AEFI/ AESI surveillance in the context of COVID-19 vaccine introduction
- Reporting -

Andrea Lohee

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AEFI – AESI in a nutshell

	AEFI	AESI in the context of COVID-19
What	Any untoward medical occurrence that follows immunization, and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.	A pre-specified event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further special studies.
Purpose of collecting information	To identify all events after vaccination – determine if serious, investigate (serious) and do causality assessment.	To identify pre-specified specific events by a set criterion and determine if the event is associated with COVID-19 vaccination.
Identification method	Identified via spontaneous reporting by vaccine recipients or their parents, or health care workers or other persons who first notice the event.	Identified via an active surveillance system in sentinel sites or electronic health record by a health care worker or other staff in the system
Case definitions	Important	Critical

AEFI – AESI in a nutshell

	AEFI	AESI in the context of COVID-19
Type of reporting	All events that follow immunization and are notified to the health care system	All events identified through active surveillance that fit the case definition, irrespective of immunization status.
Training	All frontline immunization staff in health care facilities (public and private); and other relevant staff for reporting, investigation, data analysis, and causality assessment	Immunization staff and other health care workers in sentinel sites and predefined active surveillance systems, NIP/EPI mangers, NRA, research staff, national AEFI committee.
Users	Health care workers, NIP/EPI managers, NRA, surveillance and information managers, epidemiologists, surveillance and information managers, vaccine safety partners including the community	Sentinel site staff, NIP/EPI managers, NRA, epidemiologists, national AEFI committees, study teams.

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Safety surveillance - Objectives

The goals of vaccine surveillance (including COVID-19 vaccines) are:

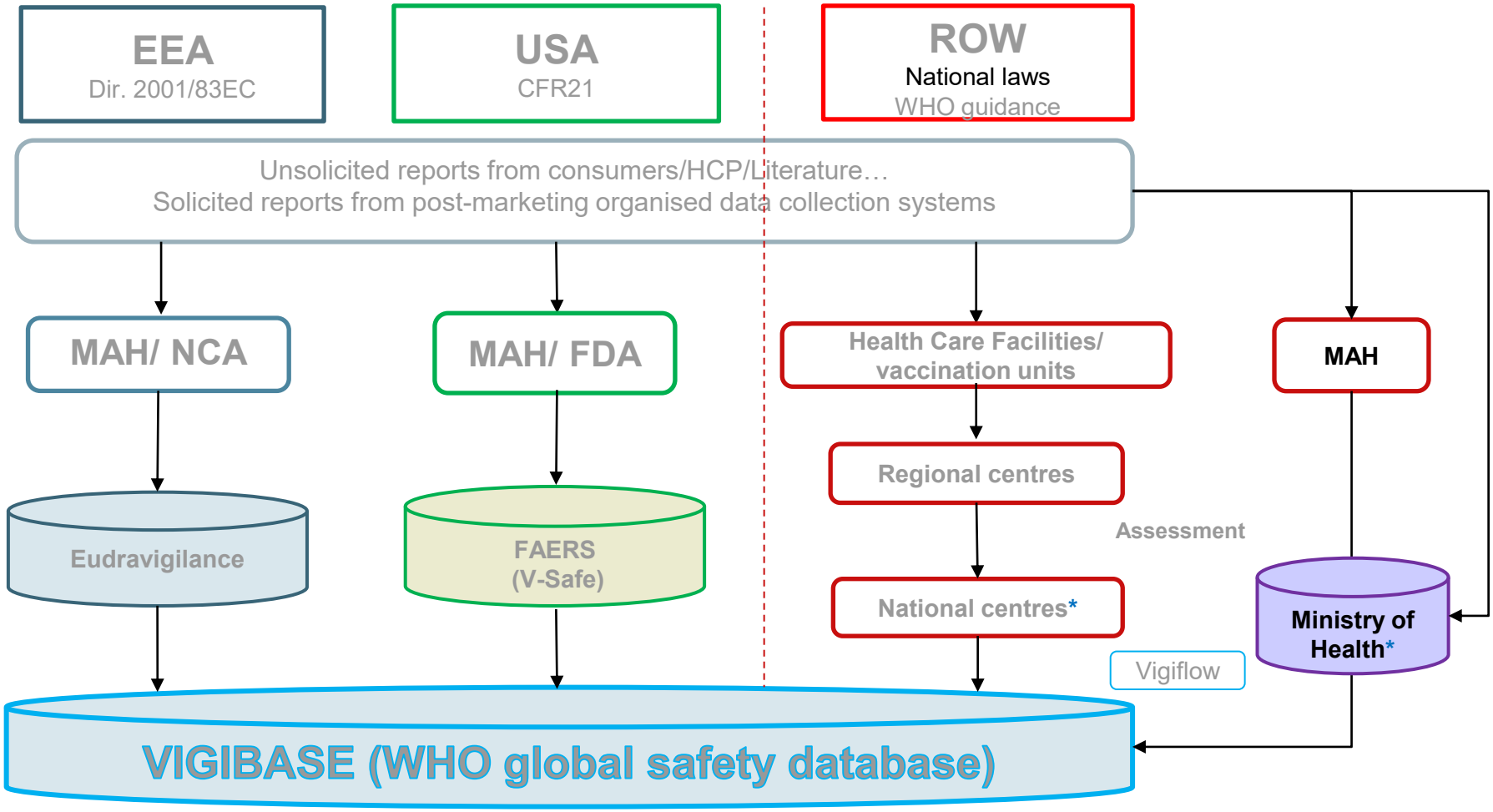
- Detect serious AEFI/AESI rapidly
- Generate date to characterize the safety of the COVID-19 vaccines
- Identify, investigate, assess validate and respond to safety signals
- Ensure high quality safety surveillance
- Maintain public and stakeholder confidence in vaccines

Safety surveillance - Objectives

To achieve this, all countries should aim at:

- Strengthening routine passive surveillance reporting systems
- Detecting, and investigate potential safety signals, clustering or serious events, immunization errors, community concerns, etc.
- Performing systematic causality assessment for AESI
- Planning and responding rapidly to any COVID-19 vaccine-related events
- Addressing concerns and maintaining public and stakeholder confidence in vaccines.

Safety Surveillance Reporting – Organisation



EEA: European Economic Area; USA: United States of America; ROW: Rest of the World; MAH: Marketing Authorisation Holder; NCA: National Competent Authority; FDA: Food and Drug Administration; HC(P): Health Care (Provider); FAERS: FDA Adverse Event Reporting System * countries part of the WHO Programme for international drug monitoring

Safety surveillance Reporting – Organisation

Organisation of pharmacovigilance is country specific and is regulated by laws and country specific guidelines.

WHO member Countries specific guidelines can be found on the UMC (Uppsala Monitoring Committee) website.

https://www.who-umc.org/global-pharmacovigilance/who-programme-for-international-drug-monitoring/country-guidelines/

Safety surveillance - Organisation

- Immunization safety surveillance is organised at different levels in the country with roles and responsibilities at each level.
- Case detection is the first important step in AEFI surveillance.
- The primary reporter (i.e the one who first reports an AEFI) may be a field health worker, hospital staff, a vaccinee or a parent, or any other person who detects the AEFI.
- Suspicion alone is sufficient for reporting and the primary reporter is not expected to report/ assess causality.

Safety surveillance – Organisation

Administrative level	Responsibilities/activities	AEFI classification status
Peripheral level person reporting the event	- AEFI **detection** and recording - Triage and reporting of serious AEFI to intermediate level - Routine **reporting** and line listing - Investigation	Preliminary classification - Serious - Non serious

Intermediate level (sub-national, district or region)	- Support to peripheral level
	  - Investigation of serious AEFI
	  - Clinical and laboratory assessment
	- Causality assessment of AEFI (preliminary)
	- **Report** to national expert committee
	- Data analysis and search for additional cases
		Provisional classification of serious AEFI
		• For referral to national level
		  • Vaccine reaction
		  • Coincidental
		  • Unknown
		• For local action
		  • Immunisation error related
		  • Immunization anxiety related

National level (national immunisation programmes)	- Provide expert support for field investigation - Monitor information collection - Assess serious AEFI - Causality assessment of AEFI (final national AEFI committee) - Data analysis and search for signals	- Final classification of all serious AEFI - Maintain repository for all cases (serious and non serious)

Safety surveillance - Challenges with Covid mass vaccinations

- New infectious disease
- Number of vaccines and various manufacturers, many using novel vaccine platforms/technologies and possibly used concomitantly in the same country
- Broad target populations (including with underlying comorbidities)
- Variable immunisation strategies adopted by different countries
- Administration on massive scale in a short time interval with minimum training and field preparation leading to large number of immunisation errors and related reactions.

Safety surveillance - Challenges with Covid mass vaccinations

- Limited data from clinical trials
- Larger numbers of immunisation anxiety-related reactions anticipated (older age groups, novelty of vaccines, rumors,…)
- Expert committees for AEFI/AESI review and causality assessment may not exist everywhere or may have limited experience in evaluation of AEFI/AESI in adults with higher comorbidities

Safety surveillance – Barriers to Reporting

Immunization service providers may not report AEFI for a number of reasons, such as:

- Considering that the event did not occur after immunization (however, all events following immunization as per the definition should be reported);
- Lack of knowledge about the reporting system and process;
- Apathy, procrastination, lack of interest or time, inability to find the reporting form;
- Fear that the report will lead to personal consequences;
- Guilt about having caused harm and being held responsible for the event; and diffidence about reporting an event when not confident about the diagnosis.

Safety surveillance - Country preparedness

- Clarify roles and responsibilities at different levels and set up relevant AEFI committees at all relevant (subnational) levels
- Identify resources available
- Define and disseminate list of events to be reported, case definitions, standard investigation procedure, AEFI forms and investigation form
- Designate and train staff (at all levels) to make reports, complete report forms and investigate AEFI.
- Inform all health workers/clinicians of the need to report immediately an AEFI, and indicate which ones should be reported
- Stimulate AEFI reporting and perform real time safety data analyses

Safety surveillance - How?

AEFI detection primarily takes place through:

- Routine passive surveillance (spontaneous reporting). This involves anyone detecting the AEFI and reporting them to any health care worker within the health care system.
- Active Vaccine Safety Surveillance (AVSS): collection of data from all individuals within a defined population, thereby minimizing the risk of under-reporting. AVSS is done via sentinel sites or through cohort event monitoring. Active surveillance aims at collecting AESIs.
- Ad hoc studies: Epidemiological studies where AEFI should be independently reported

Safety surveillance - How?

The type and scope of vaccine safety monitoring activities that countries choose to adopt to achieve these goals will depend on the resources available and the maturity of their pharmacovigilance surveillance systems but they should aim to strengthen their activities before and during COVID-19 vaccine introduction and adapt continuously to the COVID-19 situation.

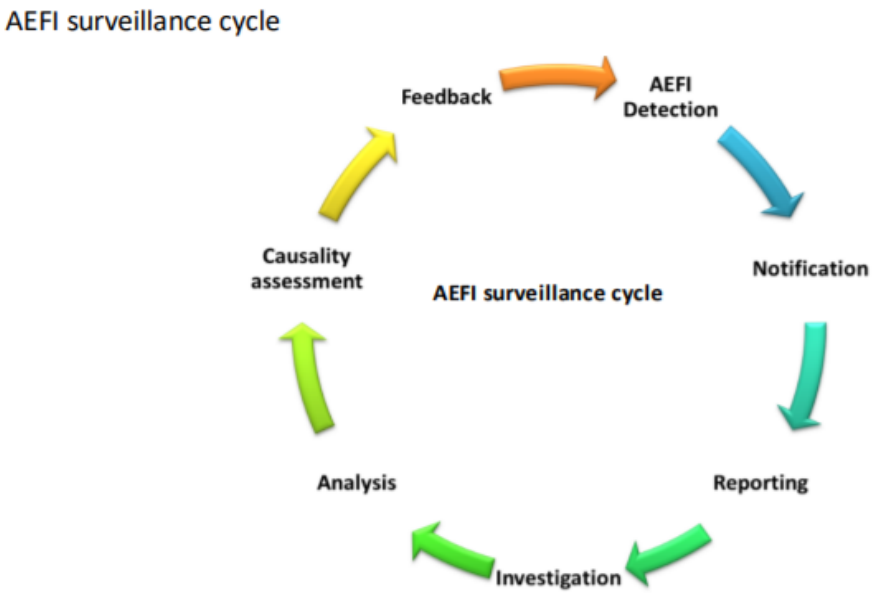
In many countries, detection will primarily take place through routine passive surveillance (AEFI reporting).

Where possible active surveillance should be implemented (AESI reporting)

Passive surveillance - AEFI reporting for Covid vaccines

At the time of vaccine introduction, all countries should have an AEFI surveillance system in place.

The surveillance cycle outlines the different steps that should be present in the surveillance model.



Passive surveillance: tools for AEFI reporting

AEFI Form

- COVID-19 AEFI form should always be used using the fastest means possible for transmitting (also country specific tools).
- When the event 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.
- Special attention should be given to the collection of brand name, manufacturer and batch number
- Usually completed by the HCW or immunization provider but may also be completed by vaccine recipients or their relatives

COVID 19_AEFI reporting form

A comprehensive complete AEFI report is the primary source for the population of the AEFI linelist

Passive surveillance - tools for AEFI reporting

AEFI linelist

Acrobat Document

When AEFI reporting form is received at the sub-national/intermediate (provincial/district) level following actions are taken:

- Assessment of seriousness*
- Decision on investigation and as transmitted to the next level

AEFI linelist, when completed, contains key descriptive epidemiological data (time, place, person) that are critical for identifying clusters and for signal detection,

The linelist serves to collate details in the reporting form and includes name of manufacturer and brand name

*An event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/ incapacity, or is a congenital anomaly/birth defect

Passive surveillance: tools for AEFI reporting

Acrobat Document

AEFI investigation form

The AEFI investigation form is intended to collect detailed information on serious AEFI that are investigated and contains COVID-19 specific questions.

A COVID-19 AEFI investigation form has been developed and can be found in the COVID-19 safety surveillance manual

https://apps.who.int/iris/bitstream/handle/10665/338400/9789240018280-eng.pdf?sequence=1&isAllowed=y

An AEFI investigation assistance software is available under the following link:

http://investigation.gvsi-aefi-tools.org/index.html#step-1

Passive surveillance: tools for reporting

- **AEFI Causality assessment form**

The AEFI causality assessment form is intended to determine the clasification of serious AEFI cases.

The form can be found in the AEFI assessment aide mémoire

Adobe Acrobat Document

https://www.who.int/vaccine_safety/initiative/investigation/New_aide_mem_causal_assmt.pdf

- An **assessment tool** (non COVID-19 specific) has been developed and may be used for this purpose.

http://gvsi-aefi-tools.org/

Passive surveillance: tools for reporting

Vaccine Adverse Event Information Management System (VAEIMS)

VAEIMS is a software that has been developed to allow the transfer of AEFI data from each national database to Vigibase.

The web-based version or off-line version of VAEIMS is available to all countries free of charge.

VigiFlow

VigiFlow is a web-based individual case safety report (ICSR) management system that is available for use by national pharmacovigilance centres of the WHO Programme for International Drug Monitoring. VigiFlow supports the collection, processing and sharing of data of ICSRs

Country specific Tools

What exists in your countries in terms of AEFI surveillance?

Active surveillance - Country preparedness

Shortlisting pre-specified AESIs before COVID-19 vaccine introduction will enable countries and regions to prepare for vaccine safety surveillance. This will involve:

- defining the events,
- ensuring suitable tools are available to detect them,
- providing training for relevant staff and identifying the disease codes and estimating the background rates for the AESIs. This is important because AESIs are generally detected and reported through active vaccine safety surveillance (AVSS) systems

AVSS also require more planning, resources, expertise as well as coordination at all reporting levels

Active surveillance - AESI detection and reporting

For countries with advanced safety surveillance system, Active Vaccine Surveillance Systems should be considered for:

- The detection of delayed AESIs
- Serious AESIs
- AESIs in specific populations
- AESI occurring during mass COVID-19 vaccination programmes

Active surveillance - AESI detection and reporting

AESIs should be identified, irrespective of exposure to COVID-19 vaccine, based on a pre-specified list, which will be unique for each country or region, and the diagnosis of each AESI case identified should match an approved case definition

These pre-specified AESI should be identified through an active process and then reported, investigated and analysed to:

- Identify signals
- Determine the rate of an event in a defined population
- Determine the relative risk of the event
- Determine the occurrence of events in both vaccinated and unvaccinated population

Active surveillance - AESI detection and reporting

Depending on the AESI surveillance methodology and the protocol (master protocols) adopted by the country, AESIs can be detected through:

- prospective surveillance, which requires that health care workers are trained to detect AESIs, using simplified case definitions, as they occur;
- retrospective surveillance, which requires designated surveillance staff to conduct systematic searches for pre-specified AESIs, using a simplified case definition, in the target population by examining patient records at facilities; or
- other electronic methods.

Active surveillance - data collection

- Collect individual data linked by unique patient identifier
- Structured data collection
- Ideally, use of electronic databases
- Different methods can be used (e.g cohort event monitoring, sentinel surveillance, etc) depending on available expertise, resources, funding.
- Several electronic tools can be used such as m-Health and e-Health to facilitate implementation and reporting

Active surveillance - data collection

Core and complete data points to be collected for AVSS

		Vaccination data	Health events or outcomes	Demographic data
Complete data set	Core data set	Vaccine brand name	Adverse event(s)	Age at onset
		Lot number	Date of onset of symptoms	Gender
		Date of vaccination	Serious	Medical conditions
		Site of vaccination	-	-
		Place of vaccination	Place of care	-
		Vaccine antigens	-	-
		Concomitant vaccines	-	-
		Route of administration	-	-

Active surveillance - tools for AESI reporting and assessment

- Unique resources are being developed for identifying and responding to AESIs, including:
  - protocols,
  - case definitions*** (developed by Brighton Collaboration),
  - **AESI reporting form*,**
  - AESI confirmation forms**,
  - **AESI linelist***,
  - **AESI investigation form***,
  - tabular checklists**,
  - **automated tools for assessments***,
  - background rates and codes.

COVID 19_AESI reporting form

COVID 19_AESI line listing

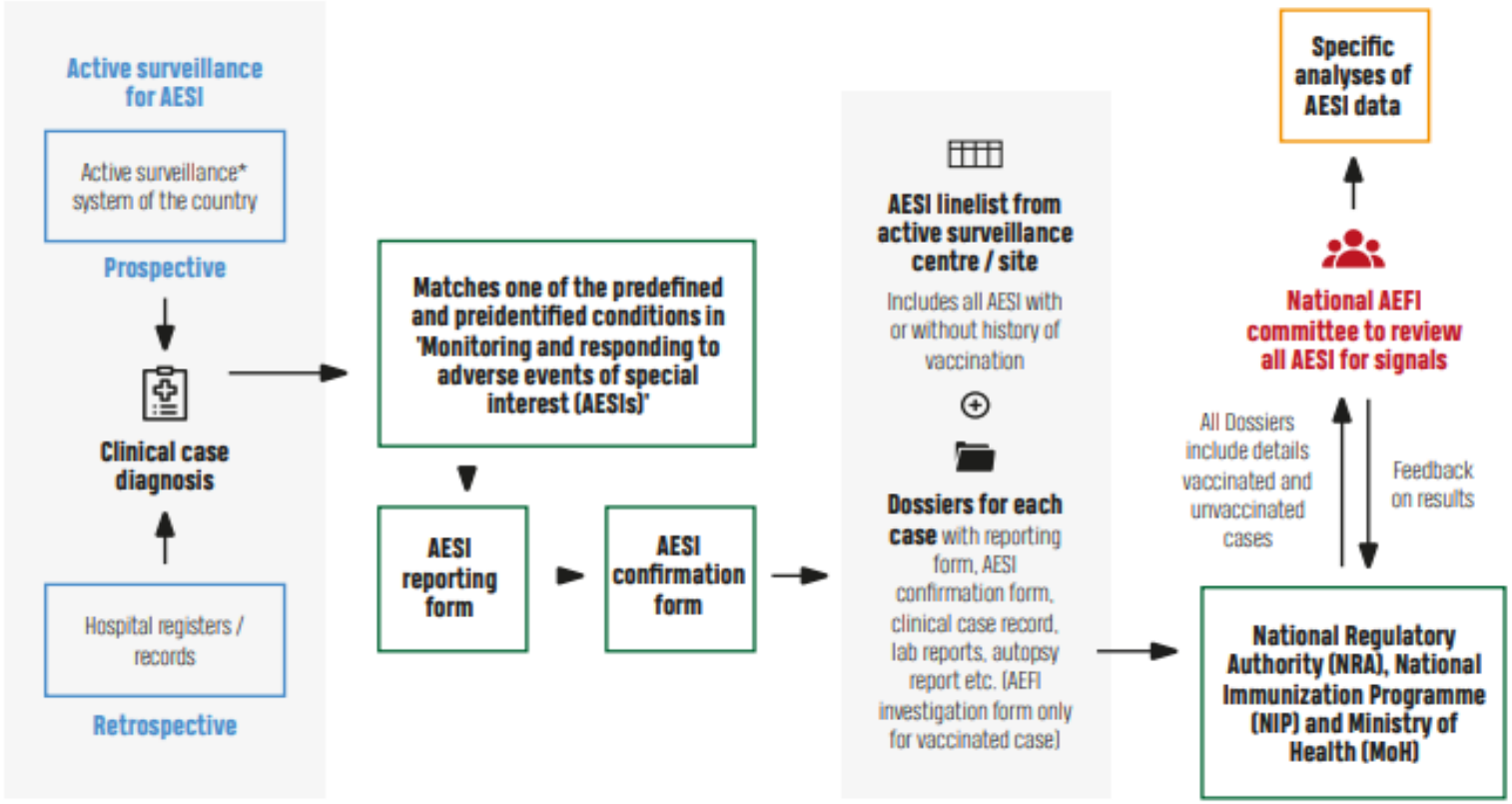
COVID 19_AESI investigation form

- Any AESI matching the list of pre-specified AESI conditions should undergo detailed investigation, unless specified otherwise in the country's protocol

*available **in development

***Case definitions: Available for some conditions and under development for others available at https://brightoncollaboration.us/covid-19/
Refer to separate presentation on AESI - case definitions

Active Safety Surveillance – in country reporting



* Data flow can be customized according to the active surveillance methods adopted by the country

What exists in your countries in terms of active surveillance?

References

- WHO Global manual on Surveillance on Adverse Events Following Immunization

https://www.who.int/vaccine_safety/publications/Global_Manual_revised_12102015.pdf

- WHO COVID-19 Vaccines: Safety Surveillance Manual

https://apps.who.int/iris/bitstream/handle/10665/338400/9789240018280-eng.pdf?sequence=1&isAllowed=y

  - Module: Responding to adverse events following COVID-19 immunization
  - Module: monitoring and responding to adverse events following immunization (AEFIs)
  - Module: monitoring and responding to adverse events of special interest (AESI)

Take Home messages

- Check your country requirements
- Check your local capacities
- Define the best strategy based on resources and qualification of personnel
- Prepare and train all stakeholders
- Strive for best quality possible


QUESTIONS

Back up slides

Glossary

Acronym	Definition
AEFI	Any untoward medical event that follows immunization and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.
AESI	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.
Causality assessment	In the context of vaccine AEFI surveillance, a systematic review of data about the AEFI case(s) to determine the likelihood of a causal association between the event and the vaccine(s) received.
Causal association	A cause-and-effect relationship between a causative (risk) factor and an outcome. Causally-associated events are also temporally associated (i.e. they occur after vaccine administration), but events that are temporally associated may not necessarily be causally associated.
VigiBase	WHO global database of individual case safety reports (ICSRs) including Adverse Drug Reactions and AEFIs, maintained by Uppsala Monitoring Centre.