Safety Monitoring of COVID-19 Vaccines in Hong Kong

This report contains data of adverse event reports up to 2 May 2021

Contents

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 2 May 2021, a total of 11,785 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.

According to the risk communication plan endorsed by the Expert Committee, the figures and summary of clinical events received will be released and updated through the designated website biweekly. When a case of suspected adverse event fulfilling the reporting criteria of an AEFI involving death within 14 days of vaccination is received, it will be announced as soon as possible. For press statements related to adverse events with history of COVID-19 vaccination, please click **here**.

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 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 2 May 2021, there were about 1,491,900 doses of COVID-19 vaccines administered. During the same period, the Department of Health had received a total of 2,402 AEFI reports (0.16% of all doses administered).

CoronaVac vaccine

Cumulative number of doses of COVID-19 vaccine administered	About **758,900** (As at 2 May)	About **598,700** (As at 18 April)
Cumulative number of AEFI reports received	**1,527** (**0.20**% of all doses administered)	**1,276** (**0.21%** of all doses administered)

Comirnaty vaccine

Cumulative number of doses of COVID-19 vaccine administered	About **733,000** (As at 2 May)	About **492,400** (As at 18 April)
Cumulative number of AEFI reports received	**875** (**0.12**% of all doses administered)	**613** (**0.12%** of all doses administered)

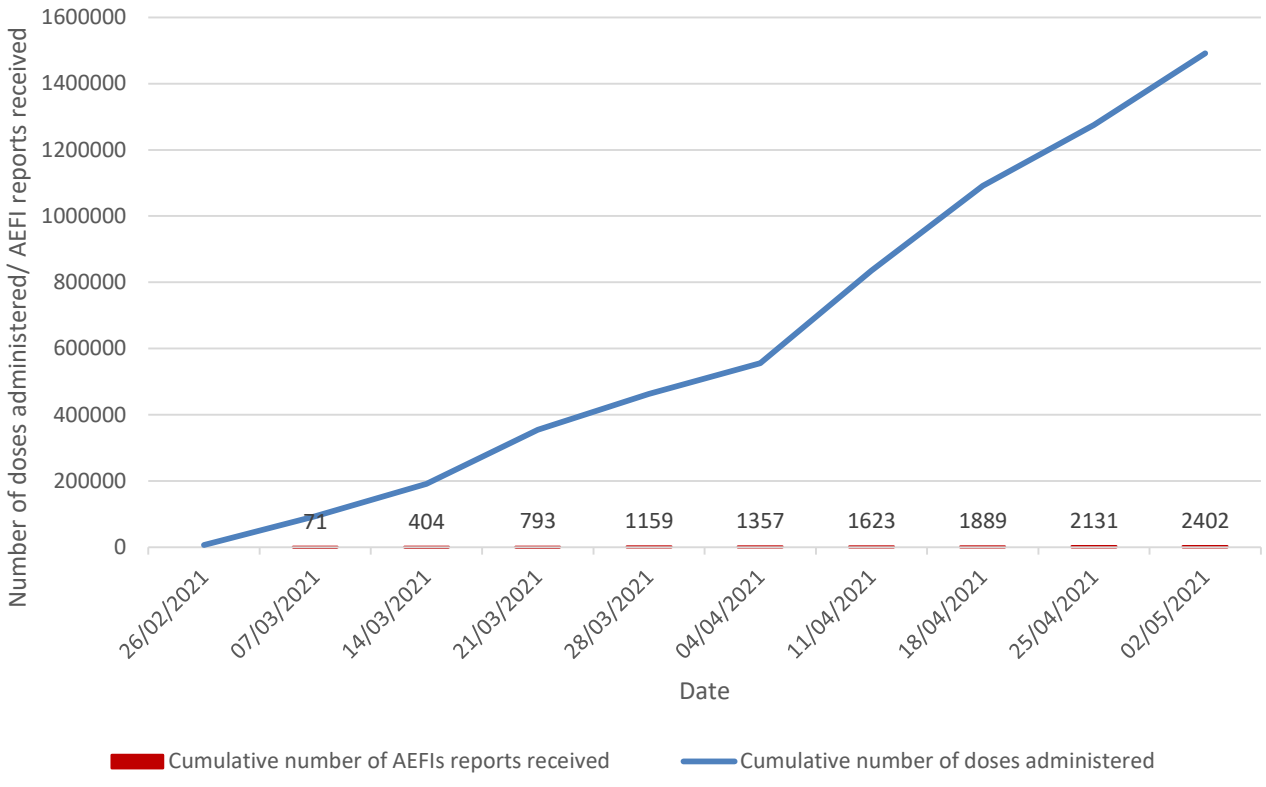
3. Statistics and charts

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 19 April and 2 May 2021, the DH received 513 AEFI reports related to CoronaVac vaccine and Comirnaty vaccine including 294 reports of hospitalization and nine reports of death cases. Four of the nine death cases had history of COVID-19 vaccination more than 14 days before the event and all reports did not have clinical evidence to support the event was caused by vaccine.

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 2 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 2 May 2021



Death

Between 19 April and 2 May 2021, the DH had received nine death cases reported as AEFIs with history of COVID-19 immunization[4]. These cases involved five males and four females aged from 43 to 76 years old. Four cases had history of COVID-19 vaccination more than 14 days before they passed away. Preliminary assessment considered no causal relationship with vaccination. From the commencement of the vaccination programme and up to 2 May, the DH had received a total of 27 death reports from the HA and one Coroner's case handled by public mortuary. Among these 28 cases, 12 had history of COVID-19 vaccination more than 14 days before they passed away. The Expert Committee concluded the causality assessment for three of these 12 cases and considered their death had no causal relationship with COVID-19 vaccination. For the remaining nine cases, the Expert Committee preliminary assessment considered no causal relationship with vaccination. These 28 cases are summarized as follows:

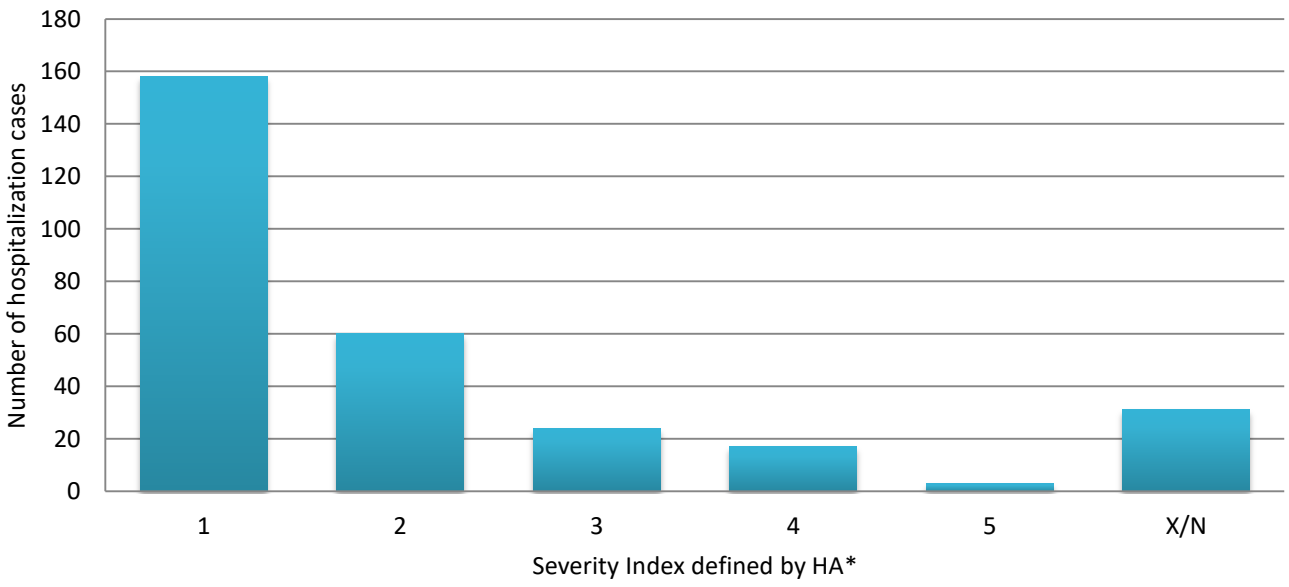
	As at 2 May	As at 18 April
Number of doses administered	About 1,491,900	About 1,091,100
Age distribution of vaccinated people	Mode: 40 – 49 Median: 40 – 49	Mode: 40 – 49 Median: 50 – 59
Total number of death case reports received (Age range)	28 (43 – 92)	19 (54 – 92)
Number of death case reports with vaccination within 14 days (Age range)	16 (43 – 80)	11 (55 – 80)
Number of death case reports with vaccination more than 14 days (Age range)	12 (54 – 92)	8 (54 – 92)

[4] For details, please refer to the press statement issued on 4 May: Expert Committee on Clinical Events Assessment Following COVID-19 Immunisation assesses serious adverse events relating to COVID-19 vaccination (info.gov.hk).

Hospitalization

There were 293 reports of hospitalization received from the HA and one from private hospital in the period between 19 April and 2 May 2021. These cases involved 178 males and 116 females, age ranged from 16 to 90 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:

Figure 2. Hospitalization cases reqported 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 mainly presented with chest discomfort, chest pain, dizziness, fever, headache, hypertension, numbness, palpitation, shortness of breath and weakness. The one case from private hospital was presented with deep vein thrombosis.

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, 211 other reports were received.

Based on the 77 AEFI reports associated with CoronaVac, the six most frequently reported events are:

Description of Events	Number of Events*
1. Dizziness	13
2. Chest pain	10
3. Chest discomfort	8
4. Palpitation	7
5. Rash	5
6. Vertigo	5

*One report may have more than one event.

Based on the 134 AEFI reports associated with Comirnaty, the five most frequently reported events are:

Description of Events	Number of Events*
1. Dizziness	26
2. Rash	16
3. Palpitation	16
4. Numbness	12
5. Chest pain	10

*One report may have more than one event.

4. Specific reports

Anaphylaxis/ anaphylactoid reactions

Between 19 April and 2 May 2021, the DH had received five reports of suspected anaphylaxis or anaphylactoid reactions with history of COVID-19 immunization. Having reviewed the available clinical data, two cases were considered hypersensitivity reaction and two cases were considered no causal relationship with COVID-19 vaccine due to the long onset time. The remaining one was anaphylactoid reactions involving a 24-year-old woman. She developed rash and throat discomfort about 30 minutes after receiving the first dose of Comirnaty. Symptoms subsided after treatment. According to the product information of the vaccine, anaphylaxis is one of the adverse reactions of the vaccine reported from clinical trials. 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 19 April and 2 May 2021, the DH had received 16 reports of suspected Bell's palsy with history of COVID-19 immunization. These cases involved 10 males and six females between 20 and 87 years old. Seven of these cases received CoronaVac vaccine and nine received Comirnaty vaccine. Having reviewed available clinical data of these cases, it was considered that three cases would require further clinical information before assessment could be concluded.

From the commencement of the vaccination programme up to 2 May 2021, the DH had received a total of 53 reports of suspected Bell's palsy. Having reviewed available clinical data of these cases, it was considered that seven cases were not Bell's palsy. For the remaining 46 cases, 30 males and 16 females between 20 and 87 years old were involved. Twenty nine cases received CoronaVac vaccine and 17 received Comirnaty

vaccine. Summary of these 46 cases are shown as follows:

	CoronaVac	Comirnaty	Total
Number of doses administered (up to 2 May 2021)	About 758,900	About 733,000	About 1,491,900
Age distribution of vaccinated people (up to 2 May 2021)	Mode: 60 – 69 Median: 50 – 59	Mode: 40 – 49 Median: 40 – 49	Mode: 40 – 49 Median: 40 – 49
Number of reports (% of doses administered) (Age range) (median)	29 (0.0038%) (26 – 87) (58)	17 (0.0023%) (20 – 78) (48)	46 (0.0031%) (20 – 87) (53)

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 65.7 new cases of Bell's palsy recorded in the period from 19 April to 2 May of 2018, 2019 and 2020. For the period from 26 February to 2 May of 2018, 2019 and 2020, there were on average 301 new cases of Bell's palsy recorded for people of 16-year-old or above[5]. 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

[5] 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.

association. The Expert Committee has yet to ascertain whether the cases collected from the pharmacovigilance system are higher than the baseline level. 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. If a signal is detected and ascertained, i.e. there is an association between Bell's palsy and the vaccines, 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.

Death

From the commencement of the vaccination programme, i.e. from 26 February to 2 May 2021, excluding 12 cases with vaccination history more than 14 days, the DH had received a total of 16 reports of deaths, involving 12 males and four females between 43 and 80 years old. Twelve of them received CoronaVac vaccine and four received Comirnaty. Based on the clinical information and preliminary autopsy findings, most cases died of ischaemic heart disease. 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, the Expert Committee had concluded the causality assessment for four of the above death cases and considered their deaths were inconsistent with COVID-19 vaccination (i.e. no causal relationship). For the remaining 12 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. Summary of the causality assessment for the death cases are shown as follows:

Causality assessment	Cases with vaccination more than 14 days	Cases with vaccination within 14 days	Total
Number of death case reports received (Age range)	12 (54 – 92)	16 (43 – 80)	28 (43 – 92)
Inconsistent with COVID-19 vaccination (i.e. no causal relationship)	3	4	7
Preliminary considered no association with COVID-19 vaccination*	9	12	21

* 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 2 May) of 2017, 2018 and 2019, there were on average 1,194 deaths due to heart diseases and on average 741 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 27 per 100,000 population and 16 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 2 May	2017	2018	2019
Number of deaths due to heart diseases among people aged 40 and above (deaths per 100,000 population)	1,205 (29.2 per 100,000 population)	1,222 (29.1 per 100,000 population)	1,154 (27 per 100,000 population)
Number of deaths due to ischaemic heart disease among people aged 40 and above (deaths per 100,000 population)	755 (18.3 per 100,000 population)	784 (18.7 per 100,000 population)	684 (16 per 100,000 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[6], 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.

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[6] 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.