Pharmacovigilance
NEWSLETTER
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The Aims of the Newsletter:

- Sharing the activities of the ADRM cell, Pharmacovigilance and COVID-19 Safety Surveillance cell and the outcomes of the National Pharmacovigilance Centre, DGDA and related committees.
- Dissemination of drug and vaccine safety information, trend of adverse events, adverse event evaluation, regulatory decisions, and pharmacovigilance enforcement activities.
- Sharing the progress of DGDA's Pharmacovigilance system towards WHO maturity level 3.

Introduction:

The Pharmacovigilance Newsletter provides the latest information on the safety of medicine, vaccines, and regulatory decisions of the DGDA. It is one of the important methods of communicating with pharmacovigilance stakeholders. The newsletter includes the status of adverse event evaluation with regulatory decisions and actions, including COVID-19 vaccines, reliance on other international regulatory authorities, introduction of Good Pharmacovigilance Practices (GVP) guidelines, training, coordination with different stakeholders, and so on.

Adverse Drug Reaction Monitoring in Bangladesh:

The Adverse Drug Reaction Monitoring (ADRM) Cell serves as the coordinating body for the national PV system in Bangladesh. From November 2021 to March 2023, the National Pharmacovigilance Centre of Bangladesh received a total of 1429 reports from different stakeholders. All these reports were primarily evaluated by the ADRM cell. Out of these 1429 reports, 638 were found complete, while 791 were deemed incomplete due to a lack of minimum information after follow up with the reporters. An electronic ADR reporting system named Pharmacovigilance Monitoring System (PViMS) development is ongoing which could eliminate submission of incomplete report. From January 2022 to May 2023, the ADRM cell organized a total of 13 workshops. So far, the committee has assessed 638 complete reports in workshop; among those reports, 555 were deemed to be not serious, and 83 to be serious*.

*"*Serious adverse reaction: An adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a birth defect". Ref. European Medicines Agency*

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Table 1: ADRM Cell Meetings, Number of ADR reports evaluated in the meetings:

Meeting	Month	No. of Report	Incomplete	Complete		
				Total	Not Serious	Serious
31-Jan-22	November	49	42	7	2	5
	December	344	121	223	200	23
7-Feb-22	January	56	52	4	4	0
3-Mar-22	February	129	76	53	42	11
6-Apr-22	March	91	63	28	26	2
12-May-22	April	91	65	26	21	5
15-Jun-22	May	50	25	25	22	3
25-Jul-22	June	33	18	15	15	0
30-Aug-22	July	40	35	5	4	1
29-Sep-22	August	8	7	1	1	0
29-Sep-22	September	25	17	8	6	2
3-Nov-22	October	13	3	10	9	1
23-March-23	Nov-Dec	372	208	164	142	22
3-May-23	Jan-March	128	59	69	61	8
	Total	**1429**	**791**	**638**	**555**	**83**

The table is showing the number of ADRM cell meeting held from January 2022 to May 2023 along with the number of ADR reports evaluated in the meeting. DGDA along with other development partners like USAID MTaPS and WHO conducted country-wide awareness programs and trainings on pharmacovigilance up to mid of the year 2022. That resulted in a significant increase in ADR reports received at DGDA. However, as the reporting system is still manual, a significant number of reports are found to be incomplete. With the support of USAID MTaPS program, DGDA is approaching to introduce an electronic PViMS that could solve this problem. The program is continuously supporting DGDA to increase the ADR reporting rate as well as improve the quality of reports.

After primary evaluation of the reports, the ADRM cell placed serious reports before the Technical Sub-committee (TSC) for causality assessment. During the period January 2022 to May 2023, the technical subcommittee held three consecutive meetings on February 13, 2022, April 20, 2022, October 10, 2022, March 29, 2023 and May, 8, 2023.The technical subcommittee evaluated a total of 128 serious ADE reports which were collected between July 2021 and March 2023. According to WHO Causality Assessment scale, all evaluated reports were classified and recorded as: Probable/Likely- 66, Possible- 25, Unlikely- 34 and Unclassifiable- 3

Adverse Drug Reaction Advisory Committee (ADRAC) Meeting for ADE evaluation:

DGDA organized 14th,15th and 16th Adverse Drug Reaction Advisory Committee (ADRAC) Meetings from 2022 to May 2023 at DGDA with the reports related to drugs and vaccines (except COVID-19 vaccines). The Director General of DGDA and Chairman of ADRAC presided over the meetings. The 14th ADRAC meeting was held on the reports received from July 2021-December 2021, the 15th meeting was on the report received from January 2022-September 2022 and the 16th meeting held on May 21, 2023 was on the reports received from October 2022 to March 2023. Out of 678 complete

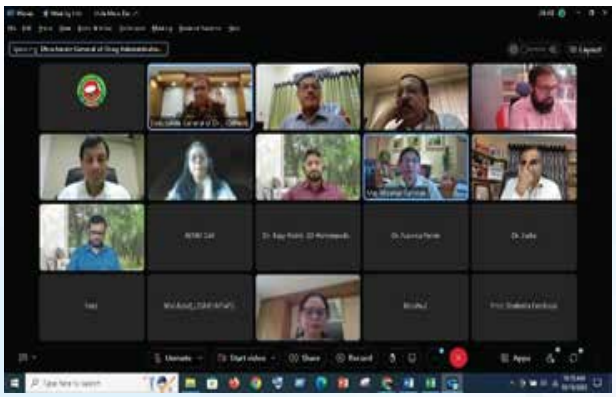


Figure 1: ADRAC Committee Members attending virtual meeting
Photo Credit: MTaPS Bangladesh

reports reviewed by technical subcommittees, 94 serious ADE reports were forwarded to the 14th,15th and 16th meetings of the Adverse Drug Reaction Advisory Committee (ADRAC) for regulatory recommendations. All those reports were finally classified by the committee as follows: Probable/Likely- 57, Possible- 15, Unlikely- 21, Unclassifiable- 1.

Table 2: Classification of serious adverse drug reactions evaluated in the meeting of ADRAC:

WHO Causality Assessment Scale	Total Serious Adverse Event Reports
Certain	0
Probable/Likely	57
Possible	15
Unlikely	21
Unclassifiable	1
Total	**63**

Regulatory decisions taken by Adverse Drug Reaction Advisory Committee:

Meeting Info	Decisions	Status
14th meeting of ADRAC held on 21st March 2022	Careful attention will be kept on Probable and Possible Case reports and necessary decisions will be taken if more reports are received in future.	Implemented
	All the reports which are classified as Probable and Possible reports as per decision taken in TSC meeting must be uploaded to Vigiflow.	Implemented
	Skin test should be done before the use of Injection Ceftriaxone in order to ensure drug safety by avoiding the hypersensitivity reactions, a letter will be sent to DGHS, Bangladesh Medical Association (BMA), Consumers Association Bangladesh (CAB), Bangladesh Pharmaceuticals Society (BPS), Bangladesh Oushodh Shilpo Shomiti, BDS and other stakeholders.	Implemented
	In order to ensure the safe use of Injection Ceftriaxone, the concerned pharmaceutical industries should conduct necessary awareness training/seminar activities for all healthcare providers including doctors, pharmacists, nurses to ensure the safety of the medicine.	Implemented
	Based on alert received from WHO Pharmaceuticals Newsletters, Issue no. 1,2022 • Association/Society of Medical Professionals will be notified about the adverse drug reaction like disturbed consciousness and potential encephalopathy on using Ivermectin medicine. • A letter will be issued to inform the Gynecologist society about the occurrence of pulmonary edema in pregnant women due to the use of Nifedipine. • Risk of serious heart-related events, cancer, blood clots on using Tofacitinib, Baricitinib and Upadacitinib should be printed in the medicine cartoon as a box warning. • The matter of Urinary Retention due to the use of Tramadol will be informed to all health professional organizations including Marketing Authorization Holder, Bangladesh Medical Association.	Implemented

15th meeting of ADRAC held on 16th October 2022	A letter will be sent to the Bangladesh Medical Association BMA and the Director General of DGHS with a request to issue necessary instructions in this regard that Carbamazepine should be administered only as per the advice of a specialist physician.	Implemented
	In the interests of patient safety, Ketorolac Tromethamine / NSAID should be used with caution in patients with Diabetes Mellitus / Hypertension - Send a letter to the Medical Association BMA and Director General, Directorate of Health with a request to issue necessary instructions in this regard.	Implemented
	Rituximab should only be administered under the direct supervision of a specialist physician, in health facilities with strong patient management facilities – A letter with request will be forwarded to the Bangladesh Medical Association and the Director General of DGHS to issue the necessary instructions in this regard.	Implemented
	National Guideline on the Pharmacovigilance System in Bangladesh is to be sent to the Ministry of Health and Family Welfare for final approval with updated organogram, job description, work flowchart and reporting form along with others information.	Implemented
	The draft GVP Guideline will be reviewed by the Working Committee as per the suggestions received in the meeting. Then it will be submitted to the Chairperson of ADRAC as well as sent to the Ministry of Health and Family Welfare for final approval.	Implemented
16th meeting of ADRAC held on May 21, 2023	Based on the information published in WHO Newsletter, Issue 1, 2023 (Signal), there is a risk of Acute Respiratory Distress Syndrome (ARDS) in taking Hydrochlorothiazide and Hypokalemia in taking Itraconazole, so a letter should be sent to MAH to include the related caution in the PIL of the two medicines.	Implemented
	A letter should be sent to the concerned institution for information/awareness regarding the sale or use of steroid medicines without a specialist doctor's prescription and not to sell or use them.	Implemented
	A letter will be sent to all medical and nursing educational institutions, pharmaceutical companies (MAH), HCPs, medical professional associations and the BMA to take adequate precautions in the application of injectable drugs including antibiotics and to seriously monitor whether the patient develops any hypersensitivity.	Implemented
	In order to increase Adverse Drug Reaction (ADR) reporting, the Directorate General of Drug Administration will provide necessary report forms, online links, instructions and other materials for easy reporting to all medical college and hospital.	Implemented
	In addition, more intense initiatives will be taken to raise awareness among the head of all health facilities.	
	A letter should be sent by thanking the organizations who provide reports and with a request for providing reports regularly attaching the necessary information to evaluate the reports accurately.	Implemented

The committee has also recommended the safety information published in the Drug Safety Information of the WHO Pharmaceuticals Newsletter, Issue No. 1, 2022. Total four alerts have been discussed in the meetings identified through literature review which were issued by other regulated country's NRA. One signal related to muscle spasms or cramps associated with Methotrexate, generated through the WHO VigiBase (a global individual case safety reports database.)

Regulatory Recommendation from ADRAC:

Important recommendations made by the 14th, 15th and 16th ADRAC meetings based on regulatory decisions of different NRAs published in the WHO Pharmaceuticals Newsletter, Issue No. 1, 2022 and Issue No. 1, 2023 are as follows:

WHO Pharmaceuticals Newsletters, Issue No. 1, 2022 এ প্রাপ্ত Alert এর ভিত্তিতে

1) Ivermectin Medicine এর Disturbed Consciousness এবং Potential encephalopathy ADR বিষয়টির মেডিকেল প্রফেশনালদের এ্যাসোসিয়েশন/সোসাইটি এর মাধ্যমে অবহিত করা হবে।

2) Nifedipine ব্যবহারের ফলে গর্ববতী মহিলাদের pulmonary oedema হওয়ার বিষয়টি Gynecologist society কে অবহিত করার জন্য পত্র প্রদান করা হবে।

3) Tofacitinib, Baricitinib and Upadacitinib ব্যবহারের ফলে serious heart-related events, cancer, blood clots হওয়ার বিষয়টি Box warning হিসেবে দেওয়া হবে।

WHO Pharmaceutical Newsletter, Issue-1, 2022 (Signal) এ প্রকাশিত তথ্যের ভিত্তিতে Methotrexate ঔষধটি গ্রহণে Muscle spasm I Muscle cramp এর ঝুঁকি রয়েছে বিধায় উক্ত ঔষধটির PIL-এ সতর্কতা হিসেবে Muscle spasm ও Muscle cramp উল্লেখ করার জন্য সংশ্লিষ্ট কোম্পনীসমূহকে পত্র প্রদান করতে হবে ।

WHO Newsletter, Issue-1, 2023 (Signal) এ প্রকাশিত তথ্যের ভিত্তিতে Hydrochlorothiazide গ্রহণে acute respiratory distress syndrome (ARDS) এবং Itraconazole গ্রহণে Hypokalaemia এর ঝুঁকি রয়েছে বিধায় উক্ত ঔষধ দুইটির PIL এর সতর্কতা হিসেবে যথাক্রমে acute respiratory distress syndrome (ARDS) এবং Hypokalaemia উল্লেখ করা যেতে পারে বলে সুপারিশ করে ।

Development of Good Pharmacovigilance Practice (GVP) Guidelines for Marketing Authorization Holders (MAHs)

DGDA formed a 17-member working committee for the development of guidelines on good pharmacovigilance practices (GVP) for marketing authorization holders (MAH) and the review of national guidelines on pharmacovigilance systems in Bangladesh.

The chair of the committee is Prof. Md. Sayedur Rahman, Chairman, Department of Pharmacology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The first workshop of the committee took place on December 19, 2021, and they worked on updating both the National PV guidelines. USAID's MTAPS program is providing support for this activity. The Good Pharmacovigilance Guideline (GVP), has been uploaded to the DGDA website (http://dgda.gov.bd) for public opinions by April 15, 2022. The final version of the draft GVP has been released after going through some review workshops. This is in line with the recommendation of WHO assessors for attaining score a in the Global Benchmarking Tool.

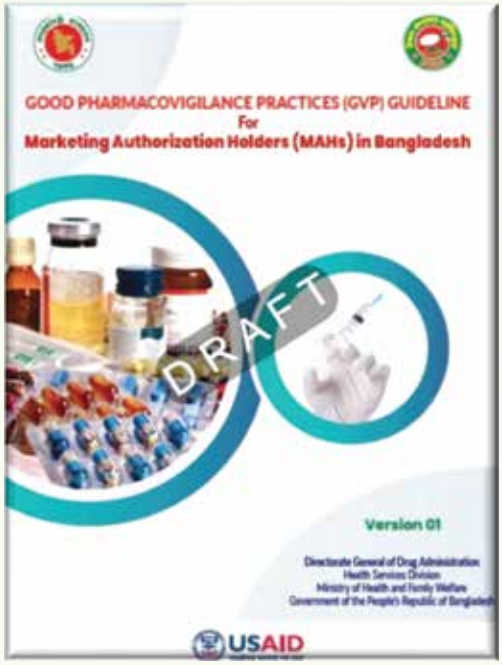


Figure 2: 17 Member working committee with Good Pharmacovigilance Guideline for MAHs in Bangladesh
Photo Credit: MTaPS Bangladesh

Awareness and scale up of Pharmacovigilance Program

DGDA, along with MTaPS, visited the National TB Control Program (NTP) on April 14, 2022, to oversee the Active TB Drug Safety Monitoring and Management (aDSM) activities. The relevant guidelines, procedures and a dedicated PV team are in place at the NTP. Periodic training program is also conducted on aDSM reporting system that is developed on eTB manager supported by MTaPS. A user access has been shared with the ADRM cell of DGDA to get the real-time aDSM status. Recommendations to the NTP was to share the aDSM reports monthly and continue the awareness and training programs to increase the number and quality of the reports. These efforts will boost up the pharmacovigilance activities and lead medicine safety

Pharmacovigilance Training Programs:

DGDA has developed standard operating procedures for monitoring the implementation of the active or proactive vigilance system and provided training. DGDA organized pharmacovigilance training for healthcare professionals like doctors, nurses, pharmacists, medical technologists, and relevant others across the country under the operation plan: Strengthening of Drug Administration (SDAM) and in collaboration with other partners such as Bangladesh Association of Pharmaceutical Industries (BAPI), USAID MTaPS, WHO and others.

Activities under SDAM OP budget by DGDA Pharmacovigilance department:

Strengthening of the Pharmacovigilance System in Bangladesh is an important goal of the DGDA. To sensitize the existing PV committees (both for Drugs and Vaccines) at the Divisional, District and City Corporation level along with the Upazila Health Complexes (UHCs), DGDA planned accordingly to educate the Healthcare Professionals (HCPs) and develop mass awareness on Pharmacovigilance nationwide. As a part of this plan, DGDA conducted eight structured workshop and training programs on pharmacovigilance for senior officials working at different administrative levels; e.g., Principals of the Medical Colleges, Divisional Health Directors, Directors of the divisional level public medical college hospitals, Professors, Consultants, Chief Health Officers (CHOs) & Health Officers of the City Corporations, District Civil Surgeons, UH&FPOs. Besides, RMOs, Health Officers, Medical Officers, EPI superintendent, Pharmacists & Nursing superintendents working in the government health facilities,

DGDA colleagues from the HQ, Division and District, and different levels of health care professionals of all the eight divisions of the country also attended. In addition, WHO consultant, Divisional Coordinators, SIMOs and USAID-MTaPS officials also participated these workshops and trainings.

Figure 3: Participants attending at workshop with Dhaka Division
Photo Credit: MTaPS Bangladesh

The Director General of DGDA chaired the programs. Additional Secretary, HSD, MoHFW, Pharmacovigilance experts from DGDA, DG Health Services, and the World Health Organization (WHO) delivered their speeches and presentations as resource persons. Active participation of the attendees and the experts in the Question and Answer sessions and open discussions made the workshops and the training programs very interactive and fruitful! All these seminar, /workshop and /training programs are being held in accordance with the requirements of WHO recent assessment, which will help in the creation of a culture of adverse events reporting to ensure medicine safety. These workshops, seminars and trainings are being supported by the DGDA's own budget from the Operational Plan (OP) for Strengthening of Drug Administration and Management (SDAM), Fiscal Year 2021-2022.

DGDA has also trained government Homoeopathy, and Unani and Ayurvedic Medical Care officers working in different government. health facilities to develop awareness on the safety monitoring of Homoeopathy and Traditional drugs. In these workshops, a total of 978 healthcare professionals have been trained on PV to cover whole country. These seminars and workshops will impact on strengthening the Pharmacovigilance system and practices within organizations and committees.

Table 3: Details of the workshops:

Workshop date	Workshop Name	Workshop method	No. of Participants	Workshop outcome
10/06/2021	Rajshahi Division	Online	135	• Awareness on the basic concepts, the working systems of Pharmacovigilance, increasing the number of the ADR/AEFI reports, including COVID-19 Vaccine • The DGDA Pharmacovigilance Department has become more connected to the health facilities all over the country, thus resulting in an improvement in the quality of ADR/AEFI reporting. • Improving the coordination and collaboration on pharmacovigilance activities among the stakeholders (The Ministry, Health facilities, Policy makers, Health Care Professionals, Academicians, DGDA officials and Development partners, etc.) • Improving the area of networking, mass awareness on of ADR/AEFI reporting, serious ADR/AEFI investigation, and causality assessment • Proper utilization of the budget allocation of the Operational Plan of SDAM for strengthening the Pharmacovigilance system and Human resource development in this regard • Engagement of the government's Homoeopathy, Unani and Ayurvedic health care professionals of different level health facilities in Pharmacovigilance activities.
13/03/2022	Sylhet & Mymensingh Division	Online	120	
12/04/2022	Khulna Division	Online	117	
20/04/2022	Chattagram Division	Online	131	
27/04/2022	Rangpur Division	Online	84	
31/05/2022	Barishal Division & Dhaka Part 1 (Faridpur, Gopalganj, Shariatpur, Madaripur, Rajbari districts)	Online	97	
08/06/2022	Dhaka Part 2	In person	62	
06/06/2022	Homoeopathy & Traditional Medicine	Online	232	
Total number of trained health care professionals			**978**	

PV Training arranged by BAPI for Pharmaceutical Companies:

DGDA provided training on the implementation of pharmacovigilance guidelines in collaboration with the Bangladesh Association of Pharmaceutical Industries (BAPI), to which 75 pharmaceutical companies were invited in three phases (25 companies per phase). BAPI organized the training programs on 12 and18 January and 16 March 2022, at the BAPI office conference hall. After that, the4th phase of the training has also been conducted on Pharmacovigilance. Thus, DGDA has provided training as BAPI targeted 100 Pharmaceutical Companies to educate, create awareness and build coordination to strengthen Pharmacovigilance. The Secretary General of BAPI, Mr. S M Shafiuzzaman; Chief Operating Officer and former DG, DGDA, Major General Md. Mustafizur Rahman; EC member & ED Operations of Square Pharmaceuticals Ltd. Mr Md Mizanur Rahman, as well as other members and participants, attended the programs.

Figure 4: Training on Pharmacovigilance at BAPI office
Photo Credit: MTaPS Bangladesh

Workshop in Dhaka Medical College Hospital:

On December 12, 2022, with technical support from USAID MTaPS, DGDA organized a workshop on "Pharmacovigilance in Hospital and the role of Healthcare Professionals" with the funding of the Operational Plan of Strengthening of Drug Administration and Management (SDAM), 4th HPNSP at Dhaka Medical College Hospital. The discussion focused on the role of healthcare professionals in reporting Adverse Drug Reactions (ADRs) and AEFIs in order to ensure greater public health safety. A total of 60 participants, including the

Figure 5: Distinguished chief guest & Special guest Additional Secretaries of MoHFW are giving their valuable speech
Photo Credit: MTaPS Bangladesh

Additional Secretaries from Health Services Division (Planning and Drug wings both), Ministry of Health and Family Welfare (MoHFW), representatives from the Dhaka divisional Adverse committee for COVID 19 vaccines, members of the DMCH of Health and Family Welfare (MoHFW) representatives from the Dhaka divisional Adverse Event Following Immunization (AEFI) causality assessment Pharmacovigilance Committee, officials of the DGDA, Directorate General of Health Services, Bangabandhu Sheikh Mujib Medical University, Bangladesh University of Health Sciences, Doctors, Pharmacists, and nurses form DMCH, as well as experts from USAID MTaPS and the World Health Organization attended the workshop. The principal, DMC, informed the audience that the hospital section had provided 10 million doses of COVID-19 Vaccines since February 2021, with effective and successful reporting of adverse events. The achievements, challenges the healthcare providers faced during the COVID-19 Vaccination program were also discussed in the workshop.

Figure 6: Honourable resource persons (Chief Scientist and advisor, former VC, BUHS, Deputy Director & Assistant Director of Pharmacovigilance Department- DGDA) are presenting lectures in the workshop
Photo Credit: MTaPS Bangladesh

Communication materials development for Pharmacovigilance of COVID-19 Vaccines:

"কোভিড-১৯ টিকাদান পরবর্তী যে কোন ধরণের পার্শ্ব বা বিরূপ প্রতিক্রিয়া যথাযথ মনিটরিং এবং কার্যকর ব্যবস্থা গ্রহণে কাজ করলে জনগণ এবং স্বাস্থ্যকর্মীদের সচেতনতা আরও বৃদ্ধি পাবে এবং ফার্মাকোভিজিল্যান্স কার্যক্রম আরও জোরদার হবে।"

Figure 7: Director General giving speech on reporting COVID 19 AEFI for documentation in video material
Photo Credit: MTaPS Bangladesh

Figure 8: Participants attending meeting for development of awareness materials on AEFI reporting
Photo Credit: MTaPS Bangladesh

DGDA conducted few meetings on the development of leaflet and video as communication materials to facilitate the creation AEFI reporting culture across the country. USAID MTaPs is providing technical assistance for this activity.

Pharmacovigilance for COVID 19 Vaccines (as of 11th May 2023):

DGDA and EPI are receiving AEFI reports of COVID-19 vaccines from vaccination centers across the country via the DGDA online AEFI reporting portal. Upon receiving a serious AEFI, primary and final investigations are carried out by the respective City Corporation or District AEFI committee headed by CHO or the Civil Surgeon respectively. The DGDA regional officers are also members of the committee. After investigation, the Divisional AEFI Causality Assessment Committee, headed by the Divisional Director of Health, determines the causal association between serious adverse events and vaccines. After that, the investigation report, together with the causality assessment report, is reviewed by the National AEFI Advisory committee, Chaired by the Director General of DGDA, with the assistance of the "Pharmacovigilance and COVID-19 Safety Surveillance Cell," DGDA.

AEFI Report Evaluation and Regulatory Decisions

DGDA conducted a series of meetings of the National AEFI Advisory Committee for COVID-19 vaccines with the support of USAID MTaPS. The committee reviewed the AEFI reports already evaluated by the district and divisional AEFI committees and made the necessary regulatory recommendations for the safe use of COVID-19 Vaccines. The Director General of DGDA chaired the meetings as Chairperson of the Committees. The COVID-19 Safety Surveillance Cell provides secretarial support to the National AEFI Advisory Committee for COVID-19 Vaccines.

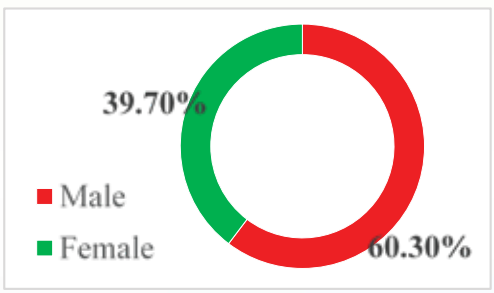
Figure 9: Virtual meeting of National AEFI Advisory Committee for COVID 19 Vaccines

Highlights:

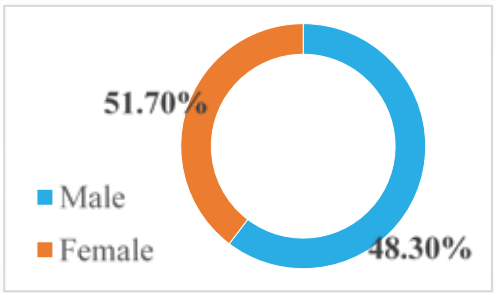
- There is a total of 4522 AEFI reports received online following 361,182,855 doses of COVID-19 Vaccine administered in Bangladesh as of May 11, 2023.
- Online reporting rate of 12.52/ million doses administered
- Of the total 4522 AEFI reports received:
- 4433 AEFI reports are non-serious (mild or moderate) (98.03% of total AEFI reports).
- 89 reports meet the definition of Serious AEFI 1.97% of total AEFI reports).
- Serious Adverse Events in 54 cases out of 89 so far resulted in death (60.67% of total serious AEFI)
- Cases recovered from the Serious Adverse Events are 35 (39.30% of total serious AEFI)

Summary of AEFI reports:

Total AEFI Reports by Gender



Serious AEFI Reports by Gender



The pie chart outlines the percentage of male and female affected with adverse events after vaccination. As of May 11, 2023, a total of 4522 AEFI reports received through online whereas 39.7% (1795) female and 60.3% (2727) was of male. But then total 82 reports were of Serious AEFI and among those reports 51.7% (46) female and 48.3% (43) was of male.

Table 4: Doses administered, spontaneous reports of suspected cases of AEFI, and Serious Adverse events following the administration of Covid-19 vaccines in Bangladesh, based on the DGHS & DGDA database as of May 2023.:

Name of Vaccine	Doses administered	Total reports of AEFI (N)	Reports of AEFI /10,00,000 doses	Non-Serious AEFI	Non-Serious AEFI /10,00,000 doses	Serious AEFI	Serious AEFI /10,00,000 doses
AstraZeneca	56,280,768	1528	27.149	1496	26.58	32	0.57
Moderna	15,808,126	833	52.694	825	52.19	8	0.51
Pfizer	80,551,732	892	11.073	878	10.89	14	0.17
Sinopharm	113,749,638	1184	10.408	1157	10.17	27	0.24
Sinovac	61,307,635	80	1.304	77	1.25	3	0.03
J & J	607,862	0	0.00	0	0.00	0	0.00
Pfizer-PF (Comirnaty)	32,877,094	5	0.152	0	0.00	5	0.15
Total	**361,182,855**	**4522**	**12.519**	**4433**	**12.27**	**89**	**0.24**

The table portrays the number of doses administered according to vaccine name and the ratio of AEFI reports against total administration of Covid-19 vaccines in Bangladesh, based on the DGHS & DGDA database as of May 11, 2023

Table 5: AEFI Reports by Covid-19 VaccineBrand?:

Name of Vaccine	Total AEFI Report	Serious AEFI		SAE Death Case		SAE Recovered	
AstraZeneca	1528	32		19		13	
Moderna	833	8		2		6	
Pfizer	892	14		9		5	
Sinopharm	1184	27		20		7	
Sinovac	80	3		2		1	
J & J	0	0		0		0	
Pfizer- PF (Comirnaty)	5	5		2		3	
Grand Total	**4522**	**89**		**54**		**35**	

Among 4522 AEFI reports the total number of serious AEFI was 89 till May 11, 2023, whereas the outcome of 54 cases was death and 35 cases was recovered

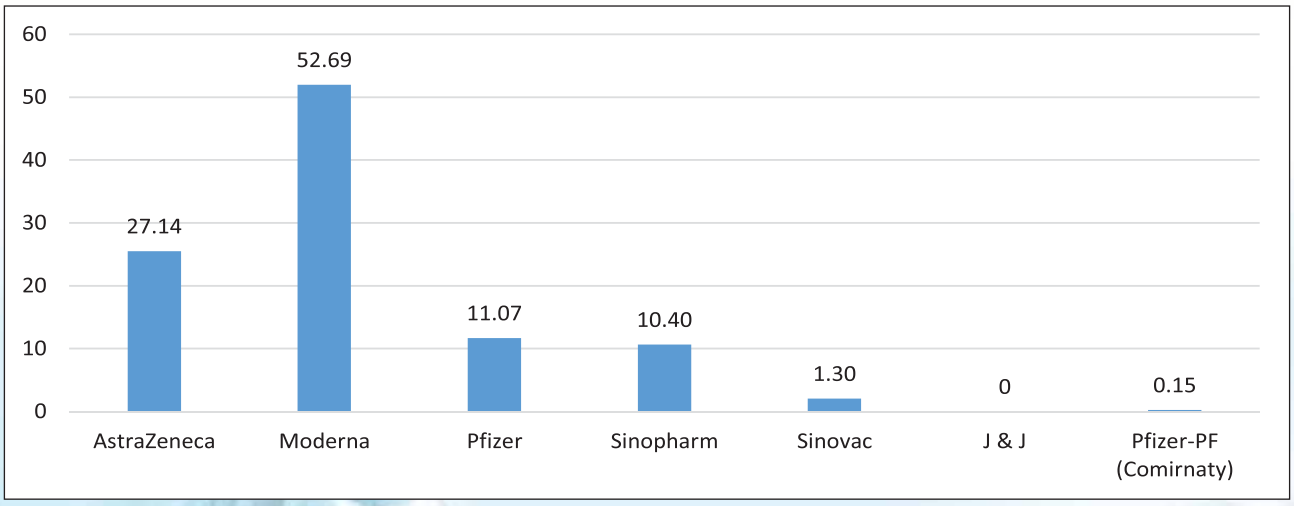
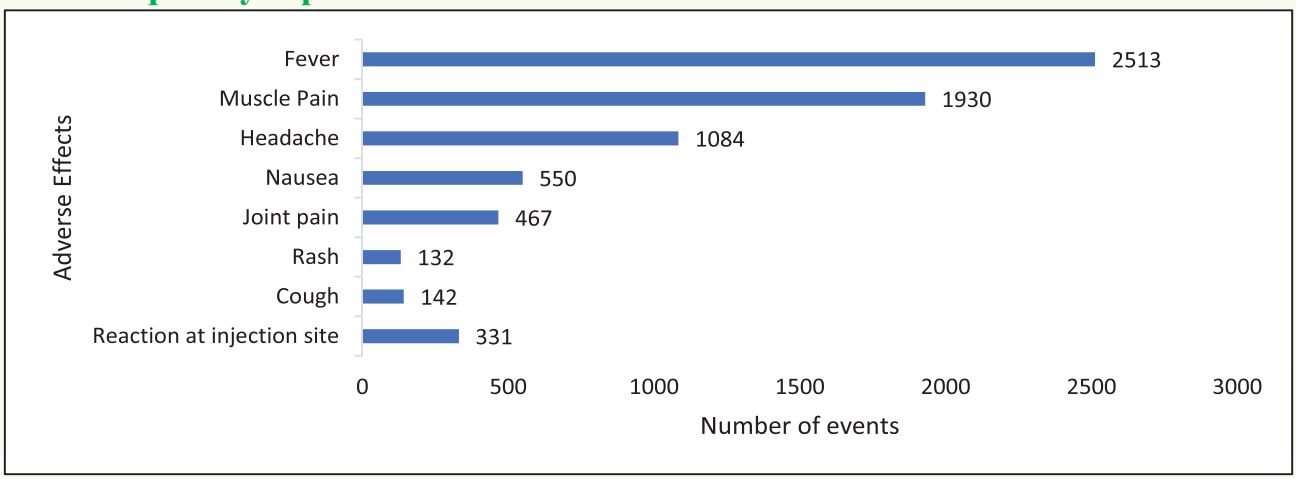


Figure 10: Proportion of reported AEFI per 1 million of administered doses by Covid-19 vaccine brand. Bangladesh, as of May 2023

The bar graph displays the proportion of reported AEFI per 1 million administered doses of different Covid-19 vaccines in Bangladesh as of May 2023. The highest proportion of AEFIs were due to vaccination with Moderna, standing at 52.69/ million doses, followed by AstraZeneca (27.14/ million doses). The Pfizer-PF (Comirnaty) vaccine was associated with the lowest proportion of AEFIs at 0.15/million doses. The proportion of adverse event for Pfizer (11.07/ million doses), Sinopharm (10.40/ million dose), Sinovac (1.30/million dose) were quite close in between.

Most frequently reported Adverse events for all COVID-19 vaccines:



Note: An AEFI report may contain multiple adverse events. So that, the sum of all advers event-specific counts will not equal to the total number of AEFI reports.

For all COVID-19 vaccines, the most commonly reported adverse events are fever and muscle pain, reported in 2513 and 1930 respectively. Besides that, headache, nausea, joint pain, rash, cough, reaction at injection site also among the most frequently reported adverse events.

Table 6: AEFI Reports by Division:

Division	Total Dose Administered	Total AEFI Reported (N)	Total AEFI /1000000 doses	Serious AEFI reported	Serious AEFI /1000000 doses	Non-Serious AEFI reported	Non-Serious /1000000 doses
Barishal	18005639	263	14.61	2	0.12	261	14.50
Chittagong	66140730	603	9.12	12	0.18	591	8.93
Dhaka	93976064	2283	24.29	27	0.29	2256	24.01
Khulna	37607160	247	6.57	7	0.19	240	6.38
Mymensingh	24389034	177	7.26	5	0.21	172	7.05
Rajshahi	43843585	570	13.00	8	0.18	562	12.82
Rangpur	35985849	229	6.36	16	0.44	213	5.92
Sylhet	22714092	137	6.03	5	0.22	132	5.81
Grand Total	342662153	4509	13.15	82	0.24	4427	12.91

The table portrays the number of total doses administered and total AEFI reported from different divisions. More than 50% of AEFI were reported from Dhaka division whereas the least number reporting division is Sylhet. Serious AEFI appear to be comparable across divisions. Almost 33% serious AEFI was reported from Dhaka whereas the least number (2.4%) received from Barishal. DGDA with the support of USAID MTaPS is striving to increase the number of AEFI reports keeping in mind this statistics.

Table 7: Number of AEFI Reports for COVID 19 Vaccines (January 2021- May 2023):

DGDA Online Platform	
Total Number of Cases	4522
Male	2727
Female	1795
Serious	89
Non-Serious	4433

The table tells that number of cases affected with AEFI is mostly males.

Table 8: Classification of 84 SAEs for COVID-19 Vaccines till May, 2023:

Classification Type	Serious AEFI Number	Vaccine Name					
		AstraZeneca	Pfizer	Sinopharm	Moderna	Sinovac	Pfizer (Comirnaty)
Vaccine Product Related Reaction	27	9	6	8	3	0	1
Coincidental	35	22	4	7	1	0	1
Immunization Anxiety Related Reaction	9	2	1	2	4		
Indeterminate	13	1	2	8	0	2	
Total	**84**	**34**	**13**	**25**	**8**	**2**	**2**

The table displays the total number of serious AEFI reviewed by the National AEFI Advisory Committee for COVID-19 Vaccines. As of May 2023, the committee reviewed a total of 86 serious AEFI and classified as: vaccine product-related reaction-27, coincidental-35, immunization anxiety related reaction- 9 and indeterminate- 13. Total 15 workshops have been accomplished till May 2023.

Besides that, the National AEFI advisory Committee for COVID 19 Vaccines made a number of regulatory and administrative decisions to further strengthen the system of COVID 19 pharmacovigilance as well as recommendations for resolving the identified issues in the country. All of the regulatory recommendations have been implemented by the DGDA with the support of MTaPS and the pharmacovigilance & COVID-19 Safety Surveillance Cell.

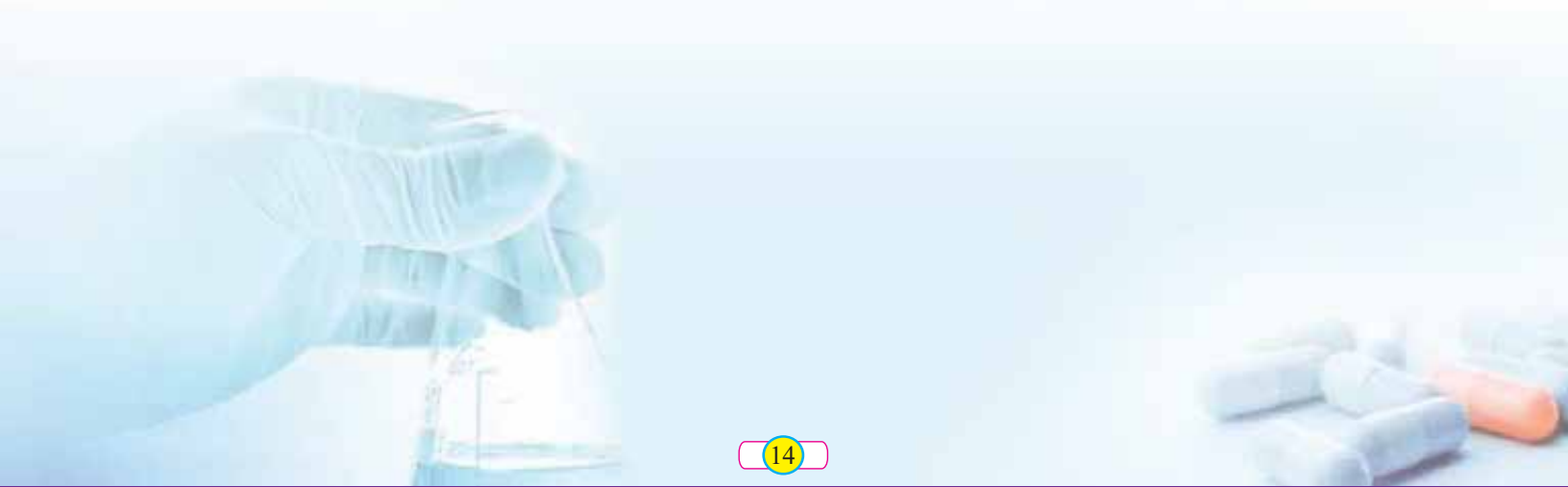


Table 9: Details of the Regulatory Decisions taken by the National AEFI Advisory Committee for COVID-19 Vaccines:

Sl.	Event	Decisions	Status
1	11th **National AEFI Advisory Committee for COVID 19 Vaccines** meeting held on January 4, 2022	An investigation team was formed to investigate the details of one case with the root cause of anaphylaxis, develop a strategy for management in the future, and submit a report to the Directorate and the Ministry of Health in order to prevent death due to serious adverse reactions like anaphylaxis after COVID-19 vaccination.	Implemented
		Reformation of the National advisory committee for COVID-19 Vaccine due to the retirement of one honorary member.	Implemented
2	12th **National AEFI Advisory Committee for COVID 19 Vaccines** meeting held on April 25, 2022.	A letter will be sent to the Director General of the DGHS to confirm at least 30 minutes of observation time in the post-vaccination waiting room at COVID-19 vaccination centers, as well as the arrangement of Adrenaline, Hydrocortisone, and Antihistamine (e.g., Promethazine) Injection for Anaphylactic Shock management at the vaccination centre.	Implemented
		To avoid potential adverse events following COVID-19 vaccination, public awareness will be raised through public announcement and mass media campaigns. A letter will be sent to the DG of DGHS to implement the decisions.	Implemented
		The National AEFI Advisory Committee for COVID-19 Vaccine will visit vaccination centers to oversee the AEFI reporting and management system across the country to avoid serious adverse events following COVID-19 Vaccination	Implemented
		Coordination meetings of DGDA, EPI, DGHS, and CDC will be organized for the purpose of implementing recommendations made by the National AEFI Advisory Committee for COVID-19 Vaccine	Implemented
		The Dhaka South City Corporation Investigation Committee will be contacted in order to re-investigate the deaths of a 12 year and 6 month old male caused by bilateral pneumonia with septic shock.	Implemented
		A letter will be re-sent to THE DG of DGHS requesting a post-mortem to find out the exact cause of "brought in dead" cases after COVID-19 Vaccination.	Implemented

3	13th **National AEFI Advisory Committee for COVID 19 Vaccines** meeting held on July 26, 2022	If anyone goes to any hospital for treatment with adverse events following the COVID-19 Vaccination, arrangements must be made to provide prompt treatment there. A letter will be sent to the Director General of DGHS with a request to provide necessary instructions to all hospitals and clinics in this regard.	Implemented
		A letter will be given to the Director General of DGHS with a request to provide instructions on the obligation to take the doctor's advice if the recipient has any fever prior to vaccination or if there is a history of convulsion, vascular event, Myocardial Infarction (MI), uncontrolled Diabetes mellitus, high blood pressure etc.	Implemented
4	14th Workshop on January, 25, 2023	Propagation of instructions to the health facilities through DGHS for the screening of any acute infection like viral, bacterial, or other causes before the COVID-19 vaccination and to defer vaccination schedule until recovery	Implemented
		Healthcare professionals must be reassured that the cases with adverse event following COVID-19 vaccination being fully investigated, accurately diagnosed and reported immediately for the safety and efficacy of the COVID-19 Vaccine	Implemented
		In case of cluster adverse events due to COVID 19 Vaccination IEDCR must be informed and a committee must be formed for systematic and integrated approach for investigating clusters.	Implemented
	15th Workshop on May, 14, 2023	Resending of letter to the Director General of DGHS with a request to provide instructions on the obligation to take the doctor's advice if the recipient has any fever prior to vaccination or if there is a history of convulsion, vascular event, Myocardial Infarction (MI), uncontrolled Diabetes mellitus, high blood pressure etc.	Under process of Implementation
		Physical Refreshment Training should be arranged for the members of National AEFI Advisory Committee, Divisional AEFI Causality Assessment Committee and District / City Corporation AEFI Investigation Committee for COVID 19 Vaccines	Under process of Implementation
		A coordination workshop will be arranged for expansion of AEFI monitoring activities after delivery of upcoming Bi-valent Vaccine for COVID-19 between technical committee and Vaccination Program AEFI Management Team.	Under process of Implementation

Coordination Meetings:

DGDA, with the support of USAID MTaPS, organized four national level coordination meetings with the relevant government counterparts within the time period from January 2022 to December 2022 in response to the COVID-19 pandemic to identify and address major issues regarding vaccination, strengthening the online AEFI reporting system, and overall management of active pharmacovigilance of Covid-19 Vaccines.

Figure 11: Director General giving speech in the Coordination Meeting on COVID 19 Pharmacovigilance
Photo Credit: MTaPS Bangladesh

Table 10: The details of the coordination meetings are given below:

Event	Participant	Objective	Outcome
Coordination Meeting held on April 21, 2022	Representatives from DGDA, DGHS (Admin), EPI, IEDCR, MIS of DGHS, a2i, USAID MTaPS, WHO district CS and others	Strengthening COVID-19 AEFI reporting and active safety surveillance	Increased quantity of the COVID-19 Vaccine AEFI reports
Coordination Meeting held on June 8, 2022	Officials of DGDA and Additional Secretary of MoH&FW, Causality Assessment Committee of Dhaka Division, AEFI Investigation Committee of 8 districts under Dhaka Division, City Corporation AEFI Investigation Committee of Dhaka.	Providing refresher orientation to the Medical Officers, Nurses and Civil surgeons from eight districts and City Corporations of Dhaka Division.	Improved COVID-19 Vaccination with sensitized AEFI reporting.

Visit to Vaccination Sites:

With the support of USAID-MTaPS, the team of the DGDA visited the vaccination centre of the 250 bed District Sadar Hospital, Cox's Bazar, on August 25, 2022, to oversee the safety compliance obligations. DGDA also organized a workshop following the monitoring of the vaccination center. The Director General of Drug Administration along with the officials of DGDA, including Pharmacovigilance Department, the Civil Surgeon of Cox's Bazar District, Superintendent of the 250 bed District Sadar Hospital, Cox's Bazar, Principal of Cox's Bazar Medical College, Doctors, Nurses, Pharmacists, the acting Country Project Director and other experts from USAID-MTaPS, and WHO attended the workshop. The discussion centered on the formation of the pharmacovigilance committee, raising awareness through the coordination workshop, and an exchange of perspectives between DGDA officials and representatives from the hospital, EPI, the Civil Surgeon Office, WHO, and USAID MTaPS on Pharmacovigilance and the adverse event reporting system and the investigation system of serious adverse events, challenges, and the way forward.

Figure 12: Distinguished participants including representatives from USAID-MTaPS and WHO provided useful insights for making Covid-19 vaccination safer.
Photo Credit: MTaPS Bangladesh

Figure 13: Director General with other Participants in the workshop at @ 250 bed District Hospital, Cox's Bazar
Photo Credit: DGDA, Bangladesh

USAID MTaPS assisted the Safety Surveillance Cell to coordinate with various stakeholders in promoting adherence to the National AEFI Advisory Committee's COVID-19 Vaccine Safety Policy and Protocols.

According to regulatory decisions taken by the National AEFI Advisory Committee for COVID-19 Vaccines DGDA visited to the COVID-19 Vaccination Center of Chittagong Medical College Hospital, Chattogram and Sylhet M.A.G Osmani Medical College Hospital, Sylhet correspondingly on February 2 and February 9, 2023, with the technical assistance of USAID MTaPS to monitor and supervise the safety compliance protocols recommended by the MTaPS supported National AEFI Advisory Committee for COVID 19 Vaccines to ensure that the vaccination centers are implementing all the safety recommendations such as: vaccination storage, handling requirements, trained staff, functionality of the AEFI committee, Guidelines, AEFI reporting form as well as the life-saving medication needed to treat anaphylaxis. The visiting team included representatives from the MoHFW, Hospital management, DGDA and MTaPS.

DGDA disseminated the safety decisions taken through the National AEFI Advisory Committee for COVID-19 Vaccines. Chittagong Medical College Hospital and Sylhet MAG Osmani Medical College Hospital agreed on decisions for further improvement.

Recommendation from the visit:

- The screening of any precipitating cause of adverse events like acute infection, uncontrolled diabetes, hypertension before the COVID-19 vaccination, counselling the patients and to defer vaccination schedule until recovery
- Doctors, nurses and Pharmacists must be reassured that the cases with adverse event following COVID-19 vaccination being fully investigated, accurately diagnosed and reported immediately for the safety and efficacy of the COVID-19 Vaccine.

Figure 14: DG of DGDA visiting to vaccination center of Chittagong Medical College Hospital on February 2, 2023

Photo Credit: Senior Technical Advisor, USAID MTaPS

Figure 15: Director, CMCH providing crest to Director General, DGDA during the visit to Chittagong Medical College Hospital on February 2, 2023

Figure 16: DG of DGDA visiting COVID-19 Vaccination Center at Sylhet MAG Osmani Medical College Hospital Sylhet during a monitoring visit to the hospital held on February 9, 2023

Pharmacovigilance Visit:

The DGDA's Pharmacovigilance Department visits pharmaceutical companies, hospitals, and health programs on a regular basis. Below are some of the snapshots to represent that. DGDA reviews the procedures and guidelines in place and the practices against them. The visit also covers training and awareness sessions on pharmacovigilance and adverse event reporting

Figure 17: visit to Square Pharmaceuticals
Photo Credit: DGDA, Bangladesh

system with training and awareness sessions on pharmacovigilance and adverse event reporting system with practical demonstration. This efforts are to oversee the organization's pharmacovigilance system and provide necessary suggestions or assistance in strengthening the safety monitoring system.

Figure 18: Visit to ACI
Photo Credit: ACI, Bangladesh

Figure 19: Visit to Renata
Photo Credit: Renata, Bangladesh

Figure 20: Visit to Shaheed Suhrawardy Medical College Hospital
Photo Credit: DGDA, Bangladesh

Figure 21: Visit to Bangladesh Specialized Hospital
Photo Credit: Bangladesh Specialized Hospital, Bangladesh

Figure 22: Visit to Navana Pharmaceuticals

World Patients Safety Day-2022 celebration:

On September 18, 2022, with the technical assistance of USAID MTaPS, the Directorate General of Drug Administration (DGDA) observed World Patient Safety Day and arranged a roundtable discussion workshop. The Director General of DGDA Major General Mohammad Yousuf, inaugurated the event as chairperson. The Director General of Medical Education participated in the program along with other dignitaries from the Bangladesh Association of Pharmaceutical

Industries (BAPI), Hospital Management, the Directorate General of Nursing and Midwifery (DGNM), the Directorate General of Family Planning (DGFP), Bangladesh Chemist and Druggist Samity (BCDS), the Regulatory Affairs Society of Bangladesh (ARAB), USAID, WHO, and so on

Figure 23: Round table discussion session
Photo Credit: Roche, Bangladesh

The theme of this year, **"Medication Without Harm,"** aims to promote safe medication practices to prevent medication errors and reduce medication-related harm.
With the purpose of spreading information and raising awareness on safe medication practice, a rally was arranged with displaying festoon balloons. Long banners were hung in front of the DGDA-HQ at different parts of the office. DGDA also developed 12 banners with the technical support of USAID MTaPS on World Patient Safety Day 2022 and disseminated those to all field offices for display

Figure 24: Rally on World Patient Safety Day Celebration
Photo Credit: Roche, Bangladesh

MedSafetyWeek-2022 and PV awareness program:

The Directorate General of Drug Administration (DGDA) celebrated #MedSafetyWeek 2022 from November 7-13 and arranged a coordination and awareness workshop in collaboration with USAID MTaPS on November 13, 2022, aligning with the global campaign of the WHO's Uppsala Monitoring Centre involving medicines regulators from 81 countries and focusing on the key role of every healthcare professional, patient and career who reports a suspected side effect and contributes to using medicines safely. The Director General of DGDA inaugurated the program as chairperson. The Vice chancellor of Chittagong Medical University, along with other distinguished guests, kept their valuable remarks regarding the issue. The slogan of the #MedSafety program was "Raising Pharmacovigilance Awareness on Social Media."The campaign materials have been posted on DGDA's social media platforms.

Figure 25: Director General, DGDA speaking in the workshop of #MedSafetyWeek 2022 @DGDA
Photo Credit: MTaPS, Bangladesh