



Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine Type 2 (nOPV2) Use

CONTENTS

- Acronyms 2
- 1. Introduction..... 3
 - a. nOPV2 background..... 3
 - b. AFP, AESI and AEFI surveillance in the context of nOPV2 introduction - key concepts 3
 - c. Audience 5
 - d. Objectives..... 6
- 2. Adverse events of special interest..... 6
 - a. List of conditions for AESI surveillance 6
 - b. Case definitions for AESIs 7
- 3. Surveillance forms and tools..... 7
- 4. Safety surveillance 8
- 5. Data flow 11
- 6. Roles and responsibilities 11
- 7. Training 13
- 8. Confidentiality 13
- 9. Limitations 13
- 10. Annexes..... 14
 - Annex 1: Example of an electronic data-sharing agreement 14
 - Annex 2: nOPV2 reporting form for adverse events of special interest (AESI) 18
 - Annex 3: nOPV2 AESI line listing form 21
 - Annex 4: nOPV2 AESI case ascertainment form 22
 - Annex 5: Examples of data abstraction forms 23
 - Anaphylaxis data abstraction form 23
 - Aseptic meningitis data abstraction form 29
 - Unexplained deaths (including SIDS) data abstraction form 32
 - Annex 6: Simplified case definitions..... 35

ACRONYMS

ADEM	Acute disseminated encephalomyelitis
AEFI	Adverse event following immunization
AESI	Adverse events of special interest
AFP	Acute flaccid paralysis
CDC	United States Centers for Disease Control and Prevention
CO	Country office
cVDPV	Circulating vaccine-derived poliovirus
EPI	Expanded Programme on Immunization
ERC	Expert Review Committee
EUL	Emergency Use Listing
GACVS	Global Advisory Committee on Vaccine Safety
GBS	Guillain-Barré Syndrome
GPEI	Global Polio Eradication Initiative
mOPV2	Monovalent oral polio vaccine type 2
NITAG	National Immunization Technical Advisory Group
nOPV2	Novel oral poliovirus vaccine type 2
NRA	National Regulatory Authority
OPD	Outpatient department
OPV	Oral polio vaccine
SAGE	Strategic Advisory Group of Experts on Immunization
SO	Surveillance officer
VAPP	Vaccine-associated paralytic poliomyelitis
VDPV	Vaccine-derived poliovirus
VRE	Vaccine-related event
WHO	World Health Organization

1. INTRODUCTION

a. nOPV2 background

Circulating vaccine-derived poliovirus (cVDPV) outbreaks occur when, in rare circumstances, the weakened strain of the poliovirus contained in the oral polio vaccine (OPV) genetically reverts into a form that can cause paralysis. This can occur when the OPV strain circulates in under-immunized populations for a long period of time, with the weakened strain contained in type 2 OPV most at risk of reverting.

A new tool developed for polio eradication is the novel oral polio vaccine (nOPV2), a modification of the existing OPV type 2 vaccine, which has been shown to provide comparable protection against poliovirus while being less likely to lead to cVDPV outbreaks. To date, the safety of nOPV2 has been evaluated through Phase 1 and Phase 2 clinical trials. The new vaccine has been well-tolerated among adults, young children and infants with no indication of any increase in general safety risk compared to monovalent oral polio vaccine type 2 (mOPV2). The Global Advisory Committee on Vaccine Safety (GACVS) reviewed data of initial use for over 70 million doses across four countries and concluded there were no serious safety concerns from the data.

nOPV2 is being made available for outbreak response through an Emergency Use Listing (EUL) procedure of the World Health Organization that ensures rigorous analysis of efficacy and safety data to address Public Health Emergencies of International Concern, such as polio. Countries wishing to use nOPV2 under an EUL will be able to introduce the vaccine in accordance with established criteria that include safety monitoring processes to facilitate rapid identification and response to safety signals, should they arise. This monitoring will be particularly important in the first two years following the introduction of nOPV2 under EUL.

This *Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine type 2 (nOPV2) Use* describes a template that can be used to implement active surveillance for adverse events of special interest (AESI) by leveraging the existing resources and processes already established for acute flaccid paralysis (AFP) surveillance.

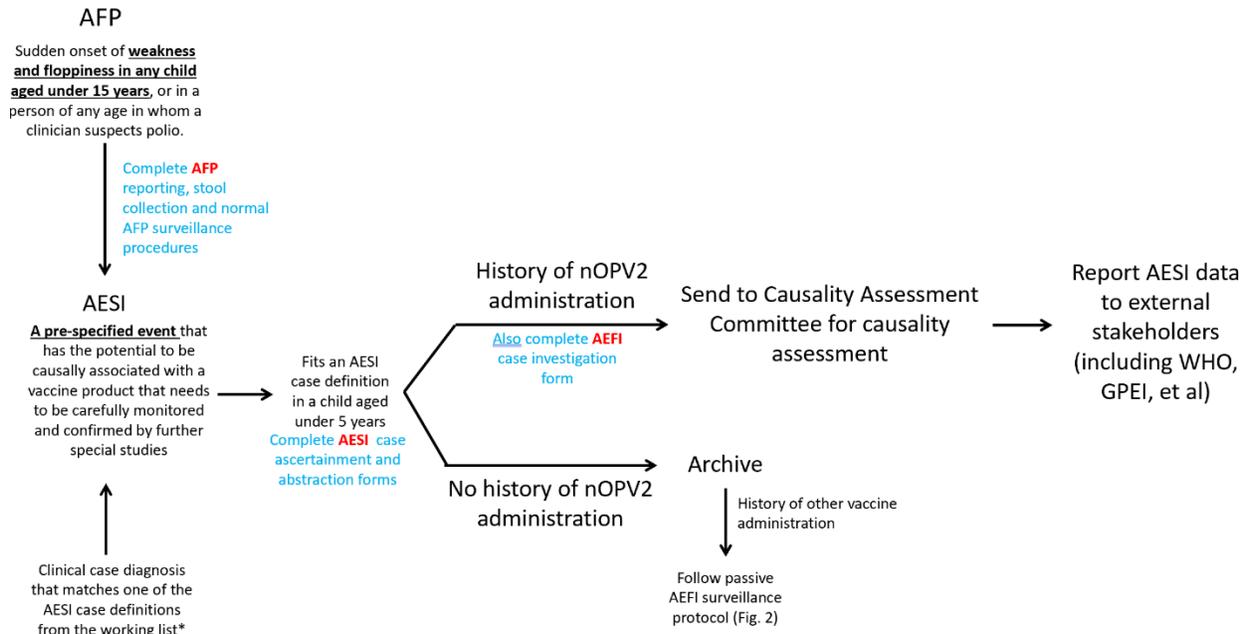
b. AFP, AESI and AEFI surveillance in the context of nOPV2 introduction - key concepts

AFP: Acute flaccid paralysis (AFP) manifests as a sudden onset of weakness and floppiness in any child aged under 15 years, or in a person of any age in whom a clinician suspects polio. Monitoring for, detecting and investigating cases of AFP have been the “gold standard” for polio surveillance. Under AFP surveillance, cases are reported to local government surveillance officers by health facility staff or a network of trained community members. Surveillance officers also perform active case search at traditional and non-traditional healthcare locations. When an AFP case is identified, surveillance officers perform detailed case investigations, asking questions about symptoms and immunization status and collecting stool samples for laboratory analysis. Confirmed cases of polio are generally diagnosed via detection of poliovirus in stool samples from AFP cases. Polio can also be diagnosed by identification of the virus in asymptomatic close contacts of the case or by assessment from a national expert review committee.

AESI: Adverse events of special interest (AESIs) are prespecified events that have the potential to be causally associated with a vaccine product (nOPV2 in this instance) that needs to be carefully monitored and confirmed by further special studies. The purpose of collecting this information is to identify prespecified specific events by a set criterion and determine if the event is associated with nOPV2 vaccination. AESIs are generally identified via an active surveillance system in sentinel sites or the electronic health record by a healthcare worker or other staff in the system. Matching the clinical and laboratory findings with prespecified case definitions for each of these pre-identified conditions are very important for AESI case confirmation. AESIs include all events identified through active surveillance that fit the case definition, irrespective of immunization status.

AFP surveillance and AESI surveillance are active processes and need the active involvement and participation of the country's immunization programme, as well as the institutions participating in surveillance activities. Fig. 1 outlines the activities and processes to be followed for AFP and AESI surveillance.

Fig. 1. Active AFP and AESI surveillance after nOPV2



* Anaphylactic reactions, aseptic meningitis/encephalitis, acute disseminated encephalomyelitis, GBS/Miller Fisher Syndrome, myelitis/transverse myelitis, AFP, unexplained deaths.

AEFI: Adverse events following immunization (AEFIs) include 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 unfavorable or unintended sign, abnormal laboratory finding, symptom or disease. AEFIs are identified through routine passive surveillance (spontaneous reporting) for all adverse events following immunization (AEFIs) for all vaccines, including nOPV2. AEFI surveillance systems typically follow a process of case identification, notification, reporting, investigation and causality assessment separate from the AFP surveillance system (Fig. 2). Although reporting structures may vary by country, National Regulatory Authorities (NRA) and national immunization programmes are typically involved. In addition, the national Vaccine Safety Advisory Committee or Causality Assessment Committee review data on serious AEFIs to conduct a causality assessment to determine the likelihood

that an event might have been caused by a vaccine or vaccination based on established WHO processes.¹

Fig. 2. Passive AEFI* surveillance after nOPV2 or other vaccines



Anywhere in the country, if reported by recipient/ representative following nOPV2 vaccine or other vaccine

During new vaccine introductions such as nOPV2, post-licensure safety monitoring is critical to detect rare or unexpected adverse events since the vaccine is given to a large number of individuals beyond those in Phase 1 and 2 clinical trials. In times of public health crises, such as during cVDPV outbreaks, enhanced vaccine safety surveillance processes can effectively and efficiently provide high-quality data for public health decision-making in settings where clinical trial data is limited. With nOPV2 use under an EUL, active surveillance for a focused list of AESIs is an important complement to the existing AFP and AEFI surveillance systems because it can assist with generating safety signals for complex conditions that may warrant timely further investigation to ensure public trust in the immunization programme.

c. Audience

This document is intended to assist countries and regions utilizing nOPV2 in implementing active AESI surveillance to generate high-quality safety data for decision-making purposes. It is developed for public health staff at the central, intermediate and peripheral levels who will contribute to the active surveillance of nOPV2 AESI, including healthcare workers, vaccinators, surveillance staff and decision-makers in public health. It is meant to complement other safety monitoring activities, including passive AEFI surveillance and AFP surveillance, and it should be adapted for individual country contexts to address the roles of different stakeholders who will be involved in nOPV2 safety monitoring efforts. These stakeholders may include the country’s Expanded Programme on Immunization (EPI), the NRA, the WHO country office (WHO CO), the Vaccine Safety Advisory Committee or Causality Assessment Committee, the Polio Expert Review Committee (ERC), GPEI agency personnel and Bio Farma, the vaccine license holder. Data will be generated primarily for use within an individual country context but

¹ Details of AEFI surveillance and its approaches are outlined in the *Global manual on surveillance of adverse events following immunization* that can be accessed online (<https://apps.who.int/iris/handle/10665/206144>).

will also benefit from comparison across countries. By standardizing the processes for AESI data collection, this guide will enable comparison of data across countries to improve the detection of safety signals across the country, regional and global levels.

d. Objectives

The objective of active AESI surveillance is to detect rare, serious, complex adverse events that may be anticipated based on what is currently known about polio vaccines. The objective of this guide is to support and strengthen the process for conducting standardized high-quality active AESI surveillance in the context of nOPV2 use in cVDPV outbreak response.

2. ADVERSE EVENTS OF SPECIAL INTEREST

a. List of conditions for AESI surveillance

AESIs are a subset of AEFI that typically fall under one of the following categories:

1. Proven association with immunization in general (e.g., anaphylaxis, VDPV, Guillain Barré Syndrome).
2. Proven association with a vaccine platform and/or adjuvant (e.g., arthritis following recombinant vesicular stomatitis virus vectored vaccine).
3. Theoretical concern based on immunopathogenesis.
4. Theoretical concern related to viral replication during wild type disease.
5. Theoretical concern because it has been demonstrated in an animal model with one or more candidate vaccine platforms.

No significant safety signals have been associated with nOPV2 thus far, though data is limited. Based on summary safety data, a working list of AESI conditions has been developed through consultation with the WHO, the United States Centers for Disease Control and Prevention (CDC) and other GPEI partners.

The AESI conditions proposed for active surveillance include:

- anaphylactic reactions;
- aseptic meningitis/ encephalitis;
- acute disseminated encephalomyelitis (ADEM);
- Guillain-Barré Syndrome (GBS)/ Miller Fisher Syndrome;
- myelitis / transverse myelitis;
- AFP due to cVDPV or vaccine-association paralytic poliomyelitis (VAPP); and
- unexplained deaths.

Additional conditions can be added by countries if they feel that there is another event of interest worth investigating further.

A harmonized approach across countries will increase the power of surveillance to detect safety signals and allow comparability of findings to guide global decision-making and document lessons learned. The final list of conditions for AESI surveillance in a particular country will need to be defined with input from country-level partners.

b. Case definitions for AESIs

Two types of case definitions are presented in this guide: (1) simplified case definitions (Annex 6); and (2) comprehensive Brighton Collaboration case definitions (Annex 5).

Simplified case definitions will be used to identify and report AESIs at the peripheral level by frontline healthcare workers and designated AESI surveillance staff. These definitions have a low level of specificity to support healthcare workers in identifying and reporting AESI. The simplified case definitions have been developed from multiple sources, including medical textbooks, WHO and country-level AEFI surveillance definitions, AFP case definitions and Brighton Collaboration case definitions and can be used in conjunction with the AESI reporting form and the AESI line listing form (described in the next section of this document).

To assist with causality assessment, Brighton Collaboration case definitions will be used in conjunction with case ascertainment/verification and data abstraction forms that will be a part of case investigation (Annex 5). Brighton Collaboration case definitions exist for: ADEM, anaphylaxis, aseptic meningitis, encephalitis, GBS/Miller Fisher Syndrome, myelitis and death.

3. SURVEILLANCE FORMS AND TOOLS

Four (4) forms assist countries in the collection of nOPV2 AESI data: (1) a reporting form; (2) a line listing form; (3) a case ascertainment form; and (4) a data abstraction form for each AESI condition. The reporting form, case ascertainment form and the line listing form are simplified or modified versions of WHO AEFI forms and tools that have been adapted for nOPV2 AESI surveillance, including the AEFI reporting form and the AEFI investigation form.² The AESI condition-specific data abstraction forms are modified versions of AESI data abstraction forms used for other AESI surveillance efforts. These form templates will be potentially further adapted for use in each country conducting nOPV2 AESI surveillance.

The **nOPV2 AESI reporting form** includes information on the patient, reporter, assessor (person who assessed the AESI), AESI, facility and vaccinations administered (see Annex 2). This form should be filled out by the staff who have identified an AESI case, including frontline healthcare workers, AFP or vaccine safety surveillance officers or others. The **nOPV2 AESI line listing form** is to be filled out by an AESI surveillance officer to keep track of potential AESI cases identified through active surveillance (see Annex 3). It also enables staff at the national and subnational levels to keep track of AESI cases and identify potential clusters in space or time, or other patterns. The **nOPV2 AESI case ascertainment form** will include clinical information obtained by surveillance staff from clinical records and patient interview (see Annex 4). The form will enable verification of AESI cases. **Data abstraction forms** have been developed for each AESI and are to be used by surveillance officers or other designated personnel as part of investigating AESI cases and as part of causality assessment (see Annex 5). These forms will aid in chart abstraction of information from patient files and provide information which will enable the classification of potential cases according to diagnostic certainty. Where appropriate, a process will be

² World Health Organization. Reporting form for Adverse Events Following Immunization (AEFI). Revised January 2016 (https://www.who.int/vaccine_safety/initiative/tools/AEFI_reporting_form_EN_Jan2016.pdf). AEFI Investigation Form (https://www.who.int/vaccine_safety/initiative/investigation/AEFI_Investigation_form_2Dec14.pdf).

undertaken to harmonize nOPV2 AESI forms with AFP surveillance forms. Electronic forms and tools will be used, if feasible.

4. SAFETY SURVEILLANCE

Once a country decides to use nOPV2, several steps can be undertaken to ensure readiness to conduct the necessary safety monitoring, as described in the Vaccine Safety Requirements in the Context of nOPV2 Use.³ Passive AEFI surveillance and active AFP surveillance should already be ongoing before nOPV2 use and should continue after nOPV2 campaigns conclude per country-specific methods. Routine passive AEFI surveillance will be particularly important in detecting unexpected adverse events. Active AESI surveillance should be undertaken to identify selected AESI in locations with nOPV2 use. The active AESI surveillance will help detect more complex adverse events that may be anticipated based on what is currently known about poliovirus and OPV. Active surveillance will continue for six (6) weeks following each nOPV2 campaign. Surveillance will focus on children in the eligible age range for nOPV2, i.e., up to five years old. Interim and final assessments of safety data will take place within each country and across countries using nOPV2 under EUL. Please note: the timing and activities described below may be modified based on field conditions, including restrictions due to COVID-19.

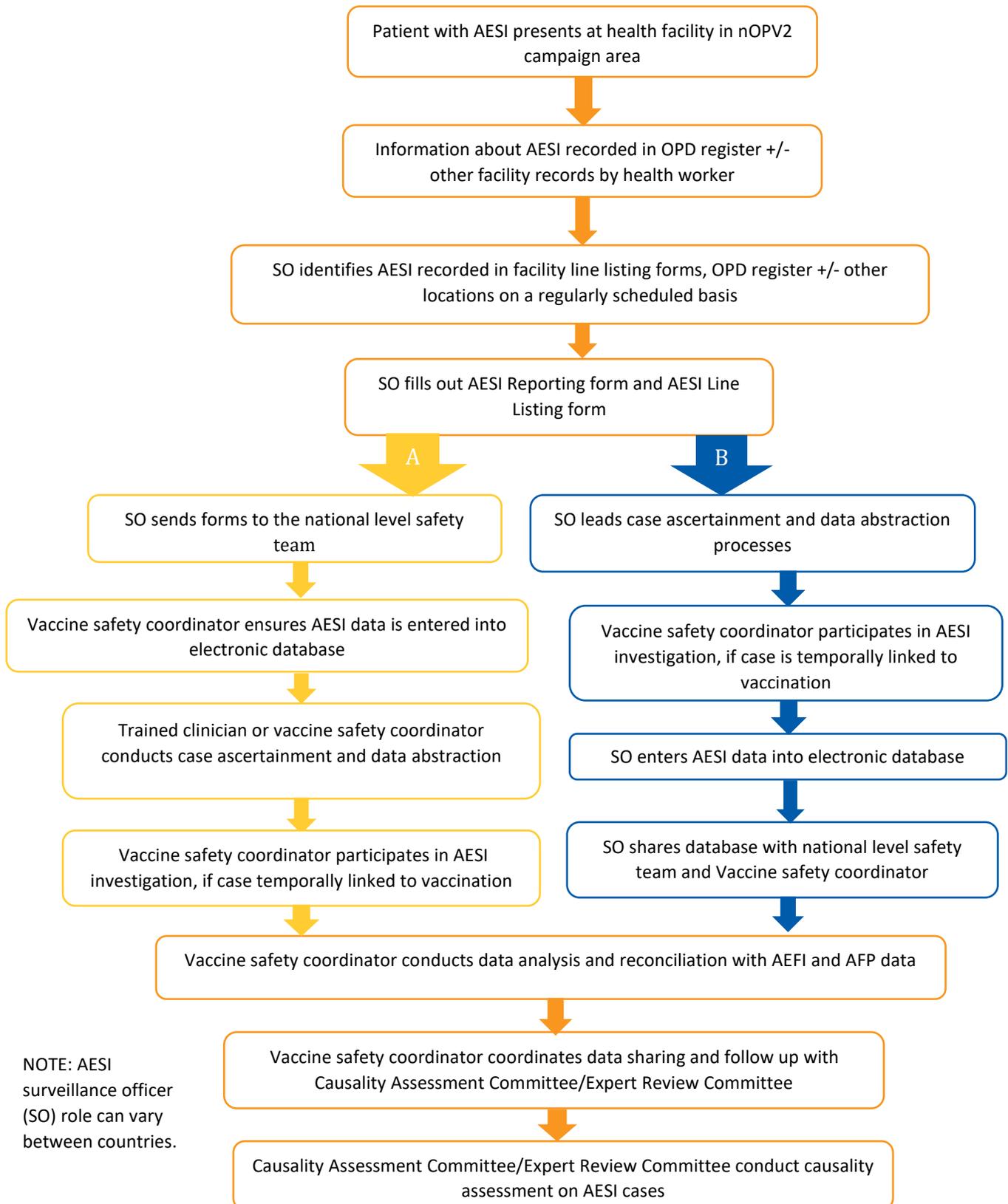
The activities necessary for AESI surveillance include AESI identification, reporting, case ascertainment/verification and chart abstraction, investigation, analysis and assessment. All AESI cases will be investigated and causally assessed if temporally linked to vaccination.

All countries using nOPV2 should consider enlisting a national or subnational vaccine safety coordinator, with the appropriate level dependent on the scope of nOPV2 SIAs, who will collaborate with the Ministry of Health, WHO, CDC and other partners to oversee and coordinate nOPV2 safety surveillance activities. Because active surveillance may generate more reports that will require special attention, having a designated person responsible for the management and coordination of AEFI/AESI information will be critical to the success of the activities.

Prospective nOPV2 AESI surveillance: The prospective AESI surveillance process starts when a patient with an AESI presents at a health facility in the nOPV2 campaign area. Information about the AESI condition, signs and/or symptoms will be recorded in facility records by a health worker. An AESI surveillance officer (AESI SO) or other designated person will visit selected facilities to identify AESI recorded in facility records on a regularly scheduled basis. The AESI SO will then report the AESI to the national safety team using an AESI reporting form (Annex 2) and will also complete an AESI line listing form (Annex 3).

³ Global Polio Eradication Initiative Vaccine Safety Requirements in the Context of nOPV2 Use. October 2021. (<http://polioeradication.org/wp-content/uploads/2021/10/nOPV2-Safety-Guidance.pdf>).

Fig. 3. Example of active AESI surveillance processes



Depending on the country context, one of the following example processes may be most appropriate:

- **Example Process A:** AESI SOs are responsible for case identification and reporting only (Fig. 3, Track A). In this scenario, SOs will complete an AESI reporting form (Annex 2) and an AESI line listing form (Annex 3) only. Case ascertainment/verification (via a case ascertainment form, Annex 4) and chart abstraction (via condition-specific data abstraction forms, Annex 5) may be done by a trained clinician (to be paid a stipend for the activity) or the national vaccine safety coordinator. The vaccine safety coordinator will coordinate or be responsible for data entry (if paper forms are used) and will participate in case investigation, as part of a case investigation team, if the case is temporally linked to vaccination.
- **Example Process B:** AESI SOs are responsible for case identification, reporting, case ascertainment and data abstraction, and data entry (Fig. 3, Track B). In this scenario SOs will complete the AESI reporting form (Annex 2), AESI case ascertainment form (Annex 4), AESI line listing form (Annex 3), and relevant condition-specific data abstraction form(s) (Annex 5). The SOs will enter relevant data into a database to be shared with the relevant stakeholders at national/subnational level. The vaccine safety coordinator will participate in case investigation, as part of a case investigation team, if the case is temporally linked to vaccination.

The final steps include data analysis and the reconciliation of AESI data with AEFI and AFP data by the vaccine safety coordinator, followed by data sharing and follow-up with the Causality Assessment Committee and ERC, who finally conduct a causality assessment.

If a country has a strong AFP surveillance infrastructure, AFP surveillance officers (AFP SOs) may be ideally positioned to fulfill the role of the AESI SO described above. If so, a process must be undertaken to integrate AESI surveillance into AFP surveillance, as well as separate processes where necessary to ensure AESI are identified, reported and investigated, with their causality assessed as described in this manual. A process should also be undertaken to review the list of surveillance sites that AFP SOs visit and add locations where AESI cases are likely to present. While some of the AESI conditions are also captured by AFP surveillance (e.g., VAPP, transverse myelitis, GBS), the AESI conditions will also have to be reported, investigated and causally assessed (for verified cases temporally linked to vaccination) as AESI *in addition* to the processes undertaken regarding AFP surveillance.

Alternately, if a country does not have a strong active AFP surveillance system, then a standalone AESI system with dedicated AESI SOs can be established for countries using nOPV2. The country may determine whether these SOs are managed by the AEFI surveillance programme or another group. Further, specific activities described above may be undertaken by trained clinicians who are provided stipends for conducting specific duties.

Countries will make the final determination as to which specific staff cadres will be used for active AESI surveillance. EPI, NRA, AFP and AEFI surveillance infrastructures and staff will all have roles in implementing the AESI surveillance system. Specific roles and responsibilities will need to be outlined depending on the country context. Because of the potential for AFP, AEFI and AESI surveillance systems to detect the same conditions, efforts should be made to reduce duplication of activities and plan for data reconciliation.

Causality assessment of reported nOPV2 AESI cases: A trained national Vaccine Safety Advisory Committee or Causality Assessment Committee can conduct AESI causality assessments jointly or independently, or a member(s) of the ERC can participate with the Causality Assessment Committee to

conduct causality assessment. Countries should consider designating an oversight body (e.g., a National Immunization Technical Advisory Group [NITAG]) to facilitate a comprehensive interpretation of the data. The Causality Assessment Committee and ERC will report to the oversight body; the oversight body will have access to the AFP, AESI and AEFI surveillance data. It will be important to clearly define roles, responsibilities and decision-making processes for this effort.

5. DATA FLOW

AESI data may reside in three separate databases: (1) a dedicated AESI database; (2) an AFP surveillance database, if the AESI is a suspected AFP; and (3) an AEFI database, for those AESI conditions that are temporally associated with vaccine administration. AESI data may be owned and managed by the country's polio programme, EPI or NRA programme, and data should be shared between these programmes. This will require commitment from all vaccine safety stakeholders to share and reconcile the data so that signals can be detected effectively and efficiently. The Vaccine Safety Advisory Committee or Causality Assessment Committee and polio ERC should have access to both AEFI and AESI data to conduct causality assessment, as should any global oversight body.

Data will flow from the peripheral to the national level following standard practices in each country. If data flows from the district to provincial to national level, the following scheme is proposed: at the district level, designated staff will ensure that all forms filled at the peripheral level are incorporated in district-level versions of the AESI and AFP surveillance databases, as appropriate, on a weekly basis. Similar processes will occur at the provincial and national levels. The AESI portion of this activity will be overseen by vaccine safety coordinator.

While these data are country-owned, a data-sharing agreement should be considered between the Country and the WHO. The agreement should indicate intent/willingness to share data from the Ministry of Health to the WHO/GPEI via the WHO country office and GPEI coordinator. The GPEI will be responsible for sharing the data with Bio Farma, CDC, regulatory/advisory boards (such as the GACVS and the Strategic Advisory Group of Experts on Immunization [SAGE]), and other stakeholders for the purposes of global public health decision making (Annex I).

6. ROLES AND RESPONSIBILITIES

Each country will determine which public health staff will conduct the activities necessary for AESI surveillance, which include AESI identification, notification, reporting, investigation, analysis and assessment. Depending on the level (e.g., national vs. subnational), roles may vary.

Table 1 describes examples of specific activities that can be undertaken to successfully roll out AESI surveillance, with the expectation of adapting to the context of each country.

Table 1: Example of roles and responsibilities of nOPV2 safety monitoring stakeholders, Country X

Activity	Role and responsibility of nOPV2 safety monitoring stakeholder		
	Polio programme	NRA	EPI
Training of stakeholders on AESI	Responsible for AESI training of AFP SOs. Responsible for AESI training of frontline campaign health workers.	Responsible for AESI training of district and regional NRA staff.	Responsible for AESI training of frontline health workers and EPI staff working on AEFI.
Provision of AESI surveillance forms	Responsible for providing AESI surveillance forms to SOs (if AFP SO responsible for AESI surveillance).		Responsible for providing AESI surveillance forms to SOs (if external SO responsible for AESI surveillance report to EPI).
AESI identification and reporting	AFP SOs will identify and report AESI (if country decides AFP SOs will be responsible for case identification and reporting) National-level safety team will receive reports from AFP SO and provide oversight.		Externally hired SO, under EPI management will identify and report AESI (if country decides to hire a new cadre for this activity) National-level safety team will receive reports, and vaccine safety coordinator will provide oversight.
AESI case ascertainment and data abstraction			Trained clinician or vaccine safety coordinator conducts case ascertainment and data abstraction OR SO conducts case ascertainment and data abstraction.
AESI case investigation		NRA staff will support AESI case investigation as needed.	Vaccine safety coordinator will participate in case investigation as part of a case investigation team.
AESI data entry	AFP SO enter AESI data into electronic database (if country determines AFP SO is responsible for data entry).		Vaccine safety coordinator enters AESI data into electronic database OR Externally hired SO under EPI management enters AESI data into electronic database.
AESI database management and analysis			Vaccine safety coordinator conducts data analysis.
Data reconciliation (AEFI/AESI/AFP)	AFP data will be shared with vaccine safety coordinator for reconciliation, if needed.		Vaccine safety coordinator reconciles data in AFP, AEFI and AESI databases and shares data with stakeholders and Causality Assessment Committee.
AESI causality assessment	National Vaccine Safety Advisory Committee/ Causality Assessment Committee and polio ERC will jointly or independently conduct causality assessment.	National Vaccine Safety Advisory Committee/ Causality Assessment Committee and polio ERC will jointly or independently conduct causality assessment.	National Vaccine Safety Advisory Committee/ Causality Assessment Committee and polio ERC will jointly or independently conduct causality assessment.

Table 1 (continued): Example of roles and responsibilities of nOPV2 safety monitoring stakeholders

Activity	Role and responsibility of nOPV2 safety monitoring stakeholder		
	Polio programme	NRA	EPI
Reporting of AESI data to external stakeholders: GPEI, WHO regional office, GACVS, SAGE, P95, Bio Farma, etc.			EPI will share data and causality assessment conclusions with stakeholders.

7. TRAINING

nOPV2 AESI surveillance includes activities related to AESI identification, notification, investigation, reporting, analysis and causality assessment. Staff specifically tasked with these safety activities should receive training on the aspects of nOPV2 AESI surveillance they will contribute to; for example, Causality Assessment Committees should be trained on causality assessment. The target audiences for the different components of AEFI surveillance will vary based on roles and responsibilities.

AEFI systems strengthening training activities should also take place for vaccine safety staff. This should include national and subnational training on AEFI processes including reporting and investigation, and training of the Vaccine Safety Advisory Committee or Causality Assessment Committee on causality assessment.

Frontline healthcare workers deployed in nOPV2 campaigns, including vaccinators, should also be trained on reporting.

8. CONFIDENTIALITY

All paper forms will be stored in locked file cabinets in a secured room. Efforts will be made to only share identifying information with those that need this information. Participants will be identified in databases through unique IDs. Persons with access to identifying information will sign a nondisclosure form.

9. LIMITATIONS

This AESI surveillance system is for the purpose of signal generation, not signal testing. Should a signal be identified and considered of importance after more detailed assessment of the available data, then further epidemiological studies to assess the signal would be required.

10. ANNEXES

Annex 1: Example of an electronic data-sharing agreement

This Electronic Data-Sharing Agreement (here-in-after **referred to as the “Agreement”**) is made this *date (dd/mm/yyyy)* between the Country A (here-in-after referred to as **“PROVIDER”**) and the WHO Country Office and GPEI (here-in-after referred to as **“RECIPIENT”**). PROVIDER and RECIPIENT may each be referred to as a “Party” or collectively referred to as “Parties”.

The parties agree as follows;

1. DEFINITIONS

1.1. **Electronic Data** – any information, communications, calculations, reports collected and stored in digital form. This term will also include any electronic files of every format generated by the software and applications used within this project.

1.2. **Sharing/transfer** – making electronic data available to parties for a stated purpose.

1.3. **“PROVIDER”** – means a person/ country providing the original data.

1.4. **“RECIPIENT”** – means a person/ organization to which the original data is sent to.

2. PURPOSE

All electronic data transferred from PROVIDER to the RECIPIENT is intended for use solely in connection with the purpose for which it is intended, i.e., nOPV2 safety surveillance and maintenance of regulatory commitments.

3. RIGHTS

RECIPIENT acknowledges that the electronic data is provided for RECIPIENT’s convenience and may be used solely for the purposes stated above. No other right, including copyright, is conveyed by transfer of the electronic data. PROVIDER retains all common laws and statutory rights in the electronic data.

4. DATA FORMAT

All electronic data shall be provided in the format in which it is commonly stored and used by PROVIDER. RECIPIENT understands that the transmission and/or conversion of electronic data from the system and the format used by PROVIDER to an alternative system or format may result in the introduction of inconsistencies, anomalies and/or errors.

There is also the possibility of electronic data being altered easily, whether inadvertently or otherwise. PROVIDER reserves the right to retain a copy of data transferred to RECIPIENT in electronic form and/or hard copy. Hence PROVIDER will have an archive of all data transmitted to RECIPIENT for the purposes of comparison and verification.

The RECIPIENT understands that the data to be transmitted would be anonymized, hence individuals cannot be traced using transmitted data.

5. REQUEST FOR DATA

PROVIDER will assign a signatory for the electronic data transfer. This signatory will be communicated to the RECIPIENT. Any request for electronic data transfer made by RECIPIENT should come with the intended purpose or usage.

PROVIDER retains the right as the owners of the data. Hence anytime there is a need for data transfer beyond the RECIPIENT, GPEI partners, or nOPV2 safety regulatory/advisory boards (including GACVS and SAGE), there must be a request from RECIPIENT. The RECIPIENT understands that one request for data by the RECIPIENT would not be used to cover all other requests.

6. RELEASE

RECIPIENT acknowledges that any alteration or modification of the transmitted electronic data may result in adverse consequences which PROVIDER can neither predict nor control. RECIPIENT hereby waives, acquits and forever discharges PROVIDER from every claim, demand and cause of action to recover any kind of damage cost, expense, fees and loss arising out of or resulting from;

- i. The further transfer of electronic data by any means,
- ii. The use, modification or misuse of electronic data by, through or under RECIPIENT (including the further processing of the electronic data),
- iii. The decline of accuracy of the electronic data,
- iv. The incompatibility of the electronic data with RECIPIENT's software or hardware or both.

7. PUBLICATIONS

In any case that the RECIPIENT wishes to publish all or any part of the electronic data transferred, it has to be jointly with co-authors from PROVIDER and there has to be official consent given by PROVIDER. In addition to seeking the official consent, the RECIPIENT shall transmit to the co-authors for review the material intended to be published at least 30 (thirty) days, for a proposed article, and fourteen (14) days, for a proposed presentation or abstract, before a proposed publication is submitted to any editor, publisher, referee or meeting organizer. At the end of the 30-day period for a proposed article or 14-day period for a proposed presentation or abstract, the publication may proceed, pending that the consent is obtained.

8. CONFIDENTIAL INFORMATION

Both parties agree that the electronic data, together with all information, discussions, communications, derivative works based on the electronic data and other matters related to this project and this agreement are confidential. RECIPIENT shall keep in confidence all information stated as confidential and shall not discuss, disclose or divulge such information to any third party without written authorization from PROVIDER. In the event disclosure of such confidential

information is required by law, RECIPIENT shall provide PROVIDER with prior written notice of such event. Such notice shall be sent in sufficient time to enable PROVIDER to seek any protective order or arrangement permitted by law.

9. MISCELLANEOUS

9.1. Mutually Binding

The parties, respectively, bind themselves, their partners, successors, assigns and legal representatives to the other party to this agreement and the other partners, successors, assigns and legal representatives to such other party with respect to all covenants of this agreement. Neither party may assign this agreement without the written consent of the other.

9.2. Severability

If any provision or any part of a provision of this Agreement shall be finally determined to be superseded, invalid, illegal or otherwise unenforceable pursuant to any applicable law or court order, such determination shall not impair or otherwise affect the validity, legality, or enforceability of the remaining provision or parts of the provision of the Agreement, which shall remain in full force and effect as if the unenforceable provision or part were deleted.

8.3. Notices and representatives

Notices are sufficient if in writing and delivered by hand, email or by regular mail to the authorized representative of the other Party; notices sent by regular mail will also be transmitted by email at the time of mailing. Unless otherwise designated in writing, the signatories to this agreement are the Parties' authorized representative for all purposes.

8.4. Titles and headings

The titles and headings used in this agreement and any other related document are for ease of reference only and shall not in any way be construed to limit or alter the meaning of any provision.

8.5. Counterparts

This agreement may be executed simultaneously in two or more counterparts, each of which shall be deemed an original. When offering proof of this agreement, it shall only be necessary to produce or account for the counterpart signed by the party against whom enforcement is sought.

This Agreement is entered into of the day and year first written above.

FOR PROVIDER

FOR RECIPIENT

(Signature)

(Signature)

(Printed Name and Title)

(Printed Name and Title)

(Address)

(Address)

(Email address)

(Email address)

Annex 2: nOPV2 AESI reporting form

AESI reporting ID number:

Today's date (DD/MM/YYYY): _/ _/ _ _ _ _
SECTION A: Reporter information
*Reporter's Name: Institution: Designation & department: Address: Telephone, WhatsApp, e-mail: Date patient notified event to health system (DD/MM/YYYY): _/ _/ _ _ _ _
SECTION B: Assessor information
*Assessor's Name: Institution: Designation & department: Address: Telephone, WhatsApp & e-mail: Date patient notified event to health system (DD/MM/YYYY): _/ _/ _ _ _ _
SECTION C: Patient information**
*Patient name:
*Patient's full address:
Telephone/WhatsApp:
Sex: <input type="checkbox"/> M <input type="checkbox"/> F
*Date of birth (DD/MM/YYYY): _/ _/ _ _ _ _

OR Age at onset: Years Months Days

OR Age group: < 1 Year 1 to < 2 years 2 + years

SECTION D: Facility information

Facility ID number:

Facility name:

Facility phone number:

Facility-in-charge name:

Facility-in-charge contact information:

Facility address:

SECTION E: AESI information

***Adverse event(s) of special interest:**

- | | |
|---|--|
| <input type="checkbox"/> Anaphylaxis | <input type="checkbox"/> Guillain-Barré syndrome (GBS) /
Miller Fisher Syndrome |
| <input type="checkbox"/> Aseptic meningitis | |
| <input type="checkbox"/> Acute disseminated encephalomyelitis | <input type="checkbox"/> Myelitis/Transverse myelitis |
| <input type="checkbox"/> Acute flaccid paralysis (VDPV) | <input type="checkbox"/> Unexplained death |
| <input type="checkbox"/> Acute flaccid paralysis (VAPP) | <input type="checkbox"/> Other (Please specify) |
| <input type="checkbox"/> Encephalitis | |

Date & Time AESI started (DD/MM/YYYY):

Hr Min

___ / ___ / _____

Describe AESI (signs and symptoms):

Source of AESI information:

***Serious: Yes / No ;** If Yes Death Life threatening Disability Hospitalization

***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 other relevant information. (e.g. other cases). *Use additional sheet if needed.*

Section F: Vaccine receipt information

Vaccinated: Yes No Unknown

*Name of vaccine	*Date of vaccination	Dose (1 st , 2 nd , etc.)	*Route of administration (ex: IM, SC, ID)
nOPV2			

National level to complete:

Date report received at national level (DD/MM/YYYY):

___ / ___ / _____

Comments:

** Compulsory field*

*** Parent/guardian's information can be provided for minors*

Annex 3: nOPV2 AESI line listing form

Date:

District:

Health facility:

Name /ID	Age or birthdate <input type="checkbox"/> UK	Sex <input type="checkbox"/> F <input type="checkbox"/> M	Address	Date onset	Initial diagnosis ^a /date Final diagnosis ^a /date	Place Hospitalized	Outcome ^b	If Vaccinated with nOPV2 Date Place	Batch Number V D	Reported as AEFI <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessed <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessment Result ^c
Name /ID	Age or birthdate <input type="checkbox"/> UK	Sex <input type="checkbox"/> F <input type="checkbox"/> M	Address	Date onset	Initial diagnosis ^a /date Final diagnosis ^a /date	Place Hospitalized	Outcome ^b	If Vaccinated with nOPV2 Date Place	Batch Number V D	Reported as AEFI <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessed <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessment Result ^c
Name /ID	Age or birthdate <input type="checkbox"/> UK	Sex <input type="checkbox"/> F <input type="checkbox"/> M	Address	Date onset	Initial diagnosis ^a /date Final diagnosis ^a /date	Place Hospitalized	Outcome ^b	If Vaccinated with nOPV2 Date Place	Batch Number V D	Reported as AEFI <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessed <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> UK	Causality Assessment Result ^c

^a a1 acute disseminated encephalomyelitis, a2 acute flaccid paralysis [for final diagnosis only: a2a acute flaccid paralysis (VAPP) a2b acute flaccid paralysis (VDPV)], a3 anaphylactic reactions, a4 aseptic meningitis/encephalitis, a5 Guillain-Barré Syndrome/Miller Fisher Syndrome, a6 myelitis/transverse myelitis, a7 unexplained death

^b b1 Recovering b2 Recovered b3 Recovered with sequelae b4 Not recovered b5 Died b6 Unknown

^c c1 A1. Vaccine product-related reaction, c2 A2.Vaccine quality defect related reaction, c3 A3. Immunization error-related reaction, c4 A4. Immunization stress related response, c5 B. Indeterminate, c6 C. Inconsistent causal association to immunization, c7 Unclassifiable

Name of the Officer: Date and signature.....

Annex 4: nOPV2 AESI case ascertainment form

Case ID _____	Today's date (DD/MM/YYYY): __/__/____
Patient name:	
Sex: <input type="checkbox"/> M <input type="checkbox"/> F	
Date of birth (DD/MM/YYYY): __/__/____ <input type="checkbox"/> UK OR Age at onset : <input type="checkbox"/> <input type="checkbox"/> Years <input type="checkbox"/> <input type="checkbox"/> Months <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> Days OR Age Group: <input type="checkbox"/> < 1 Year <input type="checkbox"/> 1 to 5 Years <input type="checkbox"/> > 5 Years	
Suspected AESI:	
Date & Time AESI started (DD/MM/YYYY): _____ / _____ / _____ <input type="checkbox"/> <input type="checkbox"/> Hr <input type="checkbox"/> <input type="checkbox"/> Min	
Name and contact information of person completing these clinical details:	
Designation:	Date/time:
<p>**Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) 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).</p>	
Signs and symptoms:	
Lab findings:	
Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information. <i>Use additional sheet if needed:</i>	
Treatment and outcome:	
Provisional and final diagnosis:	
Other findings and comments:	

Annex 5: Examples of data abstraction forms

Incorporating Brighton Collaboration case definitions

Anaphylaxis data abstraction form

Date of anaphylaxis:

Time of vaccination:

Time of onset of symptoms:

Interval from vaccination to symptom onset----

< 30 minutes

30 to 60 minutes

90 to 120 minutes

>2 hours, specify

Date of end of episode (if known):

Please fill/check the following information obtained from chart review

	Yes	No	N/A or insufficient information
Exposure of anaphylaxis suspected by Physician			
Food, specify if known			
Medication (non-vaccine)			
Insect sting			
Vaccines			
If Yes, specify the vaccine(s)			
Other, specify			
Unknown, Provider mentions that cause is unknown			

Signs and symptoms			
Is the syndrome characterized with sudden onset?			
If Yes was there a rapid progression of signs and symptoms			
Involves more than 2 organ systems?			
Major criteria			
Dermatological or mucosal			
Generalized urticarial (hives) or generalized erythema			
Angioedema, localized or generalized			
Generalized pruritus			
Cardiovascular			
Measured hypotension			
Clinical diagnosis of uncompensated shock, indicted by a combination of at least 3 of the following <ul style="list-style-type: none"> • Tachycardia • Capillary refill time > 3 seconds • Reduced central pulse volume • Decreased level of consciousness or loss of consciousness 			
Respiratory			
Bilateral wheeze (bronchospasm)			
Stridor			
Upper airway swelling (lip, tongue, throat, uvula, or larynx)			
Respiratory distress-2 or more of the following: <ul style="list-style-type: none"> • Tachypnea • Increased use of accessory respiratory muscles (sternocleidomastoid, intercostals, etc.) • Recession • Cyanosis • Grunting 			

Minor criteria			
Dermatological or mucosal			
Generalized pruritus without skin rash			
Generalized prickle sensation			
Localized injection site urticarial			
Red and itchy eyes			
Cardiovascular			
Reduced peripheral circulation as indicted by at least 2 of the following <ul style="list-style-type: none"> • Tachycardia • Capillary refill time of > 3 seconds without hypotension • Decreased level of consciousness 			
Respiratory			
Persistent dry cough			
Hoarse voice			
Difficulty breathing without wheeze or stridor			
Sensation of throat closure			
Sneezing, rhinorrhea			
Gastrointestinal			
Diarrhea			
Abdominal pain			
Nausea			
Laboratory			
Mast cell tryptase elevation > upper normal limit			

Outcome			
Full recovery			
Recovery with sequelae, specify			
Death			
Other outcome, specify			

Brighton levels of diagnostic certainty

For all levels, anaphylaxis is a clinical syndrome characterized by

- Sudden onset AND
- Rapid progression of signs and symptoms AND
- Involving multiple organs 2 or more organ systems

Level 1 of diagnostic certainty	Level 2 of diagnostic certainty	Level 3 of diagnostic certainty
≥1 major dermatological AND	≥ 1 major cardiovascular AND	≥ 1 minor cardiovascular OR respiratory criterion AND
≥ 1 major cardiovascular AND/OR	≥ 1 major respiratory criterion OR	≥ 1 I minor criterion from each of ≥ 2 different systems
≥ 1 major respiratory	≥ 1 major cardiovascular OR respiratory criterion AND	
	≥ 1 I minor criterion involving ≥ 1 different system (other than cardiovascular or respiratory) OR	
	≥ 1 major dermatologic AND ≥ 1 minor cardiovascular AND/OR minor respiratory criterion	

After review of findings, please check level of diagnostic certainty below

Level 1 []

Level 2 []

Level 3 []

Category 4: Insufficient evidence []

Identifying diagnostic level using an algorithm

Step 1: Select the categories represented by the clinical symptoms and signs of the suspect case

Major	Minor
Dermatological and mucosal (DERM) []	Dermatological & mucosal (derm) []
Cardiovascular (CVS) []	Cardiovascular (cvs) []
Respiratory (RESP) []	Gastrointestinal (gi) []
	Laboratory (lab)

Step 2: Select the column from the table representing the highest-ranking diagnostic category (major>minor, dermatology > laboratory)

Step 3: Select row from the table indicating the second highest-ranking diagnostic category

Step 4: the intersection gives the level of diagnostic certainty on the Brighton definition. Blank intersections do not fulfill any level.

		Symptom 1				
		DERM	CVS	RESP	cvs	resp
Symptom 2	CVS	1	-	2	-	2
	RESP	1	2	-	2	-
	Derm	-	2	2	3*	3*
	Cvs	2	-	2	-	3*
	Rep	2	2	-	3*	-
	Gi	-	2	2	3*	3*
	Lab	-	2	2	3*	3*

Upper case/Capital letters: 1 or more MAJOR criteria in that system

Lower case: 1 or more minor criteria. Columns or rows in Upper case/Capital letters indicate that 1 or more MAJOR criteria are present in that category.

Columns or rows in Lower case indicate that 1 or more minor criteria are present.

Level 3 diagnostic certainty requires 2 or more rows to be present in either the “cvs” or “resp” minor criteria

1-Level 1 diagnostic certainty

2- Level 2 diagnostic certainty

3-Level 3 diagnostic certainty requires 2 or more minor criteria to be present in this column

Aseptic meningitis data abstraction form

Date of vaccination:

Date of symptom onset: __/__/__

Date of diagnosis: __/__/__

Date of end of episode (if known): __/__/__

Please fill/check the following information obtained from chart review:

	Yes	No	N/A or insufficient information
Findings by physician			
Clinical evidence of acute meningitis			
Fever (38°C or above) If yes, indicate highest fever recorded			
Headache			
Vomiting			
Bulging fontanelle			
Nuchal rigidity			
Other signs of meningeal irritation Please specify			
Investigations			
CSF obtained If yes, specify date obtained Sample 1 Date: __/__/__ Sample 2 Date: __/__/__			
CSF pleocytosis If yes, specify findings			
Gram stain conducted If yes (positive), specify organism			
Bacterial culture conducted If yes, specify organism			

Antibiotic treatment If yes, specify medication and dates provided Antibiotic 1 Dates given __/__/____ Antibiotic 2 Dates given __/__/____			
Presence of alternative diagnosis If yes, specify <i>If case meets criteria for aseptic meningitis and encephalitis case definition, it should be reported as encephalitis</i>			
Outcome			
Full recovery to baseline status			
Recovery with residual symptoms If yes, specify			
Death			
Other outcome, specify			

Brighton Collaboration levels of diagnostic certainty

Aseptic meningitis

Level 1 of diagnostic certainty	Level 2 of diagnostic certainty	Level 3 of diagnostic certainty
Clinical evidence of acute meningitis such as fever, headache, vomiting, bulging fontanelle, nuchal rigidity or other signs of meningeal irritation AND	Clinical evidence of acute meningitis such as fever, headache, vomiting, bulging fontanelle, nuchal rigidity or other signs of meningeal irritation AND	Not Applicable
Pleocytosis in CSF as determined as: <ul style="list-style-type: none"> > 5WBC/mm³ in children 2 months of age or older > 15 WBC/mm³ in infants younger than 2 months of age AND 	Pleocytosis in CSF as determined as: <ul style="list-style-type: none"> > 5WBC/mm³ in children 2 months of age or older > 15 WBC/mm³ in infants younger than 2 months of age AND 	Presence of alternative diagnosis <i>If case meets criteria for aseptic meningitis and encephalitis case definition, it should be reported as encephalitis</i>
Absence of any microorganism on Gram stain of CSF AND	Absence of any microorganism on Gram stain of CSF AND	

Negative routine bacterial culture of CSF in the absence of antibiotic treatment before obtaining the first CSF sample	No bacterial culture of CSF OR negative culture in the presence of antibiotic treatment before obtaining the first CSF sample	
--	---	--

After review of findings, please check level of diagnostic certainty below:

Level 1

Level 2

Level 3

Category 4: Insufficient evidence

Category 5: Not a case of aseptic meningitis

Unexplained deaths (including SIDS) data abstraction form

Date of vaccination:

Date of symptom onset: __/__/____

Date of death: __/__/____

Cause of death (if known):

Source of information for cause of death:

Health Facility Autopsy

Verbal autopsy

Other, specify _____

The term “sudden Infant death syndrome” or SIDS should be used to describe deaths in the first year of life, which remain unexplained after excluding other causes of death.

Please fill/check the following information obtained from chart review (use additional paper, if needed):

	Yes	No	N/A or insufficient information
Information regarding death			
A. Hospital autopsy conducted			
If yes, immediate cause of death			
Underlying cause of death			
Source of information known If yes, specify • Clinical history (highlight relevant details) • History of final events (highlight relevant details)			
Clinical history available If yes, highlight relevant details:			
History of final events available If yes, highlight relevant details			
Review of autopsy report			
Macroscopic examination conducted If yes, highlight relevant details:			

Microscopic examination conducted If yes, highlight relevant details:			
Microbiologic samples taken If yes, highlight relevant details:			
Toxicological samples taken If yes, highlight relevant details:			
Screening for metabolic disease If yes, highlight relevant details:			
Radiological studies conducted If yes, highlight relevant details:			
B. Verbal Autopsy (VA)			
Date VA conducted			
Who conducted VA Doctor Other, specify			
Described cause of death			
C. Review of circumstances			
Examination of death scene If yes, please specify.			
Who conducted the examination (e.g., medical examiner)			

Brighton Collaboration levels of diagnostic certainty

Sudden unexplained death

Level 1 of diagnostic certainty	Level 2 of diagnostic certainty	Level 3 of diagnostic certainty
Unexplained deaths after a complete post-mortem investigation	Unexplained deaths after clinical and final event history and autopsy	Unexplained deaths after clinical and final event history but without autopsy
Sudden death of any child under 2 years of age which remains unexplained after excluding other causes of death by:	Sudden death of any child under 2 years of age which remains unexplained after excluding other causes of death by:	Sudden death of any child under 2 years of age which remains unexplained after excluding other causes of death by:
Review of clinical history AND	Review of clinical history AND	Review of clinical history AND
History of final events AND	History of final events AND	History of final events
Review of complete autopsy report with a standardized protocol that includes: Macroscopic examination AND	Review of incomplete autopsy result	
Microscopic examination AND		
Microbiologic examination AND		
Toxicological samples AND		
Screen for metabolic disease AND		
Radiological studies AND		
Review of circumstances of death including examination of death scene performed by suitably qualified person, such as homicide investigator or medical examiner		

After review of findings, please check level of diagnostic certainty:

Level 1

Level 2

Level 3

Category 4: Insufficient evidence

Category 5: Not a case of sudden unexplained death

Annex 6: Simplified case definitions

AESI	Potential definition based on up-to-date, modified Brighton Collaboration definition, medical dictionaries, or other sources
<p>Anaphylaxis</p>	<p>Anaphylaxis is a severe allergic reaction that occurs within minutes to hours of vaccination. It is characterized by sudden onset of signs and symptoms with shock or collapse (altered consciousness, low blood pressure, weakness or absence of peripheral pulse, cold extremities). It may be accompanied with difficulty breathing, wheezing symptoms (noisy breathing), swelling (especially of the face, mouth or throat), or skin rash (urticaria) that may be itchy. Patient may also have abdominal pain, vomiting or diarrhea, and confusion.</p> <p>Reporting criteria: Anaphylaxis diagnosed by a healthcare provider</p> <p>Sources:</p> <ul style="list-style-type: none"> • Gold MS, Gidudu J, Erlewyn-Lajeunesse M, Law B; Brighton Collaboration Working Group on Anaphylaxis. Can the Brighton Collaboration case definitions be used to improve the quality of Adverse Event Following Immunization (AEFI) reporting? Anaphylaxis as a case study. Vaccine. 2010 Jun 17;28(28):4487-98. • Rüggeberg JU, Gold MS, Bayas JM et al., Brighton Collaboration Anaphylaxis Working Group. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2007 Aug 1;25(31):5675-84.
<p>Acute flaccid paralysis</p>	<p>AFP is a syndrome characterized by rapid onset of muscle weakness and limpness (flaccidity). This weakness can be found in one or more of an individual's extremities or, more rarely, in the muscles of respiration and swallowing, progressing to maximum severity within 1-10 days. This includes Guillain-Barré Syndrome and transverse myelitis.</p> <p>Reporting criteria: Any paralytic illness described by a healthcare provider</p> <p>Source: World Health Organization. "WHO-recommended surveillance standard of poliomyelitis." http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/epidemiology_standards/en/. Last accessed May 21, 2018.</p>

<p>Aseptic meningitis</p>	<p>Aseptic meningitis is the inflammation of the meninges, membranes covering the brain and spinal cord, in patients whose cerebral spinal fluid (CSF) test results are negative for routine bacterial cultures. Common symptoms include fever, vomiting, headaches, firm neck pain, sensitivity to light, and lethargy. Aseptic meningitis is generally a mild form of meningitis.</p> <p>Reporting criteria: Aseptic meningitis as described by a healthcare provider</p> <p><i>Sources:</i></p> <ul style="list-style-type: none"> • BC case definition • Irani DN (August 2008). "Aseptic meningitis and viral myelitis". <i>Neurologic Clinics</i>. 26 (3): 635–55, vii–viii. doi:10.1016/j.ncl.2008.03.003. PMC 2728900. PMID 18657719. • Norris CM, Danis PG, Gardner TD (May 1999). "Aseptic meningitis in the newborn and young infant". <i>American Family Physician</i>. 59 (10): 2761–70. PMID 10348069.
<p>Encephalitis</p>	<p>Encephalitis, or inflammation of the brain, is an acute onset of severe illness characterized by fever and altered mental status (encephalopathy). Focal neurological findings such as focal weakness, cranial nerve palsies, sensory deficits or seizures can also be present. It occurs in approximately 2-30 days.</p> <p>Reporting criteria: Encephalitis as described by a healthcare provider</p> <p><i>Source:</i> Brighton case definition</p>
<p>Acute disseminated encephalomyelitis (ADEM)</p>	<p>ADEM is a rapidly progressive neurological condition caused by a post-infectious inflammatory reaction in the brain and spinal cord. It is characterized by altered mental status and a decreased or complete loss of one or more cranial nerves, focal weakness and lack of muscle control or coordination of voluntary movements (ataxia). It occurs in approximately 2-30 days.</p> <p>Reporting criteria: ADEM as described by a healthcare provider</p> <p><i>Source:</i> Brighton case definition</p>

Guillain-Barré Syndrome (GBS)	<p>GBS is a neurological condition in which a person's immune system attacks the peripheral nerves. It is characterized by ascending, flaccid (limp) weakness in legs to arms mostly in both sides of the body, may cause numbness (sensory loss) and eventually paralysis. It occurs in approximately 1-4 weeks.</p> <p>Reporting criteria: GBS as described by a healthcare provider</p> <p><i>Source:</i> Brighton case definition</p>
Myelitis / transverse myelitis	<p>Myelitis / transverse myelitis (TM) is a rare disorder caused by inflammation of the spinal cord. <i>Transverse</i> implies that the inflammation extends horizontally across the spinal cord. TM is characterized by: weakness in arms/legs; sensory symptoms such as numbness or tingling of the limbs, pain and discomfort as well as bowel or bladder dysfunction. The signs and symptoms depend on the area of spine involved and distribution of those symptoms may be symmetric or asymmetric affecting either legs, arms or both. It occurs within hours to weeks.</p> <p>Reporting criteria: Myelitis/TM as described by a healthcare provider</p> <p><i>Sources:</i></p> <ul style="list-style-type: none"> • Brighton case definition • West TW (October 2013). "Transverse myelitis--a review of the presentation, diagnosis, and initial management". <i>Discovery Medicine</i>. 16 (88): 167–77. PMID 24099672 • https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/transverse_myelitis/about-tm/what-is-transverse-myelitis.html
Unexplained Death	<p>Death which remains unexplained after excluding other causes of death</p> <p>Unexplained deaths, including “sudden Infant death syndrome” or SIDS in the first year of life, which remain unexplained after excluding other causes of death.</p> <p><i>Source:</i></p> <ul style="list-style-type: none"> • Brighton case definition • Verbal autopsy: Additional resource for investigating deaths occurring in community-verbal autopsy tools at https://www.who.int/healthinfo/statistics/WHO_VA_2012_RC1_Instrument.pdf?ua=1