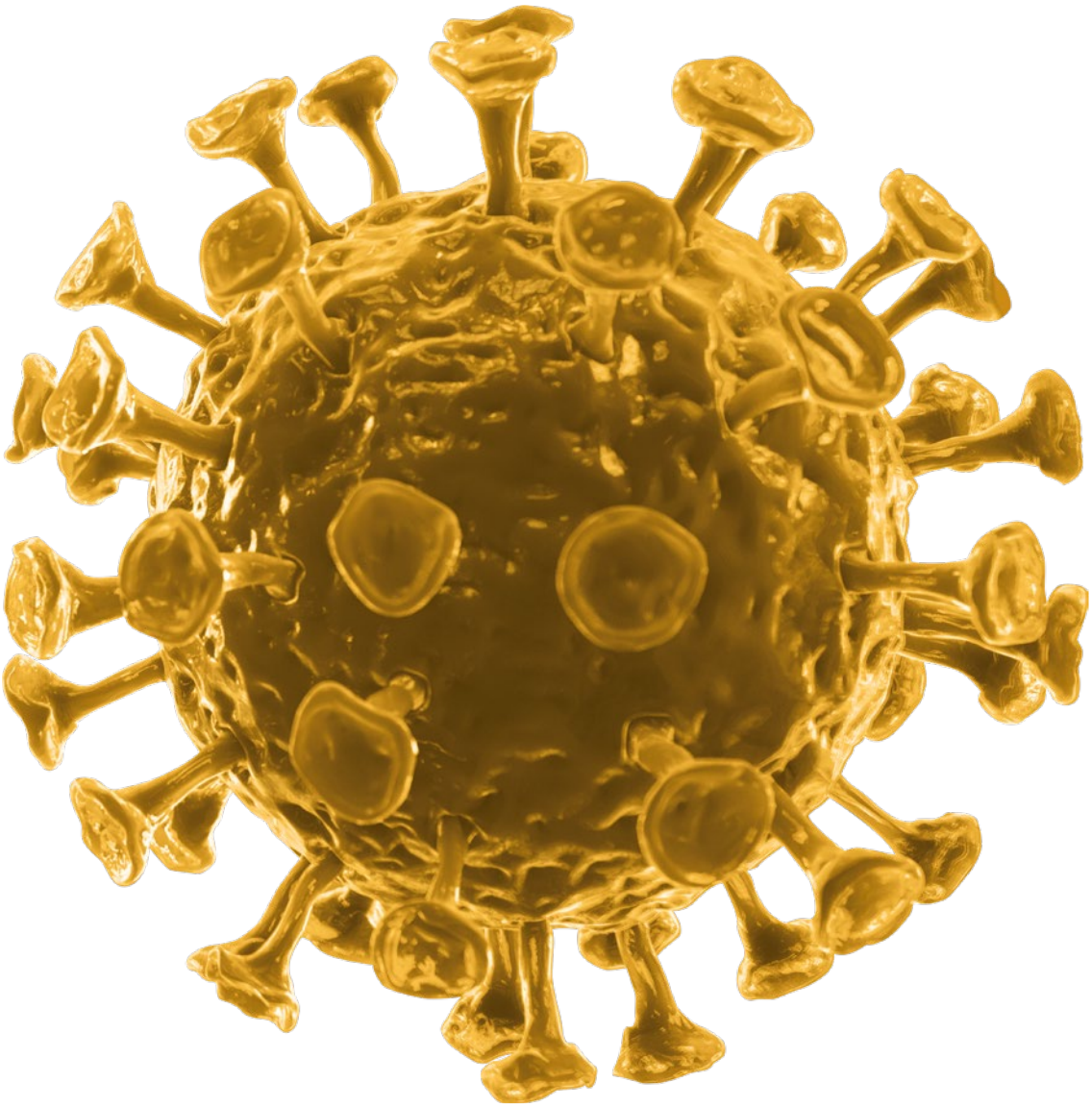
COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL

MONITORING AND RESPONDING TO ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFIS)



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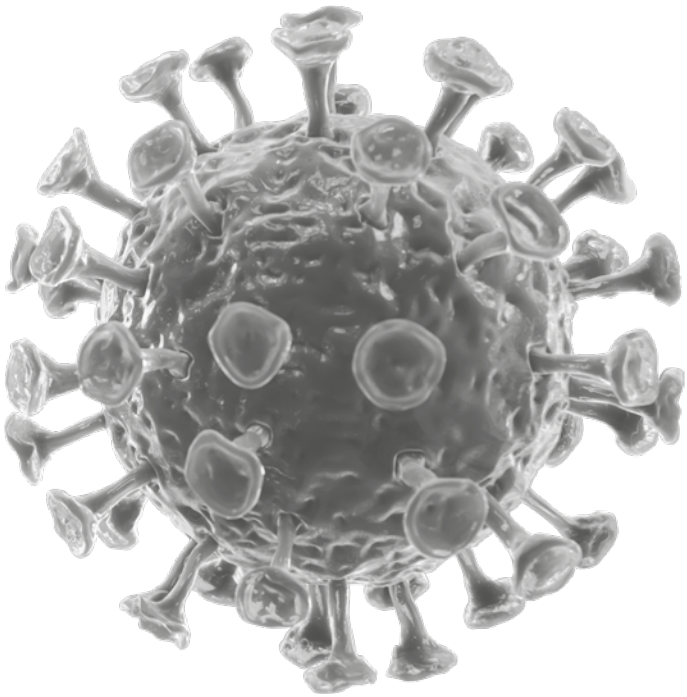

World Health Organization

Covid-19 vaccines: safety surveillance manual

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Contents

Key points

- In the context of COVID-19 vaccination, surveillance systems need to be prepared for identifying and responding to both adverse events following immunization (AEFIs) and adverse events of special interest (AESIs) as well as other safety events that may cause public concern, including incidents of substandard or counterfeit vaccines
- Specific funds should be allocated for identifying, reporting and responding to AEFIs and AESIs during the planning stage, before COVID-19 vaccination is implemented
- AEFIs are untoward medical events that follow immunization, and that do not necessarily have a causal relationship with the usage of the vaccine
- Clearly distinguishing genuine vaccine product-related events from coincidental events or concomitant medication-related AEs will be a challenge
- Immunization programmes should anticipate and prepare for clusters of AEFI following COVID-19 vaccination as the chances of immunization errors and Immunization anxiety-related reactions are much higher than that of routine immunization. Coincidental events can also occur as clusters
- AEFI detection primarily takes place primarily through routine passive surveillance (spontaneous reporting) which involves vaccine recipients, parents of immunized infants and children, health care workers and staff in immunization or health care facilities detecting the AEFIs and reporting them to any health care worker
- For COVID-19 immunization-related AEFIs, in addition to standard information, it is important to record the brand name, the manufacturer, as well as the batch numbers because it is possible that more than one COVID-19 vaccine will be in use simultaneously in a country
- All countries should establish a process for causality assessment prior to the introduction of COVID-19 vaccines
- AEFI causality assessment committees should pluri-disciplinary, including adult and elderly specialities, since COVID-19 vaccines will be administered to individuals of all ages
- The committee communication spokesperson will be responsible for communication about the AEFIs assessed by the committee, particularly with the media and other stakeholders
- AEFI causality assessment committees should anticipate an increase in reporting of serious AEFIs following the introduction of COVID-19 vaccines due to the novelty of COVID-19 vaccines, the high vigilance for AEFIs, and broad range of target populations
- Performing scientific causality assessments requires a comprehensive, completed AEFI investigation dossier, with all the necessary information including a 'valid diagnosis', details of the vaccine administered, information about medication being taken at the time of vaccination or prior to the occurrence of the AEFI and an independent AEFI causality assessment committee
- It is recommended to use existing data collection tools for data collection, collation and processing for AEFIs, that can be adapted, if necessary

01 Introduction

As outlined in the module on COVID-19 vaccine platforms, the unprecedented rapid development of the COVID-19 vaccines on novel platforms followed by their rapid deployment on a mass scale poses unique challenges for monitoring vaccine safety. Timely detection and reporting of adverse events following COVID-19 immunization is the first step in the continuous verification of vaccine safety. In the context of COVID-19 vaccination, surveillance systems need to be prepared for identifying and responding to both adverse events following immunization (AEFIs) and adverse events of special interest (AESIs) as well as other safety events that may cause public concern, including incidents of substandard or counterfeit vaccines.

AEFIs and AESIs can be detected through passive and active surveillance, respectively. However, if countries do not implement active surveillance for AESIs, all AESI-like adverse events occurring following COVID-19 immunization should be considered as AEFIs and the standard procedure for AEFI response, described below, should be adopted. In addition, the separate module on AESIs and the WHO detailed guidance on AESI following COVID-19 vaccination (to be developed) provides detailed information on AESIs including a list of potential AESIs, their case definitions, study protocols, training requirements, data collection tools (including AESI confirmation forms), processing, transmission, analysis and response.

Specific funds should be allocated for identifying, reporting and responding to AEFIs and AESIs during the planning stage before COVID-19 vaccination is implemented. This is needed because there are likely to be a lot of unknown associations since COVID-19 is a new infectious disease with many of its manifestations are still unknown, a broad target population will be exposed to one of the many new vaccines being evaluated, produced by various manufacturers, and different immunization strategies will probably be adopted by different countries.

02 Standard vaccine safety definitions and their implications in vaccine safety in the COVID-19 context

2.1 Adverse events following immunization

AEFIs are any untoward medical events that follow immunization, and that do not necessarily have a causal relationship with the immunization. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.[1] The same definition will continue to be used to identify and report all AEFIs following COVID-19 immunization.

2.2 Cause-specific definitions of AEFIs and implications COVID-19 context

Vaccine product-related reaction: An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product.

- the identification of rare (occurring in 0.01% to less than 0.1% of immunized individuals) and very rare (occurring in <0.01% of individuals) adverse events is insufficient at the time of COVID-19 vaccine licensure and more information will be needed for which AEFI surveillance has to be strengthened.

Clearly distinguishing genuine vaccine product-related events from coincidental events or concomitant medication-related AEs will be a challenge.

Vaccine quality defect-related reaction: An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the vaccine manufacturer.[2]

- Potential vaccine quality defects for new COVID-19 vaccine platforms might not be known at the time of authorization. Hence vaccine safety surveillance must be strengthened to be able to gather this knowledge.

1 Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance. Available from: https://cioms.ch/working_groups/vaccine-pharmacovigilance/. Accessed 16 November 2020.

2 For the purpose of this document, manufacturer also means marketing authorization holder.

- The rapid scaling up of vaccine production also poses additional potential risks and the identification of the exact substance in the vaccine formulation causing the adverse event will be needed.
- The likelihood of AEFIs being cause by a substandard or counterfeit version of COVID-19 vaccines should also be considered.

Immunization error-related reaction: An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and so is preventable.

- It is anticipated that COVID-19 vaccines will be administered on a massive scale in a short time interval with minimum training and field preparation and larger number of Immunization error-related reactions are anticipated. Also, staff who are not familiar with immunization may be asked to perform immunization duties. Multiple vaccines with different specifications for storage, administration, dose etc, may be in use in a country simultaneously.

Immunization anxiety-related reaction: An AEFI arising from anxiety about the immunization.

- A larger number of Immunization anxiety-related reactions are anticipated due to numerous factors including older age groups, the different vaccination environments, the novelty of the vaccines and their administration modalities.

Coincidental event: An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.

- Because of real and potential underlying comorbidities in a large number of the potential vaccinees, it will be challenging to differentiate true coincidental events from COVID-19 vaccine product related reactions or drug reactions or interactions.
- Similar challenges will occur in healthy individuals without comorbidities, especially where a higher frequency is expected based on age, gender, geographic location or ethnic background. Knowing the population-based incidence (background rates) of pre-specified adverse events of special interest (AESI) will help to anticipate and respond to such events in order to identify those that are coincidental as and those that are vaccine product-related.

2.3 Serious AEFI

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 or is a medically important event or reaction.

- The types and characteristics of serious AEFI particularly rare and very rare adverse events that could occur following COVID-19 vaccines are currently unknown, particularly rare and very rare adverse events.

2.4 Cluster

A cluster is when two or more AEFIs related in time, place or by vaccine occur. Two or more cases of the same or similar events in an AEFI cluster are usually associated with a particular vaccine manufacturer, a health facility, a vaccine batch, or a vial of vaccine, when multidose presentations are used.

- When vaccines are administered on a massive scale, it is important for immunization programmes to anticipate and prepare for clusters of AEFI as the chances of immunization errors and Immunization anxiety-related reactions are much higher than that during routine immunization. Coincidental events can also occur as clusters.

2.5 Signal

A signal is information that arises from one or multiple sources (including observations and experiments) which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verification.[3]

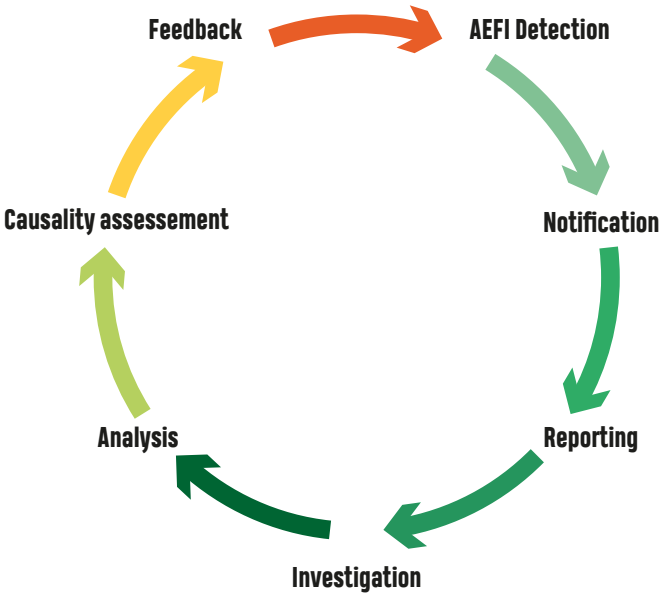
- Signal detection, verification and response is a key activity that has to be specifically addressed in the COVID-19 context. Signals can best be identified by pooling of data from multiple sources and analysing if the pooled data points to the occurrence of a new event that could be causally related to the vaccine.

3 CIOMS. Practical aspects of signal detection in pharmacovigilance. Report of CIOMS Working Group VIII. 2010. Available from: https://cioms.ch/publications/product/practical-aspects-of-signal-detection-in-pharmacovigilance-report-of-cioms-working-group-viii/. Accessed 21 November 2020.

03 AEFI surveillance in the context of COVID-19 vaccine introduction

At the time of vaccine introduction, all countries should at a minimum have an AEFI surveillance system in place as described in the *Global Manual on Surveillance of AEFI*.[4] The AEFI surveillance cycle (**Fig 1**) outlines the different steps in identification (detection), notification, reporting, investigation, data analysis, causality assessment and feedback following all AEFI, including AEFI following COVID-19 immunization.

Fig 1: AEFI surveillance cycle



3.1 AEFI detection, notification and reporting

AEFI detection primarily takes place primarily through routine passive surveillance (spontaneous reporting) in many countries. This involves vaccine recipients, parents of immunized infants and children, health care workers and staff in immunization or health care facilities detecting the AEFIs and reporting them to any health care worker within the health care system. AEFIs can also be detected through active surveillance, via sentinel sites or through cohort event monitoring. In addition, AEFIs may be detected in phase IV clinical studies of COVID-19 vaccines where they should be independently reported, assessed and processed, in compliance with

4 World Health Organization. Global manual on surveillance of adverse events following immunization. 2014. Available from: https://www.who.int/vaccine_safety/publications/aefi_surveillance/en/. Accessed 21 November 2020.

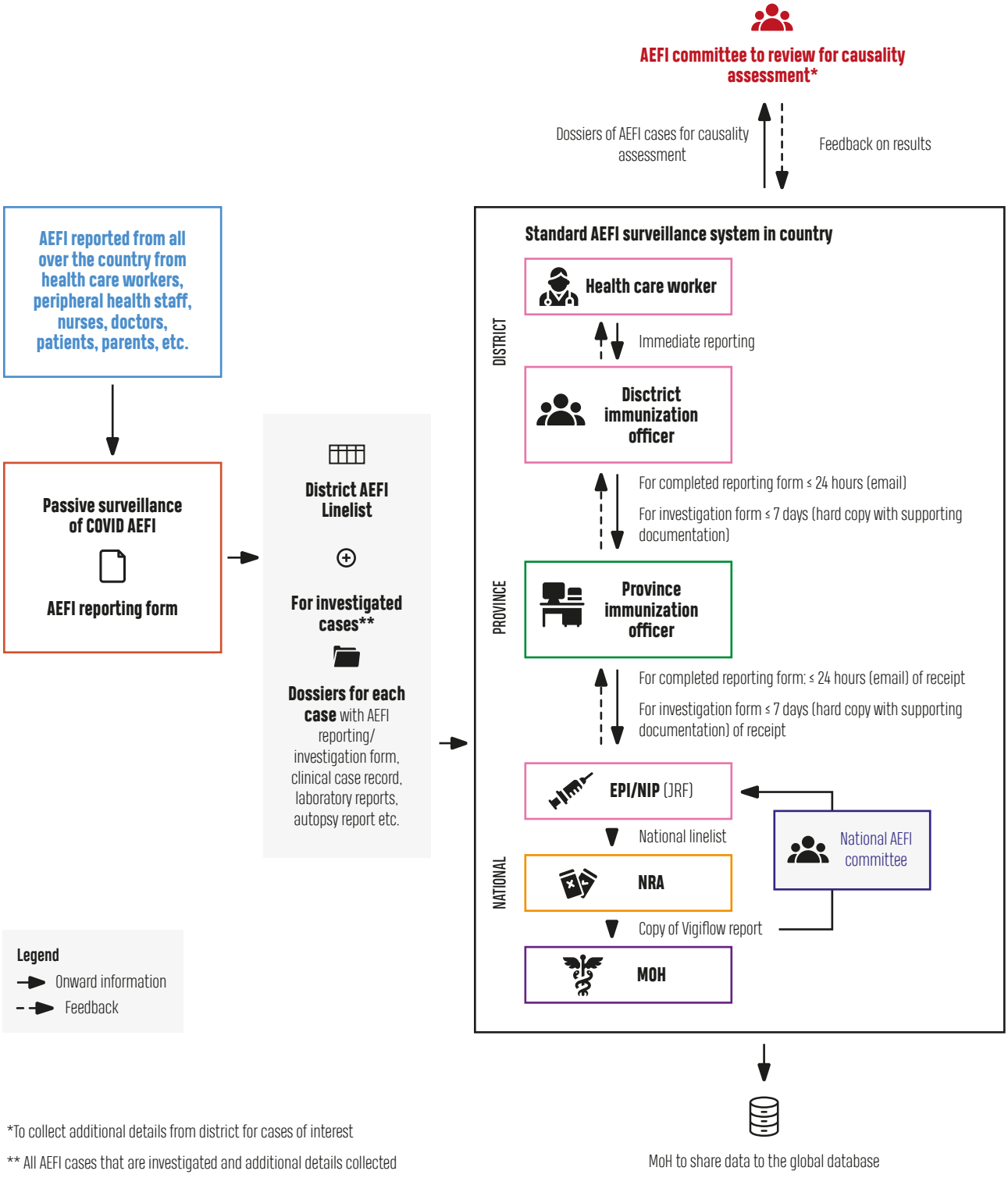
the study protocol and should not be reported through the passive reporting systems as described in this module.

3.1.1 Role of routine passive reporting systems for AEFI detection and notification

All AEFIs should be reported using the standard COVID-19 AEFI reporting form (**Appendix 5.1**) using the fastest means possible. When the AEFI is judged to be serious, reporting should also include a telephone call, direct conversation or notification via a specific application, depending on what is available in the country. AEFI reporting forms contain a minimum set of core variables in order to make the global evaluation of signals possible and thus help countries to evaluate the reported AEFIs.

For COVID-19 immunization-related AEFIs, in addition to standard information, **it is important to record the brand name, the manufacturer, as well as the batch numbers**, because vaccines in use in countries are likely to be manufactured on different platforms, with different antigen targets, adjuvants and dosage forms. A comprehensive complete AEFI report is the primary source for populating an AEFI linelist (**Appendix 5.2**) which, when processed, provides key descriptive epidemiological data (time, place and person) that are critical for identifying clusters and for signal detection. The AEFI reporting form also provides information on the quality of the passive surveillance system in terms of the completeness and timeliness of the reporting. This is important for monitoring the performance of pharmacovigilance systems. The primary reporter, i.e., the immunization provider or health care worker, are usually responsible for providing most of the information required in the COVID-19 AEFI reporting form. In some countries, vaccine recipients or their parents may complete the form themselves. AESIs may be reported spontaneously after COVID-19 immunization. These will be considered as AEFIs and will be processed through the standard AEFI surveillance system as described in this module (**Fig 2**).

Fig 2: In-country reporting and processing of AEFI



*To collect additional details from district for cases of interest

** All AEFI cases that are investigated and additional details collected

3.1.2 AEFI reporting

As outlined above, when a COVID-19 standard AEFI reporting form is received at the district, it should be reviewed for seriousness, decision taken on investigation and transmitted to the province and national levels as described in the *Global Manual on Surveillance of AEFI*.[5] If the

5 WHO. Global manual on surveillance of adverse events following immunization. Available from: https://www.who.int/vaccine_safety/publications/Global_Manual_on_Surveillance_of_AEFI.pdf. Accessed 28 October 2020

AEFI is considered to be minor or NOT serious, detailed investigation and causality assessment will not be required; this should be noted on the form. Detailed investigation and causality assessment will be required if the AEFI is considered to be:

- a serious AEFI, i.e., death, hospitalization, significant disability, life threatening, congenital anomaly, birth defect or a medically important event or reaction, or part of a cluster; or
- part of a group of events with an unexpected high rate or severity, or a suspected signal.

3.2 Investigating potential COVID-19 vaccine-related AEFIs

Chapter 6 of the *Global Manual on Surveillance of AEFI*[5] describes:

- why AEFIs should be investigated
- which AEFIs should be investigated
- who should investigate AEFIs
- when AEFIs should be investigate
- how to investigate AEFIs
- laboratory testing of specimen
- investigating AEFI clusters and investigation of deaths following immunization.

For AEFIs following COVID-19 immunization, the same processes and methodology should be followed, after the relevant staff have been trained. During the investigation, it is important to remember that, as for all other vaccines, attention should be paid to identify and rule out immunization (or programme) error-related AEFIs, immunization stress related responses and coincidental events that could manifest as a COVID-19 vaccine-related AEFI. Therefore, during AEFI investigations it will be necessary to obtain information on:

- concomitant medication, with indication and administration dates
- vaccine administration techniques
- vaccine transport, storage and handling
- immunization session environment and organization.

If the district authorities and experts feel that the AEFI investigation can be done locally, they can visit the patient and initiate the detailed investigation with appropriate members of the local health care team. If not, assistance should be solicited from the higher levels of the hierarchy. For deaths, national investigations should be led by a team from the National AEFI Committee, supported in the investigation by the Expanded Programme for Immunization (EPI) or National Immunization Programme (NIP), the National Regulatory Authority and other experts, as needed. During field investigations, the COVID-19 specific AEFI investigation form

(**Appendix 5.3**), the WHO AEFI investigation software[6] and aide mémoire[7] should be used to guide the process.

3.2.1 Causality assessment of potential COVID-19 vaccine-related AEFIs

Causality assessment is the systematic review and evaluation of available data about an AEFI to determine the likelihood of a causal association between the event(s) and the vaccine received. All countries must establish a process for causality assessment prior to the introduction of COVID-19 vaccines. In addition to having a functional post-marketing pharmacovigilance or AEFI surveillance system, there must be access to a functional expert group for causality assessment either at national, subnational, or regional levels. This step is critical for any country to ensure the scientific evaluation of potential COVID-19 vaccine-related AEFIs. Smaller countries who do not have enough experts may collaborate with neighbouring countries (or use regional resources), and larger countries may have committees at the subnational level.

The *Causality assessment of an adverse event following immunization (AEFI), user manual for the revised WHO AEFI causality assessment classification*[8] outlines the scientific basis for causality assessment and performing the assessment in a four-step process. The same causality assessment principles and process should be applied for the assessment of COVID-19 vaccine-related AEFIs.

However, because COVID-19 vaccines are novel vaccines, with multiple vaccine platforms, antigen targets and adjuvants produced by various manufacturers and will probably have differing implementation strategies adopted by different countries for broad target populations, information on risk of rare serious vaccine reactions will be limited at the time of regulatory assessment and authorization of the COVID-19 vaccines. The adaptation of causality assessment approaches must be envisaged to allow the efficient identification, monitoring and evaluation of suspected signals to ensure that the necessary regulatory and programmatic decisions are taken in a timely manner.

If phase III clinical trials are ongoing simultaneously with the widespread use of COVID-19 vaccines due to their emergency use listing, AEFI committees should have access to the periodic safety updated reports (PSURs). In addition, serious adverse events rates could be made available to the committee by the COVID-19 vaccine manufacturer. Global information and information from other regions should be available for the causality assessments, to help to identify signals and situations that could require collection of more detailed information.

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6 World Health Organization. AEFI investigation software. Available from: https://www.who.int/vaccine_safety/software-assistance-guiding-hq-AEFI-investigations/en/. Accessed 28 October 2020.

7 World Health Organization. AEFI investigation aide mémoire. Available from: https://www.who.int/vaccine_safety/initiative/investigation/New_aide-memoire_AEFI.pdf?ua=1. Accessed 28 October 2020.

8 World Health Organization. Causality assessment of an adverse event following immunization (AEFI). Updated user manual for the revised WHO classification (Second edition). Available from: https://www.who.int/vaccine_safety/publications/gvs_aefi/en/. Accessed 28 October 2020.

3.2.2 Country preparedness and capacity required for causality assessment for COVID-19 vaccine-related AEFIs

The AEFI causality assessment committee should include experts from paediatrics, neurology, general medicine, forensic medicine, pathology, microbiology, immunology and epidemiology. In addition, other external specific medical experts such as geriatricians, pulmonologists, cardiologists, nephrologists should be invited following the introduction of COVID-19 vaccines as they will be administered to individuals of all ages. If countries decide to use the AEFI committees to review AEFI cases to identify signals, the committees will need to be strengthened with additional expertise from statisticians and epidemiologists trained in research methodology. The committee communication spokesperson will be responsible for communication about the AEFI assessed by the committee, particularly with the media and other stakeholders.

The committee should be independent and should have secretarial support from both the immunization programmes (EPI or NIP) and the NRA. Alternatively, drug safety committees that evaluate adverse drug reactions could perform the causality assessment if training on AEFI causality assessments is provided. National pharmacovigilance centres play an important role in vaccine safety and their roles and responsibilities in causality assessment should be defined, taking into consideration the country context.

Countries with existing AEFI causality assessment committees do not need to establish a separate committee for COVID-19 vaccines. However, a refresher training course focusing on COVID-19 vaccine-specific AEFIs before COVID-19 vaccine introduction is warranted in the light of the unique challenges described above. Countries that do not have AEFI causality assessment committees should aim to establish such a committee prior to COVID-19 vaccine introduction to allow adequate time for training and preparation.

Decentralization should be considered in countries where the population and geographical territory are large. Sub-national AEFI causality assessment committees could be established, provided that the requisite expertise and other resources are available. This will enable timely AEFI causality assessment and reduce the workload for the national AEFI causality assessment committee. However, the sub-national committees should share all AEFI causality findings with the national committee. The sub-national level of AEFI causality assessment could also be considered as an interim stage of AEFI causality assessment for complex cases with national interest, for which the final assessment should be done by the national committee.

AEFI causality assessment committees should anticipate an increase in reporting of serious AEFIs following the introduction of COVID-19 vaccines due to the novelty of COVID-19 vaccines, the high vigilance for AEFIs, and broad range of target populations. Although this will increase their workload, the causality assessment must be performed in a timely manner to enable appropriate decision making and early response. This will be essential for maintaining the community's confidence and trust of the COVID-19 vaccines. The frequency of AEFI causality assessment committee meetings should be adjusted to meet this demand.

Countries requiring special technical expertise for causality assessment, such as specific training on COVID-19 AEFI causality assessment or advice for laboratory tests, should contact

their WHO national or regional office. Assistance is also available from WHO at the global level by contacting: gvsi@who.int.

Establishing a regional technical committee for causality assessment with collaborative mechanisms for a broader range of expertise and experience in causality assessment will support countries with limited internal expertise and resources. The success of this strategy will depend on the country willingness to share information, where necessary, while maintaining confidentiality. In addition, this regional committee could provide advice for Member States on the trends and patterns of safety signals for COVID-19 vaccines in use in the region.

3.2.3 Case selection and prerequisites for individual causality assessment

The selection of AEFI cases reported from passive surveillance systems for causality assessment should focus on the following situations:

- serious AEFIs in vaccinated patients that result in death, are life-threatening, require inpatient hospitalization or prolongation of existing hospitalization, result in persistent or significant disability/incapacity, or result in a congenital anomaly or birth defect or is a medically important event or reaction;
- the occurrence of events with an unexpected high rate or unusual severity;
- signals generated as a result of individual or clustered cases;
- significant events of unexplained cause, occurring up to 1 year after COVID-19 vaccination (and that are not listed in the product information); or
- events causing significant parental, family or community concerns.

3.2.4 Key considerations during causality assessments for COVID-19 vaccine- related AEFIs

Performing scientific causality assessments requires a comprehensive, completed AEFI investigation dossier, with all the necessary information including a valid diagnosis, details of the vaccine administered, information about medication being taken at the time of vaccination or prior to the occurrence of the AEFI and an independent AEFI causality assessment committee. At the time of assessment, the AEFI case investigation should have been completed, all details of the case such as the COVID-19 AEFI report form, case investigation form, completed clinical case record, laboratory report, autopsy report, details of field investigations should be available.

Due to unique challenges associated with COVID-19 vaccines, the AEFI causality assessment committee should consider each of the following factors:

- *Evidence for causes other than COVID-19 vaccines*: Prior knowledge on background rates of the events in the population are essential to determine if the event is associated or not with the vaccine. This is important to support for the classification of coincidental events in adult population, particularly those with chronic diseases.
- *Known causal association between COVID-19 vaccines and vaccination*: Information available from clinical trials, information published for vaccine platforms and brand-specific AEFI

rates will be useful for the assessment. In addition, risk management plans and PSURs provided by the vaccine manufacturers will be useful.

- *Novel administration technologies and handling requirements:* Administration of some COVID-19 vaccines will require specific skills for storage conditions and handling of new technology. This could increase the risk of immunization-related errors.
- *Diverse age groups:* The use of COVID-19 vaccines for the immunization of adults and adolescents and in mass campaigns could increase the risk of reporting of immunization anxiety or immunization stress-related responses.
- *Other qualifying factors for classification:* These could include previous history of a similar event, background rates of pre-existing, present and past health conditions, medications, etc.
- *Vaccine- enhanced COVID-19 disease:* Vaccine-associated enhanced disease is known to be a AEFI associated with some live attenuated vaccines. COVID-19 vaccination may be associated with an increased risk of developing COVID-19-like disease or its complications. There is also a potential risk of individuals immunized with a COVID-19 vaccine could develop severe COVID-19 disease when exposed to wild-type COVID-19 virus. At present, there is no evidence that these risks exist for COVID-19 vaccines, but they cannot be excluded. It is important to keep in mind multisystem inflammatory syndrome in children and adults during causality assessment as the relationship is currently unclear.

04 Tools for AEFI

It is recommended to use the existing data collection tools, as described in the Global Manual on Surveillance of AEFI[5] for data collection, collation and processing for AEFIs. Some of the tools need to be amended and adapted to the context of the COVID-19 vaccine safety. The details of some available tools and how to access them are provided in **Table 1**.

Table 1: Tools recommended for COVID-19 vaccine-related AEFI reporting, investigation, management and causality assessments

Description	Purpose	Status for COVID-19	Electronic tool
AEFI reporting form	To collect basic reports of all AEFI cases that have been notified	COVID-19 standard AEFI reporting form that includes the name of the manufacturer and brand name	Use in-country tools if available; if not WHO recommends Vigiflow
AEFI linelist	To collate the details in the reporting form	COVID-19 standard linelist that includes the name of the manufacturer and brand name	WHO recommends Vigiflow
AEFI investigation form	To collect detailed information when serious AEFI cases are investigated	Adapted to include COVID-19 specific questions	WHO AEFI investigation assistance software
AEFI causality assessment (available here)	To determine case classification of serious AEFI cases	Remains unchanged	Global Vaccine Safety on-line causality assessment tool

05 Appendices

Appendix 5.1: Standard COVID-19 AEFI reporting form

AEFI reporting id number:

STANDARAD REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

***Patient name or initials*:** ***Patient's full Address*:** Telephone: Sex: ☐ M ☐ F (Pregnant ☐ Lactating ☐) ***Date of birth (DD/MM/YYYY)*: _ _/_ _/_ _ _ _** *OR Age at onset :* ☐☐ *Years* ☐☐ *Months* ☐☐☐ *Days* *OR Age Group:* ☐ 0 < 1 year ☐ 1- 5 years ☐ > 5 years - 18 years ☐ > 18 years – 60 years ☐ > 60 years	***Reporter's Name*:** Institution: Designation &Department: Address: Telephone & e-mail: Date patient notified event to health system (DD/MM/YYYY): _ _/_ _/_ _ _ _ Today's date (DD/MM/YYYY): _ _/_ _/_ _ _ _

Health facility (or vaccination centre) name:

Vaccine							*Diluent*		
Name of vaccine (Generic)	****Brand Name incl. Name of Manufacturer***	****Date of vaccination***	****Time of vaccination***	Dose (1st, 2nd, etc.)	****Batch/ Lot number***	Expiry date	****Batch/ Lot number***	Expiry date	Time of reconsti tution

Adverse event (s): ☐ Severe local reaction ☐ *>3 days* ☐ *beyond nearest joint* ☐ Seizures ☐ *febrile* ☐ *afebrile* ☐ Abscess ☐ Sepsis ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Fever≥38°C ☐ Other (specify)..... Date & Time AEFI started (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ ☐☐ Hr ☐☐Min	Describe AEFI (Signs and symptoms):
Serious: Yes / No ; ➔ If Yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly ☐ Other important medical event (Specify_____)	
Outcome: ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown ☐ Died If died, date of death (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ Autopsy done: ☐Yes ☐No ☐Unknown	
Past medical history (including history of similar reaction or other allergies), concomitant medication and dates of administration (exclude those used to treat reaction) other relevant information (e.g. other cases). *Use additional sheet if needed :*	

First Decision making level to complete:

Investigation needed: ☐ Yes ☐ No	If yes, date investigation planned (DD/MM/YYYY): __ __ / __ __ / __ __ __ __

National level to complete:

Date report received at national level (DD/MM/YYYY): __ __ / __ __ / __ __ __ __	AEFI worldwide unique ID :
Comments:	

**Compulsory field*

Appendix 5.2: AEFI linelist

COVID19 AEFI linelist

Source	S. No	Patient Name/ Identifier	AEFI Reporting ID number	Patient Location (Village/Town)	Patient Location (District)	Sex (M/F)	Pregnant (Y/N)	Lactating (Y/N)	Age (Date of brith or age at onset)	Vaccine/s Brand	Manufacturer name	Dose	Vaccine Batch No	Diluent Batch No	Adverse Event	Place of vaccination	Date of Vaccination (DOV)	Date of onset (DOO)	Date of Notification (DON)	Date of Reporting (DOR)	Serious (Yes/No)	Reason for Serious	Outcome	Autopsy conducted in case of death (Y/N/NA)	Reported by	Reporter Location 1	Reporter Location 2	Investigation Planned (Y/N)	Date report recd at Natl Level

Appendix 5.3: AEFI investigation form adapted for COVID-19 immunization

Oct 2020

AEFI FOLLOWING COVID 19 VACCINATION - INVESTIGATION FORM

(Only for Serious Adverse Events Following Immunization – Death / Disability / Hospitalization / Cluster)

Section A Basic details

Province/State **District** **Case ID**

Place of vaccination (✓): ☐ Govt. health facility ☐ Private health facility ☐Other (specify) _____
Vaccination in (✓): ☐ Campaign ☐ Routine ☐ Other (specify) _____

Address of vaccination site:

Name of Reporting Officer:

Date of investigation: __ __ / __ __ / __ __ __ __
Date of filling this form: __ __ / __ __ / __ __ __ __

Designation / Position:

This report is: ☐ *First* ☐ *Interim* ☐ *Final*

Telephone # landline (with code): Mobile: e-mail:

Patient Name Sex: ☐M ☐ F

(use a separate form for each case in a cluster)

Date of birth (DD/MM/YYYY): __ __ / __ __ / __ __ __ __

OR *Age at onset: __ __ years __ __ months __ __ __ days*

OR *Age group:* ☐ *< 1 year* ☐ *1–5 years* ☐ *> 5 years - 18 years* ☐ *> 18 years – 60 years* ☐ *> 60 years*

Patient's full address with landmarks *(Street name, house number, locality, phone number etc.)*:

Brand name of vaccines (including manufacturer) /diluent received by patient	Date of vaccination	Time of vaccination	Dose (e.g. 1st, 2nd, etc.)	Batch/Lot number	Expiry date
				Vaccine Diluent	Vaccine Diluent
				Vaccine Diluent	Vaccine Diluent
				Vaccine Diluent	Vaccine Diluent
				Vaccine Diluent	Vaccine Diluent
				Vaccine Diluent	Vaccine Diluent

Type of site (✓) ☐ Fixed ☐ Mobile ☐ Outreach ☐ Other _____

Date of first/key symptom *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __ Time of first symptom (*hh/mm):* __ __ / __ __
Date of hospitalization *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __
Date first reported to the health authority *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __

Status on the date of investigation (✓): ☐ Died ☐ Disabled ☐ Recovering ☐ Recovered completely ☐Unknown

If died, date and time of death *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __ *(hh/mm):* __ __ / __ __
Autopsy done? (✓) ☐ Yes (date)_____ ☐ No ☐ Planned on (date)_____ Time_____
Attach report (if available)

Section B Relevant patient information prior to immunization

Criteria	Finding	Remarks (If yes provide details)
Past history of similar event?	Yes / No / Unkn	
Adverse event after any previous vaccination(s)?	Yes / No / Unkn	
History of allergy to vaccine, drug or food?	Yes / No / Unkn	
Pre-existing comorbidity/ congenital disorder?	Yes / No / Unkn	
Pre-existing acute illness (30 days) prior to vaccination?	Yes / No / Unkn	
Has the patient tested Covid19 positive prior to vaccination?	Yes / No / Unkn	
History of hospitalization in last 30 days, with cause?	Yes / No / Unkn	
Was the patient receiving any concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No / Unkn	
Family history of any disease (relevant to AEFI) or allergy?	Yes / No / Unkn	
For adult women • Currently pregnant? Yes (weeks) _____ / No / Unknown • Currently breastfeeding? Yes / No		

For infants

The birth was ☐ full-term ☐ pre-term ☐ post-term. Birth weight:

Delivery procedure was ☐ Normal ☐ Caesarean ☐ Assisted (forceps, vacuum etc.) ☐ with complication (specify)

Section C Details of first examination** of serious AEFI case

Source of information (✓ *all that apply*): ☐ **Examination by the investigator** ☐ **Documents** ☐ **Verbal autopsy**
☐ **Other**_____ *If from verbal autopsy, please mention source* _____

Name of the person who first examined/treated the patient:_____
Name of other persons treating the patient: _____
Other sources who provided information (specify): _____

Signs and symptoms in chronological order from the time of vaccination:

Name and contact information of person completing these clinical details:	Designation:	Date/time

****Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports, prescriptions for concomitant medication) and then complete additional information NOT AVAILABLE in existing documents, i.e.**

- ***If patient has received medical care*** – attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) and write only the information that is not available in the attached documents below
- ***If patient has not received medical care*** – obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

Provisional / Final diagnosis:

Section D Details of vaccines provided at the site linked to AEFI on the corresponding day

Number immunized for each antigen at session site. Attach record if available.	Vaccine name									
	Number of doses									

a)	When was the patient immunized? (✓ the ☐ below and respond to ALL questions)	
	☐ Within the first vaccinations of the session ☐ Within the last vaccinations of the session ☐ Unknown	
	In case of multidose vials, was the vaccine given ☐ within the first few doses of the vial administered? ☐ within the last doses of the vial administered? ☐ unknown?	
b)	Was there an error in prescribing or non-adherence to recommendations for use of this vaccine?	Yes* / No
c)	Based on your investigation, do you feel that the vaccine (ingredients) administered could have been unsterile?	Yes* / No / Unable to assess
d)	Based on your investigation, do you feel that the vaccine's physical condition (e.g. colour, turbidity, foreign substances etc.) was abnormal at the time of administration?	Yes* / No / Unable to assess
e)	Based on your investigation, do you feel that there was an error in vaccine reconstitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)?	Yes* / No / Unable to assess
f)	Based on your investigation, do you feel that there was an error in vaccine handling (e.g. break in cold chain during transport, storage and/or immunization session etc.)?	Yes* / No / Unable to assess
g)	Based on your investigation, do you feel that the vaccine was administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size, not following good injection practice etc.)?	Yes* / No / Unable to assess
h)	Number immunized from the concerned vaccine vial/ampoule	
i)	Number immunized with the concerned vaccine in the same session	
j)	Number immunized with the concerned vaccine having the same batch number in other locations. Specify locations: _____	
k)	Could the vaccine given to this patient have a quality defect or is substandard or falsified?	Yes* / No / Unable to assess
l)	Could this event be a stress response related to immunization (e.g. acute stress response, vasovagal reaction, hyperventilation, dissociative neurological symptom reaction etc.)?	Yes* / No / Unable to assess
m)	Is this case a part of a cluster?	Yes* / No / Unkn
i.	If yes, how many other cases have been detected in the cluster?	
a.	Did all the cases in the cluster receive vaccine from the same vial?	Yes* / No / Unkn
b.	If no, number of vials used in the cluster (enter details separately)	

* ***It is compulsory for you to provide explanations for these answers separately***

Section E Immunization practices at the place(s) where concerned vaccine was used

(Complete this section by asking and/or observing practice)

Syringes and needles used:

• Are AD syringes used for immunization?	Yes / No / Unkn

If no, specify the type of syringes used: ☐ Glass ☐ Disposable ☐ Recycled disposable ☐ Other _____

Specific key findings/additional observations and comments:

Reconstitution: (complete only if applicable, ✓ NA if not applicable)

	Status		
• Reconstitution procedure (✓)			
Same reconstitution syringe used for multiple vials of same vaccine?	Yes	No	NA
Same reconstitution syringe used for reconstituting different vaccines?	Yes	No	NA
Separate reconstitution syringe for each vaccine vial?	Yes	No	NA
Separate reconstitution syringe for each vaccination?	Yes	No	NA
• Are the vaccines and diluents used the same as those recommended by the manufacturer?	Yes	No	NA

Specific key findings/additional observations and comments:

Injection technique in vaccinator(s): (Observe another session in the same locality – same or different place)	
• Correct dose and route?	Yes / No
• Time of reconstitution mentioned on the vial? (in case of freeze dried vaccines)	Yes / No
• Non-touch technique followed?	Yes / No
• Contraindications screened prior to vaccination?	Yes / No
• How many AEFI were reported from the centre that distributed the vaccine in the last 30 days?	
• Training received by the vaccinator? (If Yes, specify the date of last training _____)	Yes / No
Specific key findings/ additional observations and comments?	

Section F Cold chain and transport *(Complete this section by asking and/or observing practice)*	
Last vaccine storage point:	
• Is the temperature of the vaccine storage refrigerator monitored?	Yes / No
○ If "yes", was there any deviation outside of 2–8° C after the vaccine was placed inside?	Yes / No
○ If "yes", provide details of monitoring separately.	
• Was the correct procedure for storing vaccines, diluents and syringes followed?	Yes / No / Unkn
• Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer?	Yes / No / Unkn
• Were any partially used reconstituted vaccines in the refrigerator?	Yes / No / Unkn
• Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator?	Yes / No / Unkn
• Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store?	Yes / No / Unkn
Specific key findings/additional observations and comments:	
Vaccine transportation:	
• Type of vaccine carrier used	
• Was the vaccine carrier sent to the site on the same day as vaccination?	Yes / No / Unkn
• Was the vaccine carrier returned from the site on the same day as vaccination?	Yes / No / Unkn
• Was a conditioned ice-pack used?	Yes / No / Unkn
Specific key findings/additional observations and comments:	

Section G Community investigation (Please visit locality and interview parents/others)

Were any similar events reported within a time period similar to when the adverse event occurred and in the same locality? Yes / No / Unknown If yes, describe:

If yes, how many events/episodes?

Of those effected, how many are
- Vaccinated:_____
- Not vaccinated:_____
- Unknown:_____

Other comments:

Section H Other findings/observations/comments

COVID-19 VACCINES:

SAFETY SURVEILLANCE MANUAL

World Health Organization

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