Safety Monitoring of COVID-19 Vaccines in Hong Kong

This report contains data of adverse event reports up to 30 May 2021

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1. COVID-19 vaccines and pharmacovigilance system in Hong Kong

The ongoing COVID-19 pandemic causes a significant disease burden worldwide. In Hong Kong, cases and outbreaks continue to be reported. As of 30 May 2021, a total of 11,838 persons have been infected with COVID-19 and 210 died of the disease. To reduce the impacts of COVID-19 on health and society, vaccines against COVID-19 is considered an important public health tool for containing the pandemic in the medium and long term.

The two COVID-19 vaccines authorized for use in Hong Kong have been rigorously evaluated by the Advisory Panel on COVID-19 Vaccines ("Advisory Panel") established under the Prevention and Control of Disease (Use of Vaccines) Regulation, Cap. 599K ("the Regulation") that they are safe, effective and of good quality. Current scientific evidence indicates that the benefits of the two COVID-19 vaccines outweigh their risks for use as active immunization to prevent COVID-19 caused by SARS-CoV-2 virus. The vaccines not only protect individuals from COVID-19 infection, available data also

support that the vaccines could reduce the seriousness of the COVID-19 even if infected.

The rapid development of COVID-19 vaccines may require close monitoring to ensure the safety and to identify potential signals that may indicate causal association between previously unknown adverse events and the vaccines. Therefore, the Department of Health ("DH") has put in place a pharmacovigilance system for COVID-19 immunization, including receiving reports of Adverse Events Following Immunization ("AEFIs")[1] related to the COVID-19 vaccines used in Hong Kong from healthcare professionals and pharmaceutical industries. **The main purpose of the pharmacovigilance system is to detect signals of possible side effects of the vaccines.**

Pursuant to the requirements of the Regulation to monitor any adverse event that occurs to the recipient associated with the administration of the relevant vaccine, the Director of Health appointed the Expert Committee on Clinical Events Assessment Following COVID-19 Immunization ("Expert Committee") to provide independent assessment of potential causal link between AEFIs and COVID-19 vaccines used in Hong Kong and to provide expert advice to the Government on safety-related matters.

The DH also partners with the University of Hong Kong ("HKU") to conduct an active surveillance programme for Adverse Events of Special Interest ("AESIs")[2] related to COVID-19 vaccines, i.e. the COVID-19 vaccines Adverse events Response and Evaluation Programme (CARE Programme). Through big-data analysis and scientific

[1] According to World Health Organization, Adverse Events Following Immunization refers to any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine.

[2] According to the World Health Organization, Adverse Event of Special Interest ("AESI") is a preidentified and predefined medically-significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies. The list of AESI is available at https://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/adr_reporting/index.html

studies designed when indicated, the CARE Programme would provide more data on the safety profile of the COVID-19 vaccines.

With reference to the experience since the commencement of the COVID-19 Vaccination Programme, the Expert Committee has recently updated the risk communication plan on clinical events following immunization. As endorsed by the Expert Committee, report on safety monitoring of COVID-19 vaccines will continue to be published in the Government's designated website and updated on a monthly basis. Relevant statistics will also be released through the website regularly.

2. Summary of AEFI reports received

The information of adverse events provided below is based on the reports received from healthcare professionals via the COVID-19 Vaccine Adverse Event on-line Reporting System (link click **here**) and via the established reporting channel with the Hospital Authority ("HA"). In addition, healthcare professionals are encouraged to report 15 items (link click **here**) of serious or unexpected AEFIs for close monitoring of the safety of the vaccines.

According to the World Health Organization ("WHO"), AEFI refers to any medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. Upon receipt of reports from the HA on the above 15 items, the DH will immediately contact the HA for further information. According to the established mechanism, all the important cases will be considered by the Expert Committee while all other serious or unexpected AEFI cases will be assessed by DH based on the causality assessment algorithm of the WHO[3]. **The ultimate goal of causality assessment is to detect signals of possible side effects of the vaccines.**

Currently, the Government Vaccination Programme provides two different types of COVID-19 vaccines, namely:

1. Inactivated virus technology platform - CoronaVac COVID-19 Vaccine (Vero Cell), Inactivated by Sinovac Biotech (Hong Kong) Limited; and

2. mRNA technology platform - Comirnaty COVID-19 mRNA Vaccine (BNT162b2) Concentrate for Dispersion for Injection by Fosun Pharma in collaboration with the German drug manufacturer BioNTech.

[3] WHO Causality assessment of an adverse event following immunization (AEFI) (CausalityAssessmentAEFI_EN.pdf (who.int))

Up to and including 30 May 2021, there were about 2,364,000 doses of COVID-19 vaccines administered. During the same period, the Department of Health had received a total of 3,289 AEFI reports (0.14% of all doses administered).

CoronaVac vaccine

Cumulative number of doses of COVID-19 vaccine administered	**About 1,014,800 (As at 30 May)**	**About 873,200 (As at 16 May)**
Cumulative number of AEFI reports received	**1,787** (**0.18%** of all doses administered)	**1,664** (**0.19%** of all doses administered)

Comirnaty vaccine

Cumulative number of doses of COVID-19 vaccine administered	**About 1,349,200 (As at 30 May)**	**About 1,081,900 (As at 16 May)**
Cumulative number of AEFI reports received	**1,502** (**0.11%** of all doses administered)	**1,226** (**0.11%** of all doses administered)

3. Statistics and charts

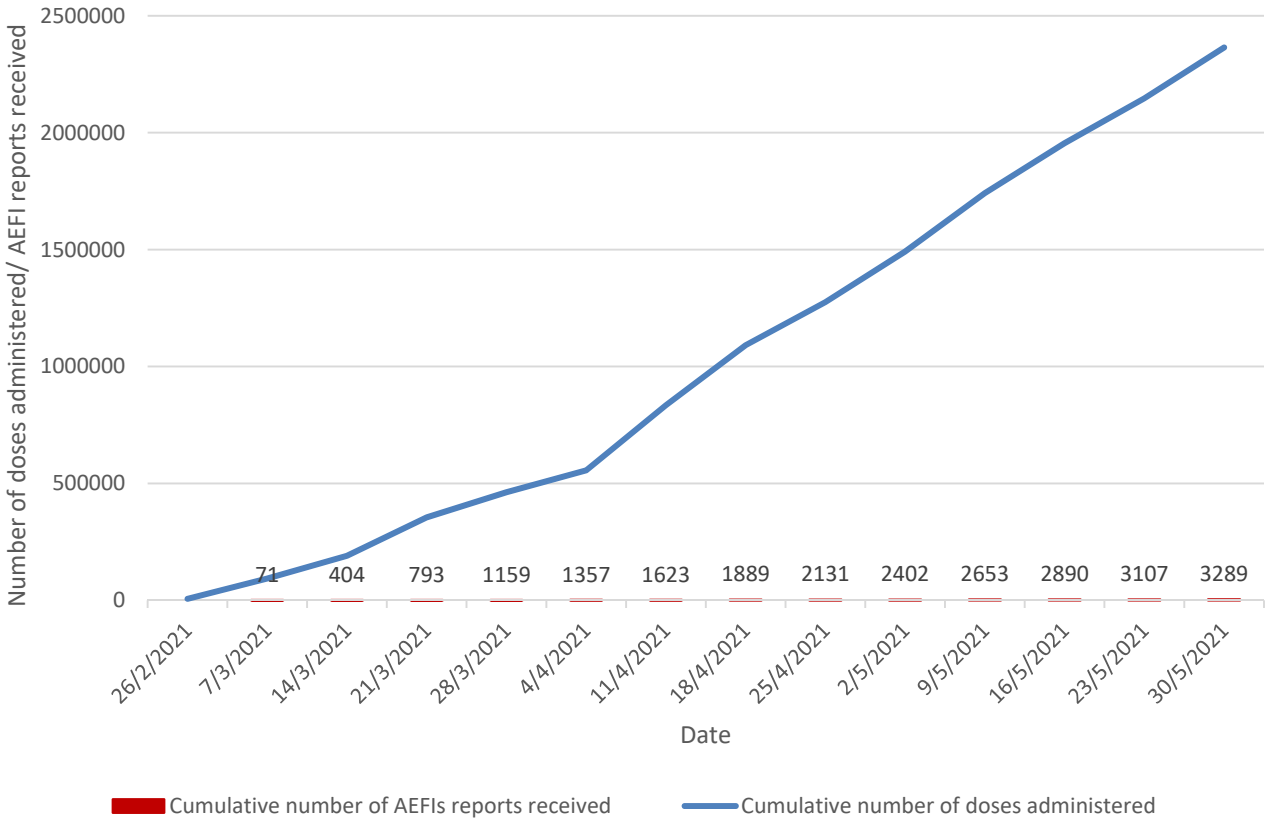
The below information gives an overview of the number of AEFI reports received and the proportion of AEFI. Information may be subjected to change when further information is available.

For the period between 17 May and 30 May 2021, the DH received 399 AEFI reports related to CoronaVac vaccine and Comirnaty vaccine including 52 reports of hospitalization and one report of death case. The death report did not have clinical evidence to support the event was caused by vaccine. Summary of these cases are shown as follows:

For the period between 17 May and 30 May 2021	CoronaVac	Comirnaty	Total
Death cases	0	1	1
Hospitalization cases reported by HA	16	32	48
Hospitalization cases reported by private hospitals	2	2	4
Other reports	108	238	346
Total	126	273	399

The cumulative number of doses of COVID-19 vaccines administrated and the cumulative number of AEFI reports received from the commencement of the COVID-19 vaccination programme up to 30 May 2021 are shown in Figure 1.

Figure 1. Cumlative number of doses of COVID-19 vaccines administered and cumulative number of AEFI reports received up to and including 30 May 2021



Death

Between 17 May and 30 May 2021, the DH had received one death case fulfilling the criteria for reporting as serious AEFIs. The case involved a 44 years old female. From the commencement of the vaccination programme and up to 30 May, about 2.364 million doses of COVID-19 vaccines had been administered for member of the public. The DH had received a total of 21 death reports of AEFI (9 cases per 1 million doses administered [0.0009%]) with history of COVID-19 vaccination within 14 days before they passed away[4] (20 cases from the HA and one Coroner's case handled by public mortuary). Details of these death cases are summarized as follows:

[4] Death cases with COVID-19 vaccination history of more than 14 days and no clinical evidence to indicate association with vaccine would be captured and analyzed by the HKU under the CARE Programme as AESI.

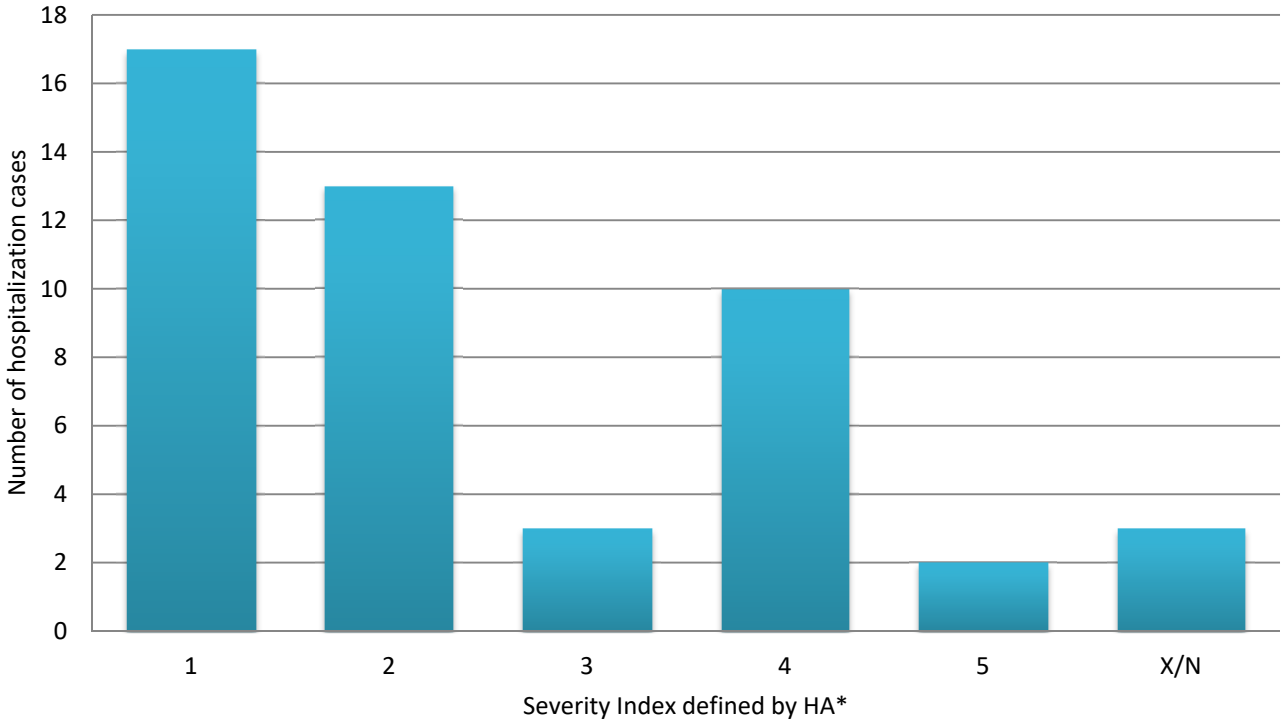
	As of 30 May	As at 16 May
Number of doses administered	About 2,364,000	About 1,955,100
Age distribution of vaccinated people	Mode: 40 – 49 Median: 40 – 49	Mode: 40 – 49 Median: 40 – 49
Number of death case reports with vaccination within 14 days (Age range)	21 (9 cases per 1 million doses administered [0.0009%]) (43 – 80)	20 (10 cases per 1 million doses administered [0.0010%]) (43 – 80)

Hospitalization

There were 48 reports of hospitalization received from the HA[5] and four reports from private hospitals in the period between 17 May and 30 May 2021. These cases involved 27 males and 25 females, age ranged from 22 to 81 years old. For the cases reported by the HA, the distribution of the severity index of these cases as defined by HA is shown in Figure 2 as follows:

[5] During the period, the HA provided updated information about a hospitalization case first reported on 24 May. The case involved a 58-year-old man who passed away on 28 May due to brain death secondary to stroke. He received the second dose of CoronaVac vaccine 11 days prior to his death. There was no clinical evidence to indicate the event was caused by vaccine. Based on the clinical information, the Expert Committee preliminarily considered the event was not associated with vaccination. The case would be included in HKU's CARE Programme for analysis.

Figure 2. Hospitalization cases reported by Hospital Authority (HA)



* Severity index defined by HA:
1 = Incident occurred but no injury sustained.
2 = Minor injury.
3 = Temporary morbidity.
4 = Significant morbidity.
5 = Major permanent loss of function / disability
X/N = Not known or Not applicable

Most of the cases from the HA were reported as incident occurred but no injury sustained or minor injury (around 62.5% of total hospitalization cases). They were mainly presented with chest pain, fever, headache, loss of consciousness, numbness, palpitation and weakness. The cases from private hospitals were presented with fever, headache, itchy rash and slurred speech.

Adverse events reported are not necessarily caused by the vaccine. As a whole population, people with acute medical conditions with various severity are admitted to the hospitals every day. With the commencement of the vaccination programme, it is anticipated that more patients with acute medical conditions will have received vaccines and reports of such cases might increase with the increasing vaccination uptakes. It is important for the

surveillance system in place to monitor these adverse events following COVID-19 vaccination and to conduct causality assessments based on scientific and objective approach to ensure that any untoward outcome would not go unnoticed.

Other Reports

Apart from the reports of hospitalization and death cases, 346 other reports were received.

Based on the 108 AEFI reports associated with CoronaVac, the most frequently reported events are:

Description of Events	Number of Events*
1. Dizziness	28
2. Chest discomfort	26
3. Headache	12
4. Rash	10
5. Numbness	8
6. Palpitation	8

*One report may have more than one event.

Based on the 238 AEFI reports associated with Comirnaty, the most frequently reported events are:

Description of Events	Number of Events*
1. Dizziness	47
2. Headache	34
3. Chest discomfort	32
4. Rash	28
5. Palpitation	26

*One report may have more than one event.

4. Specific reports

Anaphylaxis/ anaphylactoid reactions

Between 17 May and 30 May 2021, the DH had received 2 reports of suspected anaphylaxis or anaphylactoid reactions with history of COVID-19 immunization. Having reviewed the available clinical data, both cases were considered not related to vaccination due to long onset time.

From the commencement of the vaccination programme up to 30 May 2021, the DH received a total of 18 reports of suspected anaphylaxis or anaphylactoid reactions with history of COVID-19 immunization. Having reviewed the available clinical data, there were 1 case of anaphylaxis (0.42 cases per 1 million doses administered [0.000042%]) and 2 cases of anaphylactoid reactions (0.85 cases per 1 million doses administered [0.000085%]). The remaining 15 cases were considered to be either non-anaphylactic allergic reactions or due to non-related conditions not related to vaccination.

It was noted that reports of suspected anaphylaxis and anaphylactoid reactions had increased but in most cases the events were neither anaphylaxis nor anaphylactoid reactions. As reported in overseas, this may be due to elevated levels of concern and anxiety triggered by various reports on vaccines. Nevertheless, healthcare providers should be able to recognize the signs and symptoms of anaphylaxis and anaphylactoid reactions and provide appropriate treatment. People with previous severe allergic reactions to vaccine should not receive COVID-19 vaccination, unless advised by specialists in Immunology and Allergy.

Bell's palsy

Between 17 May and 30 May 2021, the DH had received 14 reports of suspected Bell's palsy with history of COVID-19 immunization. These cases involved 10 males and four

females between 27 and 76 years old. Four of these cases received CoronaVac vaccine and 10 received Comirnaty vaccine. Having reviewed available clinical data of these cases, it was considered that eight cases would require further clinical information before assessment could be concluded.

From the commencement of the vaccination programme up to 30 May 2021, the DH had received a total of 87 reports of suspected Bell's palsy. Having reviewed available clinical data of these cases, it was considered that ten cases were not Bell's palsy. For the remaining 77 cases, 49 males and 28 females between 20 and 87 years old were involved. 38 cases received CoronaVac vaccine and 39 received Comirnaty vaccine. Summary of these 77 cases are shown as follows:

	CoronaVac	Comirnaty	Total
Number of doses administered (up to 30 May 2021)	About 1,014,800	About 1,349,200	About 2,364,000
Age distribution of vaccinated people (up to 30 May 2021)	Mode: 50 – 59 Median: 50 – 59	Mode: 40 – 49 Median: 40 – 49	Mode: 40 – 49 Median: 40 – 49
Number of reports **(number of case per 1 million doses administered)** **(% of doses administered)** **(Age range)** **(median)**	38 (37) (0.0037%) (26 – 87) (57)	39 (29) (0.0029%) (20 – 78) (46)	77 (33) (0.0033%) (20 – 87) (50)

Bell's palsy (acute peripheral facial paralysis) is a common neurologic disorder. Majority of the patients will have complete recovery even without treatment and early use of a short course of treatment within 3 days of symptoms onset will further enhance the recovery rate. It is also one of the listed rare side effects of Comirnaty.

According to the preliminary information collected by the University of Hong Kong

from HA, for people of 16-year-old or above, there were on average 72.3 new cases of Bell's palsy recorded in the period from 17 May to 30 May of 2018, 2019 and 2020. For the period from 26 February to 30 May of 2018, 2019 and 2020, there were on average 437.7 new cases of Bell's palsy recorded for people of 16-year-old or above[6]. Summary of these records are shown as follows:

Figures for the period of 26 February to 30 May (collected from HA)	2018	2019	2020
Number of new cases of Bell's palsy recorded	424	459	430
Cases per 100,000 population for people of 16-year-old or above	6.5	7.0	6.6

It is worth to note that many cases of Bell's palsy are not serious and many patients may seek medical attention in the private sector. The above figures may not fully reflect the local background incidence.

The Expert Committee noted a number of Bell's palsy cases reported after vaccination of CoronaVac vaccine and preliminary analysis suggested that there might be a potential association. To further look into the association between COVID-19 vaccines and Bell's palsy, the HKU has already commenced a study to further analyze the association between Bell's palsy and the vaccines. After the concerned signal is ascertained, the Expert Committee will forward the assessment with recommended regulatory measures to be taken to the Advisory Panel for consideration. Meanwhile, the DH according to the established mechanism has provided summary information of relevant case reports to both suppliers of the vaccines for global monitoring and analysis.

[6] The figures presented above are generated from data collected from a database of the Hospital Authority. The database is regularly audited and updated to ensure the validity of the data. Therefore, any update to the figures above may result in a difference from the current version due to the dynamic nature of the database.

Death

From the commencement of the vaccination programme, i.e. from 26 February to 30 May 2021, excluding cases with vaccination history more than 14 days received, the DH had received a total of 21 reports of deaths, involving 15 males and six females between 43 and 80 years old. Thirteen of them received CoronaVac vaccine and eight received Comirnaty vaccine. The Expert Committee conducted causality assessment of individual cases based on the algorithm of the WHO and all available information, including the medical conditions and history of the patient with relevant clinical data, vaccine information and preliminary autopsy findings. **So far, there is no case identified as having causal relationship with the COVID-19 vaccination.** The Expert Committee had concluded the causality assessment for six of the above death cases and considered their deaths were inconsistent with COVID-19 vaccination (i.e. no causal relationship). For the remaining 15 cases, the Expert Committee preliminary considered that the outcomes of the deceased persons were not associated with COVID-19 vaccination. However, full autopsy reports would be required for the Expert Committee to conclude the causality assessment.

Causality assessment	Cases with vaccination within 14 days
Number of death case reports received (Age range)	21 (43 – 80)
Inconsistent with COVID-19 vaccination (i.e. no causal relationship)	6
Preliminary considered no association with COVID-19 vaccination*	15

* Based on medical history, clinical data, vaccination information and preliminary autopsy findings.

According to the local mortality data, in the same period (i.e. 26 February to 30 May) of 2017, 2018 and 2019, there were on average 1,678 deaths due to heart diseases and on average 1,039 deaths due to ischaemic heart disease, among people aged 40 and above. In 2019, the death rates due to heart diseases and ischaemic heart disease in this age group were 38.3 per 100,000 population and 22.4 per 100,000 respectively in the same period of time. These mortality data are summarized as follows:

Figures for the period of 26 February to 30 May	2017	2018	2019
Number of deaths due to heart diseases among people aged 40 and above (deaths per 100,000 population)	1,670 (40.4 per 100,000 population)	1,729 (41.2 per 100,000 population)	1,635 (38.3 per 100,000 population)
Number of deaths due to ischaemic heart disease among people aged 40 and above (deaths per 100,000 population)	1,069 (25.9 per 100,000 population)	1,090 (26.0 per 100,000 population)	957 (22.4 per 100,000 population)

According to HA, daily average numbers of deaths in public hospitals in the period from 3 May to 30 May are shown as follows:

Deaths in Public Hospitals	3 May to 30 May in 2021	Historical Figures		
		3 May to 30 May in 2020	3 May to 30 May in 2019	3 May to 30 May in 2018
Deaths† in Public Hospitals / Day	121	121	119	110.5
Inpatient Deaths / Day	103.5	102.1	104.9	95.7
Deaths at AED / Day	17.5	18.9	14.1	14.9

† Refers to inpatient deaths and deaths at Accident and Emergency Department (AED).

In addition, the HA has provided following rate per 10,000 population for deaths in public hospitals by whether inoculation record can be identified in the period from 3 May to 30 May:

Deaths in Public Hospitals	3 May to 30 May in 2021		
	Cases with inoculation record@	Cases without inoculation record@	Overall
	per 10K pop^	per 10K pop*	per 10K pop
Deaths† in Public Hospitals	0.29	5.48	4.53
Inpatient Deaths	0.17	4.7	3.88
Deaths at AED	0.13	0.77	0.65

† Refers to inpatient deaths and deaths at AED.

@ Inoculation data of patients was obtained via vaccination database of Department of Health during patient encounters at public hospitals, and were used to identify inoculation record of patients. Episodes with adverse events for the cases with inoculation record were counted regardless of the inoculation date and whether the events were related to vaccination or not. Not all events were reported to the Department of Health as adverse events following COVID-19 immunization.

^ Inoculation population refers to population with 1st dose of COVID-19 vaccine since the start of the COVID-19 vaccination programme up to 30 May 2021.

* Non-inoculated population refers to "2020 year-end population" minus "inoculated population^".

The Expert Committee reviewed these data and considered there is no unusual pattern identified so far. Moreover, the existing available information of the reported cases also does not show any causal relationship with the vaccines. The Expert Committee will continue to closely monitor the situation and further collect more data for assessment. For death cases outside the reporting criteria for AEFI[7], including death of all causes and sudden death as listed AESI, they would be actively monitored and analyzed under the CARE Programme conducted by the HKU.

[7] Death cases with vaccination history of more than 14 days (unless with evidence of association with COVID-19 vaccine) or cases with obvious cause(s) of death, other than vaccination, are outside the reporting criteria for AEFI. These cases would be included in the HKU's CARE Programme for big-data analysis.

Guillain-Barre syndrome

Between 17 May and 30 May 2021, the DH received a report of suspected Guillain-Barre syndrome (GBS) with history of COVID-19 immunization. The affected was a 65-year-old male. He presented with numbness over bilateral feet five days after receiving Comirnaty vaccine. He was admitted to hospital for management and remained in stable condition. GBS is a rare neurological disorder causing paralysis and even respiratory difficulties. Most people recover completely but some have chronic weakness. GBS can develop following a variety of infections, including influenza. GBS was identified as a possible adverse event requiring specific safety monitoring activities. According to the data provided by the HA to the Centre for Health Protection[8], the average number of newly admitted GBS cases to HA for the past ten years (2011-2020) was 59.3 cases per year. In 2021[9] (up to 30 April), there were 8 cases of newly admitted GBS. So far, there was no evidence indicating that the GBS cases exceeds the background incidence. The Expert Committee will continue to closely monitor the situation.

Thrombocytopenia

The Expert Committee also reviewed one report of thrombocytopenia (TP) with history of COVID-19 immunization. The affected was a 40-year-old female. She presented with multiple bruises over body one day after receiving Comirnaty vaccine. She was admitted to hospital and her platelet count had normalized after treatment. TP refers to an abnormally low platelet count. The pathogenesis of TP following immunization is not known and clinically apparent TP after immunization is rare. Most post-immunization episodes of TP resolve within three months. TP was also identified as a possible adverse event requiring specific safety monitoring activities. The Expert

[8] Centre for Health Protection - Monthly number of newly admitted Guillain-Barré Syndrome (GBS) cases in Hong Kong (chp.gov.hk)

[9] Provisional data

Committee will continue to closely monitor the situation.

4 June 2021