatory agencies and non-government organizations have been helping the FDA in strengthening and enhancing the pharmacovigilance in the country.

Signal detection process

The Therapeutic Goods Administration (TGA), through the Australian Government's commitment to help other countries have access to safe and effective medicines and vaccines, provided technical assistance to the pharmacovigilance staff of FDA Philippines. With the aim to improve and strengthen the signal detection process, a series of meetings were conducted on signal detection, signal prioritization, and signal evaluation through its International Regulatory Branch.

Risk management plan

The Pharmaceutical and Medical Devices Agency provided a PV webinar to the FDA Philippines with topics on risk management plan, its structure, and its evaluation and assessment. The evaluation and assessment of PSUR/PBRER was also discussed.

Technical assistance

The Medicines, Technologies, and Pharmaceutical Services (MTaPS) program offers assistance to the FDA in different aspects of Pharmacovigilance from advocacies to strengthening of PV regulations. In 2022, they held a three-day workshop entitled "Pharmacovigilance Best Practices Learning Session and Workshop." The workshop consisted of a lecture and group activities on the drafting of targeted spontaneous reporting procedure and revision of the administrative order on pharmacovigilance.

Figure 7. FDA with TGA

GLOBAL BENCHMARKING TOOL

The Global Benchmarking Tool (GBT) is a globally standardized assessment tool developed by the WHO to serve as the primary means to evaluate objectively regulatory systems, as per provisions of World Health Assembly Resolution 67.20 on Regulatory System Strengthening for Medical Products. (WHO, n.d.)

GBT Vigilance (VL) indicator is used for evaluating the performance of pharmacovigilance systems in the country. The tool helps identify gaps in PV regulatory capacity and provide guidance on how to improve them. The WHO classification for assessing the maturity level of pharmacovigilance is carried out based on its PV indicators, which measure inputs, processes, outputs, outcomes, and impacts. These indicators provide information on how well a pharmacovigilance system is achieving its objectives.

FDA has made significant strides as national regulatory agency improving its regulatory processes. It has implemented various initiatives such as streamlining registration procedures for drugs, strengthening post-market surveillance activities, and enhancing collaboration with international regulatory agencies.