REPORT N° 8

ADVERSE EVENTS FOLLOWING IMMUNIZATION WITH COVID-19 VACCINES IN LEBANON

COVID-19 Vaccines - Lebanon

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February 14, 2021 - January 19, 2022

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EXECUTIVE SUMMARY

This executive summary provides an overview of Adverse Events Following Immunization (AEFIs) that were temporally associated (i.e., occurred after administration of the vaccine) to the four COVID-19 vaccines (Pfizer-BioNTech Vaccine, AstraZeneca Vaccine, Sputnik V Vaccine and Sinopharm Vaccine) available in Lebanon during the mass campaign immunization between February 14th, 2021, and January 19th, 2022. According to the World Health Organization (WHO), an AEFI is any untoward medical occurrence that follows immunization and does not necessarily have a causal relationship with the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.

The following information summarizes COVID-19 vaccines doses since their first deployment in Lebanon, from February 14th, 2021, until January 19th, 2022:

TOTAL NUMBER OF REGISTERED PERSONS
5,658,190

TOTAL NUMBER OF ADMINISTERED DOSES
4,765,458

FIRST DOSE
2,404,201
(50.5%)

SECOND DOSE
1,959,448
(41.1%)

THIRD DOSE
400,209
(8.4%)

TOTAL PFIZER-BIONTECH DOSES
3,903,866
(81.92%)

TOTAL ASTRAZENECA DOSES
711,566
(14.93%)

TOTAL SPUTNIK V DOSES
123,340
(2.5%)

TOTAL SINOPHARM DOSES
17,281
(0.36%)

As per the COVID-19 vaccination dashboard provided by IMPACT platform on January 19th, 2022

All percentages are calculated with respect to the total administered doses

BACKGROUND

Within the scope of the AEFI surveillance related to the available COVID-19 Vaccines in Lebanon, the Pharmacovigilance (PV) Program established a procedure for the management of reported AEFIs. Vaccine recipients experiencing any AEFI can report through one of the following means: 1214 Hotline Call Center, IMPACT Platform, Vaccination Sites/Hospital Sites through "Kobo toolbox: AEFIs Software for reporting" or by direct contact with the PV program, and other sources including Preventive Medicine, Epidemiology Surveillance Program, Health Education and other departments from the Ministry of Public Health (MoPH). A case report refers to a report received by the PV Program which pertains to one individual vaccine recipient who reported at least one adverse event after receiving the COVID-19 vaccine (i.e., temporally associated with the vaccine). All case reports are screened and validated for data completion. Incomplete or inconsistent case reports are followed-up directly with the initial reporter. The case reports are classified as serious or non-serious cases. The non-serious case reports are entered directly into the national web-based report management system, VigiFlow, while serious cases go through a follow–up/ investigation, causality assessment and validation by the Serious AEFI Special Committee before they are entered into VigiFlow. The surveillance aims to establish a rigorous safety profile regarding the COVID-19 vaccines administered in Lebanon.

HIGHLIGHTS

- A total of 6,578 case reports and 24,237 AEFIs were received following the administration of 4,765,458 doses of COVID-19 vaccines (Pfizer-BioNTech, AstraZeneca, Sputnik V and Sinopharm) in Lebanon between the 14th of February 2021 and the 19th of January 2022:
  - This is equivalent to a reporting rate of 1.38 case reports and 5.08 AEFIs per 1,000 doses administered
  - This represents an increase of 540 case reports and 1,798 AEFIs in comparison with the previous report dated from February 14th to November 19th, 2021
  - The age group of vaccine recipients who mostly reported AEFIs was between 18 and 44 years old (54.6%), with females reporting more than males (60.9% vs. 39.1%) (Table 4)
  - Most of the reporters were vaccine recipients (84.6%)

- The 6,578 case reports were received through one of the following means (Table 1):
  - IMPACT Platform: 3,783 case reports (57.5%)
  - 1214 Hotline Call Center: 1,884 case reports (28.64%)
  - Vaccination Sites/Hospital Sites through "Kobo toolbox: AEFIs Software for reporting" or by direct contact with the PV program: 846 case reports (12.86%)
  - Other reporting sources which may include Preventive Medicine, Epidemiology Surveillance Program, Health Education and other departments from the MoPH: 65 case reports (1.0%)

- Out of the 6,578 case reports (Table 2):
  - 5,123 case reports were associated with dose 1 of vaccination (77.9%)
  - 1,307 case reports were associated with dose 2 of vaccination (19.86%)
  - 142 case reports were associated with dose 3 of vaccination (2.15%)
  - 6 case reports were missing this information (0.09%)

- Out of the 6,578 case reports (Figure 2, Table 3):
  - 6,146 case reports were non-serious (93.43% of total case reports)
  - 432 case reports included serious AEFIs (6.57% of total case reports) as per the WHO definition (refer to Technical Notes for serious cases definition as per WHO), out of which:
    - o 311 case reports included serious AEFIs that did not require hospitalization nor lead to death. These were identified as other medically important events (4.73% of total case reports)
    - o 121 case reports resulted in either hospital admission or death representing 1.84% of all case reports and a reporting rate of 0.025 per 1,000 doses of vaccines

- Of the total received AEFIs, the 5 most frequently reported AEFIs with the four COVID-19 vaccines available in Lebanon were (Table 6):
  - Injection site pain (43.2% of total reported AEFIs)
  - Fatigue (41.8% of total reported AEFIs)
  - General pain which may correspond to body pain or joint pain (41.4% of total reported AEFIs)
  - Headache (37.3% of total reported AEFIs)
  - Pyrexia (33.2% of total reported AEFIs)

- Of the total received AEFIs, the most reported AEFIs by System Organ Class (SOC) with the four COVID-19 vaccines available in Lebanon were (Table 11):
  - General Disorders and Administration Site Conditions (84.2% of total reported AEFIs per SOC)
  - Nervous System Disorders (45.0% of total reported AEFIs per SOC)
  - Gastrointestinal Disorders (26.6% of total reported AEFIs per SOC)

- The most frequently reported AEFIs per vaccine were (Table 7, 8, 9, 10):
  - Injection site pain was the most frequently reported non-serious adverse event following the Pfizer-BioNTech Vaccine (37.4% of total reported AEFIs)
  - Fatigue was the most common adverse event following all other vaccines: 56.3% of the total reported AEFIs related to AstraZeneca Vaccine, 65.9% of the total reported AEFIs related to Sputnik V Vaccine, and 50.0% of the total reported AEFIs related to Sinopharm Vaccine

REPORTING OVERVIEW

a. Global Analysis

Table 1 summarizes the case reports by reporting means: 1214 Hotline Call Center, IMPACT Platform, Vaccination Sites/Hospital Sites through "Kobo toolbox: AEFIs Software for reporting" or direct contact with the PV program, and other sources including Preventive Medicine, Epidemiology Surveillance Program, Health Education, and other departments from the MoPH.

Table 1: Summary of case reports by means of reporting

Means of Reporting	IMPACT Platform	1214 Hotline	Vaccination Sites/ Hospital Sites	Others
Number of Case Reports	3,783	1,884	846	65
Percentage	57.50%	28.64%	12.86%	1.0%

Table 2 classifies the 6,578 reported cases according to their occurrence: after the 1st, 2nd and 3rd dose of COVID-19 vaccines. Out of these 6,578 case reports, 5,123 case reports (77.9%) were after the 1st dose, 1,307 case reports (19.86%) were after the 2nd dose and 142 case reports (2.15%) were after the 3rd dose (booster dose). The remaining 6 case reports (0.09%) were missing the dose number. Of the total registered persons, 34.63% have completed their primary COVID-19 vaccination series (dose 1 and 2).

Table 2. Summary of case reports according to received dose*

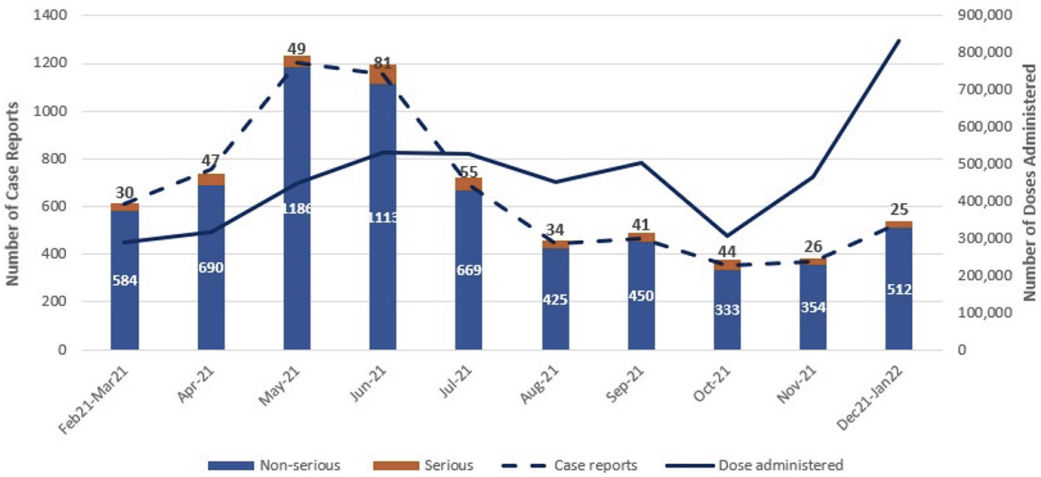
	All Vaccines Combined	Pfizer-BioNTech	AstraZeneca	Sputnik V	Sinopharm
Total Case Reports (%)	6,578 (100)	4,035 (61.34)	2,292 (34.84)	235 (3.57)	16 (0.25)
Dose 1 (%)	5,123 (77.9)	2,817 (69.81)	2,121 (92.54)	175 (74.46)	10 (62.5)
Dose 2 (%)	1,307 (19.86)	1,074 (26.62)	167 (7.29)	60 (25.54)	6 (37.5)
Dose 3 (%)	142 (2.15)	141 (3.50)	1 (0.04)	0 (0)	0 (0)

**Six case reports were missing the dose number (0.09%).*

Table 3. Summary of all case reports related to COVID-19 vaccines available in Lebanon, from February 14th, 2021, to January 19th, 2022

	All Vaccines Combined	Pfizer-BioNTech	AstraZeneca	Sputnik V	Sinopharm
Total Doses Administered	4,765,458	3,903,866	711,566	123,340	17,281
Total case reports (%)	6,578 (100)	4,033 (61.31)	2,294 (34.87)	235 (3.57)	16 (0.25)
Non serious case reports* (%)	6,146 (93.43)	3,747 (92.9)	2,162 (94.25)	225 (95.74)	12 (75.0)
Serious case reports** (%)	432 (6.57)	286 (7.1)	132 (5.75)	10 (4.26)	4 (25.0)
Total reporting rate per 1,000 doses administered	1.38	1.03	3.22	1.91	0.92
Serious reporting rate per 1,000 doses administered	0.09	0.07	0.19	0.08	0.23

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1)
**Non serious cases include expected local and systemic AEFIs resolved without the need for further follow up or investigation*
***Serious cases are those who meet the WHO seriousness criteria (refer to Technical Notes)*



*Numbers presented on the blue and red bars reflect the number of case reports reported by month

Figure 1: Number of case reports*, doses administered, non-serious and serious cases by month of the four COVID-19 Vaccines' administration in Lebanon, from February 14th, 2021, to January 19th, 2022

Case reports are assessed based on the date of vaccine administration. The administration period ranges from February 14th, 2021 to January 19th, 2022. Accordingly, case reports were received as of February 14th, 2021, with an increase in both serious and non-serious case reports. The highest reporting rate was during the month of May for the non-serious cases and June for the serious cases.

b. Demographics

Tables 4 and 5 present a summary of case reports related to the COVID-19 vaccines by age group, gender, and reporter qualification.

Table 4. Summary of all case reports by age group and gender related to the four COVID-19 vaccines available in Lebanon, from February 14th, 2021, to January 19th, 2022

Gender	COUNT	PERCENTAGE
Female	4,003	60.9%
Male	2,575	39.1%
Age		
12- 17 years	228	3.5%
18 - 44 years	3,594	54.6%
45 - 64 years	1,950	29.6%
65 - 74 years	339	5.2%
≥ 75 years	421	6.4%
Unknown	46	0.7%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1)
Note: Age represents the age at time of vaccination. Some case reports may be missing the date of birth

Table 5. Summary of all case reports by reporter qualification related to the four COVID-19 vaccines available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reporter Qualification	COUNT	PERCENTAGE
Physician	229	3.5%
Pharmacist	190	2.9%
Other Health Professional	592	9.0%
Vaccine Recipients	5,567	84.6%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1)

c. Non serious Adverse Events Following Immunization

A case report refers to a report received by the PV Program, which pertains to one individual vaccine recipient who has reported at least one adverse event after receiving one of the COVID-19 vaccines (i.e., temporally associated with the vaccine).

The tables below give an overview of the top reported non-serious AEFIs.

c.i. Most Reported Non-Serious AEFIs Related to COVID-19 Vaccines:

Table 6. Top 15 AEFIs by reported Preferred Terms (PTs)* related to the four COVID-19 vaccines available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reported Preferred Terms* (MedDRA)	COUNT	PERCENTAGE
Injection site pain	2,654	43.2%
Fatigue	2,570	41.8%
Pain	2,544	41.4%
Headache	2,295	37.3%
Pyrexia	2,040	33.2%
Chills	1,870	30.4%
Nausea	1,028	16.7%
Injection site swelling	598	9.7%
Dyspnea	492	8.0%
Abdominal pain	466	7.6%
Diarrhea	445	7.2%
Injection site erythema	406	6.6%
Cough	398	6.5%
Dizziness	339	5.5%
Vomiting	322	5.2%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
**Preferred Terms (PTs) are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.*

c.ii. Non serious AEFIs per specific vaccine:

Table 7. Top 10 AEFIs by reported Preferred Terms (PTs)* related to the Pfizer-BioNTech COVID-19 vaccine available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reported Preferred Terms (MedDRA)	COUNT	PERCENTAGE
Injection site pain	1,402	37.4%
Pain	1,323	35.3%
Fatigue	1,198	32.0%
Headache	1,109	29.6%
Pyrexia	936	25.0%
Chills	832	22.2%
Nausea	477	12.7%
Injection site swelling	378	10.1%
Dyspnea	280	7.5%
Injection site erythema	242	6.5%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
**Preferred Terms (PTs) are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.*

Table 8. Top 10 AEFIs by reported Preferred Terms (PTs)* related to the AstraZeneca COVID-19 vaccine available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reported Preferred Terms (MedDRA)	COUNT	PERCENTAGE
Fatigue	1,217	56.3%
Injection site pain	1,135	52.5%
Pain	1,100	50.9%
Headache	1,074	49.7%
Pyrexia	1,003	46.4%
Chills	926	42.9%
Nausea	496	23.0%
Abdominal pain	221	10.2%
Injection site swelling	203	9.4%
Dyspnea	197	9.1%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
**Preferred Terms (PTs) are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.*

Table 9. Top 10 AEFIs by reported Preferred Terms (PTs)* related to the Sputnik V COVID-19 vaccine available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reported Preferred Terms (MedDRA)	COUNT	PERCENTAGE
Fatigue	149	65.9%
Pain	118	52.2%
Injection site pain	112	49.6%
Chills	111	49.1%
Headache	110	48.7%
Pyrexia	98	43.4%
Nausea	52	23.0%
Diarrhea	20	8.8%
Injection site swelling	17	7.5%
Cough	15	6.6%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
**Preferred Terms (PTs) are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.*

Table 10. Top 10 AEFIs by reported Preferred Terms (PTs)* related to the Sinopharm COVID-19 vaccine available in Lebanon, from February 14th, 2021, to January 19th, 2022

Reported Preferred Terms (MedDRA)	COUNT	PERCENTAGE
Fatigue	6	50.0%
Injection site pain	5	41.7%
Dyspnea	3	25.0%
Nausea	3	25.0%
Pain	3	25.0%
Pyrexia	3	25.0%
Chest pain	2	16.7%
Cough	2	16.7%
Dizziness	2	16.7%
Headache	2	16.7%

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
**Preferred Terms (PTs) are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.*

Table 11. Summary of number and percentage of reported non-serious AEFIs by System Organ Class (SOC)* related to the four COVID-19 vaccines available in Lebanon, from February 14th , 2021, to January 19th, 2022

System Organ Class (SOC)	All Vaccines Combined	Pfizer-BioNTech	AstraZeneca	Sputnik V	Sinopharm
General disorders and administration site conditions	5,172 (84.2)	2,998 (80.0)	1,953 (90.4)	211 (93.4)	10 (83.3)
Nervous system disorders	2,764 (45.0)	1,420 (37.9)	1,220 (56.5)	119 (52.7)	5 (41.7)
Gastrointestinal disorders	1,637 (26.6)	813 (21.7)	751 (34.8)	70 (31.0)	3 (25.0)
Respiratory, thoracic and mediastinal disorders	745 (12.1)	460 (12.3)	262 (12.1)	20 (8.8)	3 (25.0)
Musculoskeletal and connective tissue disorders	659 (10.7)	374 (10.0)	268 (12.4)	16 (7.1)	1 (8.3)
Skin and subcutaneous tissue disorders	491 (8.0)	284 (7.6)	189 (8.7)	17 (7.5)	1 (8.3)
Vascular disorders	227 (3.7)	164 (4.4)	63 (2.9)	0 (0)	0 (0)
Cardiac disorders	158 (2.6)	113 (3.0)	45 (2.1)	0 (0)	0 (0)
Investigations**	131 (2.1)	89 (2.4)	41 (1.9)	0 (0)	1 (8.3)
Eye disorders	116 (1.9)	60 (1.6)	53 (2.5)	2 (0.9)	1 (8.3)
Infections and infestations	89 (1.4)	64 (1.7)	21 (1.0)	3 (1.3)	1 (8.3)
Blood and lymphatic system disorders	73 (1.2)	61 (1.6)	9 (0.4)	3 (1.3)	0 (0)
Ear and labyrinth disorders	60 (1.0)	40 (1.1)	16 (0.7)	4 (1.8)	0 (0)
Reproductive system and breast disorders	42 (0.7)	21 (0.6)	20 (0.9)	1 (0.4)	0 (0)
Injury, poisoning and procedural complications	37 (0.6)	16 (0.4)	21 (1.0)	0 (0)	0 (0)
Psychiatric disorders	37 (0.6)	16 (0.4)	21 (1.0)	0 (0)	0 (0)
Metabolism and nutrition disorders	34 (0.6)	12 (0.3)	22 (1.0)	0 (0)	0 (0)
Immune system disorders	31 (0.5)	18 (0.5)	13 (0.6)	0 (0)	0 (0)
Renal and urinary disorders	13 (0.2)	7 (0.2)	6 (0.3)	0 (0)	0 (0)
Surgical and medical procedures	2 (0)	2 (0.1)	0 (0)	0 (0)	0 (0)
Endocrine Disorders	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1)
**System Organ Classes (SOCs) are groupings by etiology (e.g., Infections and infestations), manifestation site (e.g., Gastrointestinal disorders) or purpose (e.g., Surgical and medical procedures)*
*** Investigations include cases of abnormal blood pressure, increased blood pressure, decreased blood pressure, increased systolic blood pressure, increased heart rate, irregular heart rate, increased Fibrin D-Dimer, decreased weight, decreased oxygen saturation, increased blood glucose levels, decreased blood iron, increased blood pH, increased intraocular pressure, red blood cells in urine, decreased urine output and cases who tested positive or negative for SARS-CoV-2.*

d. Serious Adverse Events Following Immunization

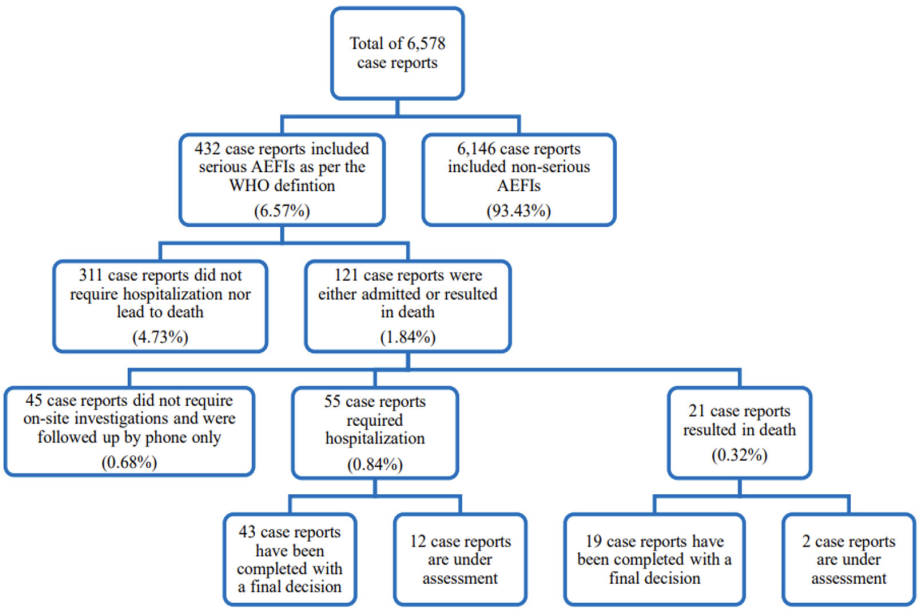
According to the WHO, a serious AEFI is an event that results in death, hospitalization, or prolongation of an existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth, defect or is life-threatening. The ICH E2A and E2D Guidelines (refer to Technical Notes) have also stated that other situations such as other medically important event or reaction which may jeopardize the patient or may require intervention to prevent one of the outcomes stated in the serious case definition, should also be considered serious after applying medical and scientific judgment. Those "other situations" are open to interpretation and could vary from jurisdiction to jurisdiction. In this report, serious case reports following immunization were classified as follows:

- **Other Medically Important Events :** This includes unexpected AEFIs, local or systemic, that may be serious in their nature but did not require hospitalization nor resulted in death. They may include ER visits and may or may not be resolved in the next 48 hours. These case reports are followed by the PV team over the phone without further investigation.
- **Serious Cases :** This includes cases that resulted in death, hospitalization, disability, congenital abnormalities, or were life threatening. These are investigated and evaluated for causality assessment.

432 case reports included serious AEFIs as per the WHO definition, out of which 311 case reports did not require hospitalization nor lead to death. These were identified as other medically important events. 121 case reports were serious cases that were either admitted to the hospital or resulted in death (Figure 2).

Serious Cases:

Out of the 121 cases mentioned above, 45 case reports fit the WHO definition of seriousness criteria, but they did not require on-site investigations and they were followed up by phone only; 76 cases were serious reports that required full investigation. Of the 76 serious cases, 62 reports have been completed with a final decision by the Serious AEFI Special Committee at the Ministry of Public Health. The remaining 14 case reports are still under assessment by the PV team. Tables 12, 13 and 14 show detailed description of the 76 serious cases.



**As per the WHO definition (refer to Technical Notes for serious cases definition as per WHO)*

Figure 2. Classification of case reports by seriousness criteria* related to the four COVID-19 vaccines available in Lebanon, from February 14th , 2021, to January 19th, 2022

Table 12. Summary of 62 serious case reports that have been completed with a final decision by the Serious AEFI Special Committee

	All Cases	Pfizer-BioNTech	AstraZeneca	Sinopharm
Number of case report (%)	62 (100)	51 (82.26)	10 (16.13)	1 (1.61)
Age (years)				
12 - 17 years	1	1	0	0
18 - 44 years	9	6	2	1
45 - 64 years	18	11	7	0
65 - 74 years	10	9	1	0
≥ 75 years	24	24	0	0
Median Age in years (range)	67.5 (16-95)	73 (16-95)	54.5 (29-65)	43
Sex (%)				
Male	33 (53.23)	28 (54.9)	5 (50)	0
Female	29 (46.77)	23 (45.1)	5 (50)	1 (100)
Dose number (%)				
1st	39 (62.90)	30 (58.83)	8 (80)	1 (100)
2nd	20 (32.26)	19 (37.25)	1 (10)	0
3rd	2 (3.23)	2 (3.92)	0	0
1st and 2nd *	1 (1.61)	0	1 (10)	0
Median TTO in days (range)**	4.5 (0-93)	4 (0-93)	8 (2-32)	20
Median TTO in days (range) per dose				
1st	5 (0-32)	5 (0-26)	10.5 (2-32)	20
2nd	3 (0-93)	3 (0-93)	2	0
3rd	0.5 (0-1)	0.5 (0-1)	0	0
1st and 2nd *	9	0	9	0
Mean TTO in days (SD) per dose***				
1st	8.82 (8.11)	7.6 (7.31)	12 (10)	20
2nd	9.95 (20.47)	10.37 (20.94)	2	0
3rd	0.5 (0.71)	0.5 (0.71)	0	0
1st and 2nd *	9	0	9	0
Seriousness Criteria (%)				
Fatal	19 (30.65)	15 (29.41)	3 (30.)	1 (100)
Hospitalized	43 (69.35)	36 (70.59)	7 (70)	0
AEFI Committee Decision (%)				
Coincidental	34 (54.9)	29 (56.86)	4 (40)	1 (100)
Indeterminate	23 (37.1)	19 (37.26)	4 (40)	0
Consistent	5 (8.1)	3 (5.88)	2 (20)	0

**This is an immunization-error case in which the patient received both doses during the same vaccination session*
***TTO: Time to onset*
****SD: Standard deviation*

Table 13. Summary of reported AEFIs for the 62 completed serious cases

Vaccine Brand / AEFI		Pfizer-BioNTech (N=51)	AstraZeneca (N=10)	Sinopharm (N=1)
Acute Bronchitis		1	0	0
Acute Disseminated Encephalomyelitis		0	1	0
Amyotrophic Lateral Sclerosis (ALS)		1	0	0
Aspiration Peumonia with Respiratory Failure		1	0	0
Atrial Fibrillation with Ischemic Cerebrovascular Accident (CVA)		1	0	0
Pneumonia		1	0	0
Cardiac Arrest		7	1	0
Cerebral Hemorrhage		0	1	0
Cerebrovascular Accident (CVA)	Hemorrhagic	0	1	0
	Ischemic	13	1	0
	Transient Ischemic Attack	2	0	0
Epilepsy		1	0	0
Extensive Portal Vein Thrombosis extending to the Superior Mesenteric Vein		0	1	0
Fatal Atrial Fibrillation		1	0	0
Febrile Neutropenia		1	0	0
Guillain-Barré Syndrome		4	0	0
Hyperstimulation of Immune System		1	0	0
Hypertensive emergency with Ischemic Stroke		1	0	0
Kounis Syndrome		1	0	0
Pulmonary Actinomycosis		0	1	0
Myocardial Infarction		4	1	0
Myocarditis		1	0	0
Oxygen Desaturation with Dyspnea		1	0	0
Polypnea, Cyanosis and Hypotension		0	0	1
Post-Surgical Bleeding		0	1	0
Pulmonary Edema		1	0	0
Pulmonary Embolism		1	0	0
Sepsis		1	0	0

Severe Allergic Reaction	Acute Severe Urticaria	1	0	0
	Anaphylactic Shock	1	0	0
Vascular Disease	Deep Vein Thrombosis	1	0	0
	Thrombosis of Left Axillary Artery	1	0	0
	Pulmonary Embolism	1	0	0
Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)		0	1	0

Table 14. Summary of 14 serious case reports that are still under assessment by the PV team

	All Cases	Pfizer-BioNTech	AstraZeneca
Number of case report (%)	14 (100)	10(71.43)	4 (28.57)
Age (years)			
12 - 17 years	2	2	0
18 - 44 years	4	2	2
45 - 64 years	5	3	2
65 - 74 years	3	3	0
≥ 75 years	0	0	0
Median Age in years (range)	50 (12-71)	54.5 (12-71)	44.5 (32-52)
Sex (%)			
Male	5 (42.86)	4 (40)	2 (50)
Female	8 (57.14)	6 (60)	2 (50)
Dose number (%)			
1st	7 (50)	4 (40)	3 (75)
2nd	5 (35.71)	4 (40)	1 (25)
3rd	2 (14.29)	2 (20)	0
Median TTO in days (range)*	7.5 (0-44)	8.5 (0-44)	6 (2-16)
Median TTO in days (range) per dose			
1st	7 (0-16)	4.5 (0-15)	7 (7-16)
2nd	5 (1-39)	5.5 (1-39)	5
3rd	32.5 (21-44)	32.5 (21-44)	0
Mean TTO in days (SD) per dose**			
1st	7 (6.53)	6 (6.98)	8.33 (7.09)
2nd	11.2 (15.85)	12.75 (17.86)	5
3rd	32.5 (16.26)	32.5 (16.26)	0
Seriousness Criteria (%)			
Fatal	2 (14.29)	1 (10)	1 (25)
Hospitalized	12 (85.71)	9 (90)	3 (75)

*TTO: Time to onset
**SD: Standard deviation

e. Safety Signals

The PV team has adopted two sources for identifying signals (refer to Technical Notes) associated with AEFIs following Pfizer-BioNTech and AstraZeneca COVID-19 Vaccine: The French National Security Agency of Medicines and Health Products (ANSM) and the World Health Organization-Uppsala Monitoring Center (WHO-UMC) Classification.

Tables 15 and 16 summarize the reported AEFIs in Lebanon during the time of this report which may be either potential or confirmed signals for Pfizer-BioNTech and AstraZeneca COVID-19 vaccines according to the ANSM reports and/or the WHO-UMC Vigibase.

Table 15. Confirmed signals identified in Lebanon

Pfizer-BioNTech COVID-19 vaccine		AstraZeneca COVID-19 vaccine	
Safety Signal	**Count**	**Safety Signal**	**Count**
Arterial Hypertension†	121	Flu-Like Syndrome	33
Myocarditis	2	Immune Thrombocytopenia	1
Pericarditis	3	Transverse Myelitis	1
Trigeminal Neuralgia§	4	Trigeminal Neuralgia§	1
Photophobia	1	Photophobia	3
Tinnitus	11	Tinnitus	8
Deafness	1	Deafness	1

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
Data Source: ANSM (13/01/2022)
Data Source: World Health Organization-Uppsala Monitoring Center (WHO-UMC)
†Cases of arterial hypertension included the terms: blood pressure abnormal, blood pressure systolic increase, blood pressure increased, hypertension, hypertensive crisis, and hypertensive emergency.
§Cases of trigeminal neuralgia included the term: facial paralysis.

Table 16. Potential signals identified in Lebanon

Pfizer-BioNTech COVID-19 vaccine		AstraZeneca COVID-19 vaccine	
Safety Signal	**Count**	**Safety Signal**	**Count**
Shingles†	11	Mucocutaneous Bleeding¶	45
Cardiac Rhythm Disorders§	170	Shingles	5
Menstrual Irregularities‖	17	Elevated Blood Pressure¶¶	56
Cerebral Vein Thrombosis‡	13	Erythema nodosum#	169
		Arrhythmias	71
		Pancreatitis	2

Data Source: VigiLyze (Dataset date: 19/01/2022, MedDRA version: 24.1).
Data Source: ANSM (13/01/2022)
†Cases of shingles included the terms: oral herpes, herpes zoster, herpes zoster infection neurological, herpes zoster reactivation, Human herpes virus infection reactivation, and herpes virus infection.
§Cases of cardiac rhythm disorders included the terms: tachycardia, palpitations, bradycardia, cardiac arrest, increased heart rate, arrhythmia, sinus bradycardia, Atrial fibrillation, and irregular heart rate.
‖Case of menstrual irregularities included the terms: menstruation irregular, menstruation delayed, menstrual disorder, and vaginal hemorrhage.
‡Cases of cerebral vein thrombosis included the terms: ischemic stroke, ischemic cerebral infarction, cerebral ischemia, and transient ischemic attack.
¶Cases of mucocutaneous bleeding included the terms: contusion, injection site bruising, epistaxis, and oral contusion.
¶¶Cases of elevated blood pressure included the terms: blood pressure abnormal, blood pressure systolic increase, blood pressure increased, hypertension, hypertensive crisis, and hypertensive emergency.
#Cases of erythema nodosum included the terms: rash erythematous, injection site erythema, and erythema.

DESCRIPTION OF SERIOUS ADVERSE EVENTS FOLLOWING IMMUNIZATION

AEFIs requiring Hospitalization or with Fatal Outcome (Tables 12, 13, 14)

AEFIs are classified as serious according to the seriousness criteria of WHO (refer to the Technical Notes). These cases either require a phone call only or an investigation followed by a causality assessment to evaluate the potential relationship between the AEFI and the vaccine, and to implement the appropriate follow-up actions. The investigation is carried out by the PV team members. It includes an extensive and rigorous scientific evaluation based on available information about the vaccination site, the patient's medical records, laboratory results, and information retrieved from the vaccine recipient and/or their relatives. After collecting all the available information, an investigation report is filled, and a causality assessment is performed by a group of experts to review the potential causal association between the AEFI and the vaccine. WHO forms and tools are used to carry out both the investigation and the causality assessment. Findings are discussed with the Serious AEFI Special Committee at Ministry of Public Health. In the period covered by this report, there were 121 case reports classified as serious per the WHO-UMC definition that resulted in either hospitalization or death, representing 1.84% of all case reports and a reporting rate of 0.025 per 1,000 doses of vaccines.

Overview of completed serious case reports (Table 12, 13)

Out of the 62 serious case reports that were completed with a final decision by the Serious AEFI Special Committee, there are 43 cases of hospitalization and 19 cases of death temporally associated with the administration of COVID-19 vaccines.

For the 43 suspected hospitalization cases post-vaccination (21 Males, 22 Females), the vaccine recipients' age range was between 16 and 95 years old. Twenty-eight hospitalizations occurred after the 1st dose, twelve hospitalizations occurred after the 2nd dose, while the remaining two hospitalizations occurred after the 3rd dose. There is one case of immunization error where the patient received both doses during the same vaccination session. The 43 vaccine recipients experienced AEFIs within few minutes to 32 days' post-vaccination. The Serious AEFI Special Committee at the Ministry of Public Health confirmed the coincidental causality assessment in 24 case reports. Fifteen case reports were considered as indeterminate, and four case reports were classified as consistent (one case of immunization error, one case of anaphylactic shock and two cases of Guillain-Barré).

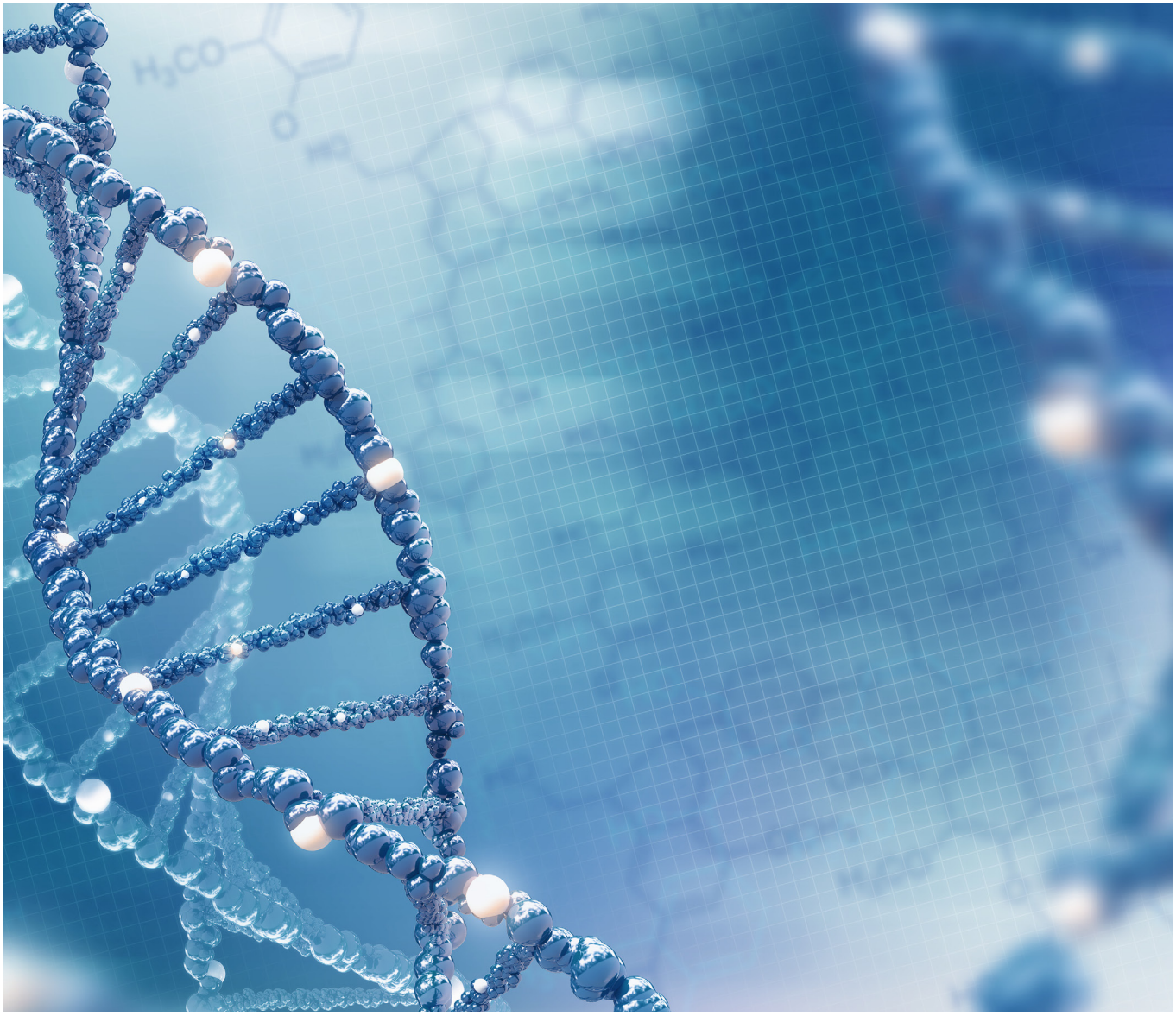
In the 19 suspected cases of death post-vaccination (11 Males, 8 Females), the vaccine recipients' age range was between 29 and 92 years old. Eleven death cases were after the 1st dose while the remaining eight cases were after the 2nd dose. The 19 vaccine recipients experienced AEFIs within 30 minutes to 93 days' post-vaccination. The Serious AEFI Special Committee at the MoPH confirmed the coincidental classification in ten case reports. Eight case reports were considered as indeterminate, and one case report showed a consistent association due to the lack of other clearly attributing factors.

Overview of serious case reports under assessment (Table 14)

Out of the 14 serious case reports that are still under assessment by the PV team, there are 12 cases of hospitalization and 2 cases of death temporally associated with the administration of COVID-19 vaccines.

For the 12 suspected hospitalization cases post-vaccination (5 Males, 7 Females) the vaccine recipients' age range was between 12 and 71 years old. Six hospitalizations occurred after the 1st dose, four hospitalizations occurred after the 2nd dose, and two hospitalizations occurred after the 3rd dose. The 12 vaccine recipients experienced AEFIs within few hours to 44 days' post-vaccination.

In the 2 suspected cases of death post-vaccination (1 Male, 1 Female), the vaccine recipient's age was 57 and 32 years old, respectively. Death occurred 8 days after the 1st dose in the case of the male vaccine recipient while it occurred 5 days after the 2nd dose in the case of the female vaccine recipient (Table 14).



INTERNATIONAL DATA OVERVIEW RELATED TO SERIOUS AEFI WITH COVID-19 VACCINES

After a thorough literature review, the following data was retrieved from other countries regarding AEFI with COVID-19 vaccines. It is important to mention that each country has its own way of reporting AEFI with COVID-19 vaccines.

United-States of America (CDC)

According to the CDC, death reports after COVID-19 vaccination are rare. From December 14th, 2020, through January 18th, 2022, more than 529 million doses of COVID-19 vaccines were administered in the United States. Vaccine Adverse Event Reporting System (VAERS) received 11,468 death reports (0.0022%) among people who received a COVID-19 vaccine.

Ontario, Canada (Public Health Ontario)

Based on the weekly surveillance summary published by Public Health Ontario (PHO) regarding AEFI for COVID-19 in Ontario, covering the period between December 13th, 2020, to January 16th, 2022, 978 AEFI reports have been classified as serious, representing 5.6% of the total AEFI reports and a serious AEFI reporting rate of 3.4 per 100,000 doses administered for all vaccine products combined. 547 serious cases were reported following Pfizer-BioNTech COVID-19 vaccine, which represented a reporting rate of 2.8 per 100,000 doses administered, and 121 serious cases were reported following AstraZeneca COVID-19 vaccine, which represents a reporting rate of 11.1 per 100,000 doses administered. Of the 978 reports, 967 reports required hospital admission related to the adverse event and 11 were reports of death.

United Kingdom (Medicines and Healthcare Products Regulatory Agency)

Based on the weekly summary of the Yellow Card reporting by the Medicines and Healthcare products Regulatory Agency (MHRA), up to and including the 12th of January 2022, 158,933 UK Yellow Cards were received and analyzed from people who have received the Pfizer-BioNTech COVID-19 Vaccine, and a total of 242,148 UK reports of suspected AEFIs were received from people who have received the AstraZeneca COVID-19 Vaccine. The MHRA has received 696 UK reports of suspected AEFIs to the Pfizer-BioNTech COVID-19 Vaccine in which the patient died shortly after vaccination, and 1,190 reports for the AstraZeneca COVID-19 vaccine.

CONCLUSION

In Lebanon, from January 3rd, 2020, to January 24th, 2022, there have been 865,229 confirmed cases of SARS-CoV-2 with 9,487 deaths, reported to the WHO. Vaccination is the single and most effective way to reduce deaths and hospitalizations from COVID-19. The national immunization campaign was first deployed on February 14th, 2021. Pfizer-BioNTech, AstraZeneca, Sputnik V, and Sinopharm, are the four COVID-19 vaccines available in Lebanon. Most COVID-19 vaccines administered are Pfizer-BioNTech and AstraZeneca.

In this report, 93.43% were classified as non-serious case reports, and only 6.57% were classified as serious. It is important to note that reports of adverse events following vaccination, including hospitalizations and deaths, do not necessarily mean that they are caused by the vaccine.

The PV Program at the Ministry of Public Health continues to conduct constant monitoring for the safety of COVID-19 vaccines in collaboration with its partners, including individual case review, daily analysis of surveillance data for vaccine safety signals, and regular reporting.

TECHNICAL NOTES

- Important Medical Event Terms List: The EudraVigilance Expert Working Group (EV-EWG) has coordinated the development of an Important Medical Event Terms (IME, MedDRA version: 24.0) list. This IME list aims to facilitate the classification of suspected adverse reactions as well as aggregated data analysis and case assessment in the frame of the day-to-day PV activities of stakeholders. The IME list is intended for guidance purposes only.

- EudraVigilance is the system for managing and analyzing information on suspected adverse reactions to medicines which have been authorized or being studied in clinical trials in the European Economic Area (EEA). The European Medicines Agency (EMA) operates the system on behalf of the European Union (EU) medicines regulatory network.

- MedDRA (Medical Dictionary for Regulatory Activities) is a standardized medical terminology, published by the International Council for Harmonization, used for coding cases of adverse effects in clinical study reports and pharmacovigilance databases, and to facilitate searches in these databases.

- PIDM: The WHO Program for International Drug Monitoring (PIDM), established in 1968, provides a forum for WHO Member States to collaborate in the monitoring of drug safety, and notably, the identification and analysis of new adverse reaction signals from data submitted to the WHO global individual case safety report (ICSR) database by member countries.

- Seriousness Criteria: According to the WHO, a serious AEFI is an event that results in death, hospitalization, or prolongation of an existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth, defect or is life-threatening.

- ICH E2A Guidelines: Aims to develop standard definitions and terminology for key aspects of clinical safety reporting. It also provides guidance on the appropriate mechanism for handling expedited (rapid) reporting, in the investigational (i.e., pre-approval) phase.

- Safety Signal: According to the World Health Organization (WHO), a "signal" is a reported information on a possible causal relationship between an AE and a drug, the relationship being unknown or incompletely documented previously. Usually more than one report is required to generate a signal, depending on the seriousness of the event and the quality of the information.

- Trigeminal Neuralgia: is a neuropathic pain condition affecting the fifth cranial nerve and causing one of the most severe pains to be experienced. Symptoms include extreme, sporadic, sudden burning or shock like pain lasting from seconds up to two minutes and is usually unilateral.

- Myocarditis: An inflammation of the heart muscle (myocardium). Common myocarditis signs and symptoms include chest pain, rapid or abnormal heartbeat (arrhythmias), shortness of breath, or fluid buildup with leg swelling.

- Photophobia: Abnormal light sensitivity. It can occur as a symptom of various condition such as migraine headache or ophthalmic inflammation.

- VigiFlow is a web-based individual case safety report (ICSR) management system that is available for use by national PV centers of the WHO Program for International Drug Monitoring.

- VigiBase is the WHO global ICSR database that contains ICSRs submitted by the participating member states enrolled under WHO's international drug monitoring program. It is the single largest drug safety data repository in the world.

- VigiLyze supports the collection, processing, and sharing of data of case reports to facilitate effective data analysis. VigiLyze is a signal detection and management system that can use national, regional, or global data as the starting point for quantitative signal detection.

DATA CAVEATS

- Each case report refers to a reporter who reported an AEFI after receiving a dose of COVID-19 vaccine. A case report may contain multiple AEFIs. Therefore, the total number of AEFIs can exceed the number of individual case reports reported in a given time frame. Case reports that did not contain an AEFI at the time of data extraction or was missing the Vaccine name have been excluded.
- AEFI reporting rates were calculated using the number of vaccines' specific AEFIs reported in the specified time period in Lebanon divided by the doses of vaccines administered in the same time period in Lebanon.
- The information available in this report does not represent Uppsala Monitoring Center (UMC) nor WHO's opinions.

DISCLAIMER:

CITATION:

Ministry of Public Health – Quality Assurance of Pharmaceutical Products – Pharmacovigilance Program (2022). Adverse Events Following Immunization for COVID-19 Vaccines in Lebanon: February 14th, 2021 to January 19th, 2022; Beirut, Lebanon.

FOR FURTHER INFORMATION:

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