POLIO GLOBAL ERADICATION INITIATIVE

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

Contents

ACRONYMNS

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
EUL	Emergency Use Listing
GACVS	Global Advisory Committee on Vaccine Safety
GBS	Guillain-Barré syndrome
GPEI	Global Polio Eradication Initiative
mOPV	Monovalent Oral Poliovirus Vaccine
NITAG	National Immunization Technical Advisory Group
nOPV2	Novel Oral Poliovirus Vaccine
NRA	National Regulatory Authority
OPD	outpatient department
OPV	oral poliovirus vaccine
SAGE	Strategic Advisory Group of Experts
SO	Surveillance officer
VAPP	Vaccine Associated Paralytic Polio
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 the weakened strain of the poliovirus contained in the oral polio vaccine (OPV) genetically reverts into a form that can cause paralysis. In rare circumstances, 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.

nOPV2 is being made available for outbreak response through WHO's Emergency Use Listing (EUL) procedure, a 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.

To date, the safety of nOPV2 has been evaluated through phase 1 and phase 2 clinical trials. It 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 (mOPV2). There have also been no serious adverse events that are considered to be causally related to vaccination with nOPV2 have been identified. Still, countries will benefit from enhanced nOPV2 safety monitoring processes that will facilitate rapid identification and response to safety signals should they arise. This monitoring will be particularly important during the approximately 3-month initial global use period, as well as the approximately 24 months following the initial use period. Here, we describe 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 and AEFI surveillance background

Global surveillance for polio includes monitoring for Acute Flaccid Paralysis (AFP) cases. AFP cases are reported to local government area-level surveillance officers by health facility staff or a network of trained community members. Surveillance officers also perform active case finding 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.

In addition to AFP surveillance, countries perform routine passive surveillance for all adverse events following immunization (AEFI). AEFI are any untoward medical occurrence which follow immunization and which do not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be an unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. Although reporting structures may vary by country, these systems typically involve both National Regulatory Authorities (NRA) and National Immunization Programs and follow a process of case identification, reporting, and investigation separate from the AFP surveillance system. In addition, the national Vaccine Safety Advisory Committee/AEFI Causality Committee review data on serious AEFI and

signal clusters to conduct a causality assessment based on established WHO processes. Causality assessment is a systematic evaluation to determine the likelihood that an event might have been caused by a vaccine or vaccination.

During new vaccine introductions, post-licensure safety monitoring is critical to detect rare or unexpected adverse events since the vaccine is given to 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. Active surveillance for a focused list of adverse events of special interest (AESI) during the initial phase of use is an important complement to 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 program.

c. For whom is the guide intended?

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 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 Program on Immunization (EPI), the NRA, the WHO Country Office (WHO CO), the Vaccine Safety Advisory Committee/AEFI Causality Committee, the Polio Expert Review Committee, GPEI and Bio Farma, the license holder. Data will be generated primarily for use by countries but will also benefit 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 at a regional and global level.

d. Objectives of the guide

The objective of this guide is to describe the process for conducting standardized high-quality active AESI surveillance during nOPV2 initial use in cVDPV outbreak response.

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 vaccine.

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.

There have been no significant safety signals associated with nOPV2 thus far, though data is limited. Based on summary safety data from WHO, a number of conditions are likely to be of interest for nOPV2 AESI surveillance.

A working list of AESI conditions has been developed through consultation with WHO, the United States Centers for Disease Control and Prevention (CDC), and GPEI partners. The AESI conditions proposed for active surveillance include:

- anaphylactic reactions
- aseptic meningitis/encephalitis
- acute disseminated encephalomyelitis (ADEM)
- Guillain-Barré syndrome (GBS)/ Fishers Syndrome
- myelitis/transverse myelitis
- acute flaccid paralysis (VAPP); AFP (cVDPV)
- unexplained deaths

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 manual: (1) simplified case definitions (Annex 6); and (2) comprehensive Brighton Collaboration Case definitions (Annex 5).

Simplified case definitions will be used at the peripheral level by frontline healthcare workers and designated AESI surveillance staff to identify and report AESI. These definitions have a low level of specificity, needing to be usable by health care workers to identify and report AESI. Simplified case definitions can be used in conjunction with the AESI Reporting Form and the AESI line listing form (described in the next section of this document). 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.

Brighton Collaboration case definitions will be used in the context of case ascertainment/verification and data abstraction forms that will be a part of case investigation (Annex 5) and to assist with causality assessment. Brighton Collaboration case definitions exist for: anaphylaxis, aseptic meningitis, Guillain–Barré syndrome/Fisher's Syndrome, encephalitis, myelitis, ADEM, and death.

3. FORMS AND TOOL DEVELOPMENT

A total of 4 forms have been developed to assist countries in the collection of nOPV2 AESI data: a reporting form (Annex 2), a line listing form (Annex 3), a case ascertainment form (Annex 4), and a data abstraction forms for each AESI condition (Annex 5). The Reporting form, Case Ascertainment form, and the Line Listing form are simplified and/or modified versions of WHO AEFI forms and tools[1] that have been adapted for the purposes of nOPV2 AESI surveillance, including the Reporting form for Adverse Events Following Immunization (AEFI) and the AEFI Line Listing Form. The AESI condition-specific data abstraction forms are modified versions of AESI data abstraction forms used for other AESI surveillance efforts. These draft forms will potentially be further adapted for use in each country conducting nOPV2 AESI surveillance.

The nOPV2 AESI Reporting form includes information on the patient, reporter, assessor (person that assessed the AESI), AESI, facility, and vaccinations administered. This form should be filled out by the staff that have identified an AESI case, including frontline health care 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. It also enables staff at the national and subnational level 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. 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. 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 undertaken to harmonize nOPV2 AESI forms with AFP surveillance forms. All forms and tools will be piloted before use and 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 assure readiness to conduct AESI surveillance, as described in the nOPV2 Vaccine Deployment Readiness Checklist. Passive AEFI surveillance, environmental surveillance, and active AFP surveillance should already be ongoing before nOPV2 use and continue after nOPV2 campaigns conclude per country-specific methods. Environmental surveillance can help detect wild type virus or VDPV. Routine passive AEFI surveillance will be particularly important in detecting unexpected adverse events. Active AESI surveillance should be undertaken to identify selected AESI in the areas with nOPV2 administration. The active AESI surveillance will help detect more complex adverse events that may be anticipated based on what is currently known about polio virus and OPV. The active surveillance will continue for 6 weeks following each nOPV2 campaign. It is recommended that AESI conditions occurring six months prior to the nOPV2 campaign are retrospectively identified to capture baseline rates. 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. A robust vaccine related event (VRE) response, described in the nOPV2 VRE Response plan, will ensure adverse event and

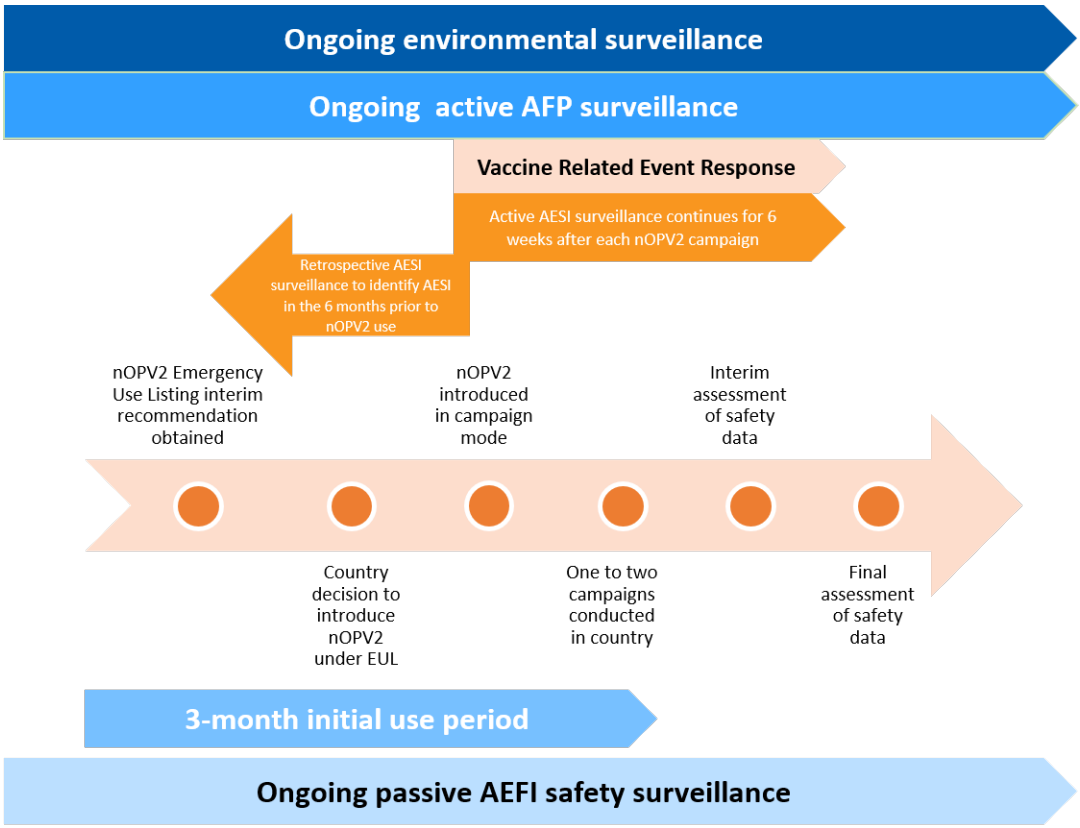
[1] WHO Reporting form for Adverse Events Following Immunization (AEFI) and the AEFI Line Listing Form link: https://www.who.int/vaccine_safety/initiative/tools/AEFI_reporting_form_EN_Jan2016.pdf?ua=1

communication responses are aligned and coordinated (Figure 1). 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 causality assessed, if temporally linked to vaccination.

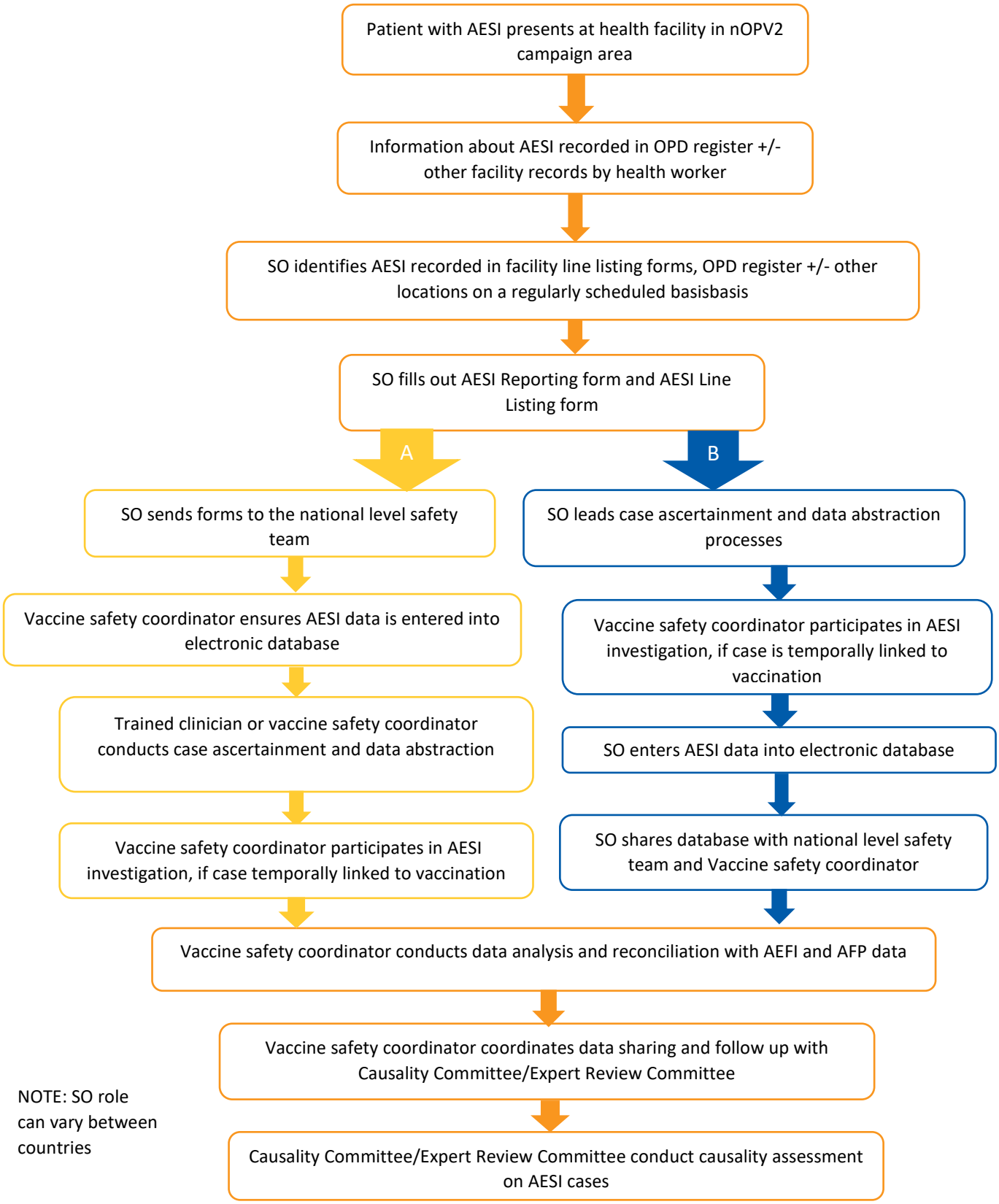
All countries using nOPV2 during in the initial use phase should consider enlisting a national or subnational- level Vaccine safety coordinator (level will depend on scope of SIAs), who will collaborate with the Ministry of Health, WHO, CDC and other partners to oversee and coordinate nOPV2 safety surveillance 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

Figure 1: Timeline for nOPV2 AESI surveillance



Prospective nOPV2 AESI surveillance: Figure 2 below describes an example of a proposed prospective AESI surveillance flow. The process starts with a patient with an AESI presenting 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 level safety team using an AESI Reporting form (Annex 2) and will also complete an AESI Line Listing form (Annex 3).

Figure 2: Example of active AESI surveillance processes



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

AESI SOs are responsible for case identification and reporting only (Figure 2, 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.

AESI SOs are responsible for case identification, reporting, case ascertainment and data abstraction, and data entry (Figure 2, 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 and polio expert review committee. Finally, the Causality Committee or Polio Expert Review Committee conducts a causality assessment.

Depending on the strength of the country's AFP surveillance infrastructure, AFP surveillance officers 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 to ensure AESI get identified, reported, investigated, and causally assessed as described in this manual. A process should also be undertaken to review the list of surveillance sites that AFP surveillance officers visit and add locations where AESI cases are likely to present. While some of the AESI conditions are also captured by AFP surveillance (ex: VAPP, transverse myelitis, GBS), the AESI conditions will also have to be reported, and 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 during the initial use period. The country may determine whether these SOs are managed by the AEFI surveillance program 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. The surveillance flow figure above (Figure 2) serves as an example.

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.

Retrospective nOPV2 AESI surveillance: For the recommended *retrospective* identification of AESI cases, the AFP or designated AESI surveillance officer will be responsible for reviewing records from active surveillance sites for a recommended period of 6 months prior to vaccine introduction. All data will be entered into a separate database to establish a baseline to which prospective AESI data may be compared and shared with the appropriate vaccine safety stakeholders in country and globally.

Causality Assessment of reported nOPV2 AESI cases: A trained national Vaccine Safety Advisory Committee/AEFI Causality Committee and polio Expert Review Committee can conduct AESI causality assessments jointly or independently, or a member(s) of the ERC can participate with the Causality Committee to conduct causality assessment. Countries should consider designating an oversight body (e.g. a National Immunization Technical Advisory Group (NITAG)), for this group to facilitate a comprehensive interpretation of the data. The Causality Committee and Expert Review Committee 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) dedicated AESI database; (2) AFP surveillance database, if the AESI is a suspected AFP; and (3) AEFI database, for those AESI conditions that are temporally associated with vaccine administration. Environmental surveillance data may be managed by a separate surveillance system. AESI data may be owned and managed by the country's polio program, EPI program, or NRA program, and data should be shared between these programs. 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/AEFI Causality Committee and polio Expert Review Committee 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 with external partners such as WHO, Bio Farma, CDC, 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. These activities include AESI identification, notification, reporting, investigation, analysis, and assessment. Depending on the level (ex: 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 program	**NRA**	**EPI**
Training of stakeholders on AESI	Responsible for AESI training of AFP surveillance officers. 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 surveillance officers will identify and report AESI (if country decides APF surveillance officers 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
AESI Causality assessment	National Vaccine Safety Advisory Committee/AEFI Causality Committee and polio Expert Review Committee will jointly or independently	National Vaccine Safety Advisory Committee/AEFI Causality Committee and polio Expert Review Committee will jointly or	National Vaccine Safety Advisory Committee/AEFI Causality Committee and polio Expert Review Committee will jointly or

	conduct causality assessment	independently conduct causality assessment	independently conduct causality assessment
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/AEFI Causality Committee on causality assessment.

Front-line health care workers working 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 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 ELECTRONIC DATA SHARING AGREEMENT

ELECTRONIC DATA SHARING AGREEMENT

This Electronic Data Sharing Agreement dated, XXX is between the Country A, its officers, its directors, its employees and related entities hereafter collectively referred to as Country A and Organizations A, B, and C, hereafter referred to as Receiver. Collectively, COUNTRY A and Receiver are 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.

2. PURPOSE

All electronic data transferred from COUNTRY A to the Receiver is intended for use solely in connection with the purpose for which it is intended, i.e. nOPV2 safety surveillance.

3. RIGHTS

Receiver acknowledges that the electronic data is provided for receiver'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. COUNTRY A 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 COUNTRY A. Receiver understands that the transmission and/or conversion of electronica data from the system and the format used by COUNTRY A 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, COUNTRY A reserves the right to retain a copy of data transferred to receiver in electronic form and/or hard copy. Hence COUNTRY A will have an archive of all data transmitted to receiver for the purposes of comparison and verification.

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

5. REQUEST FOR DATA

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

COUNTRY A retains the right as the owners of the data, hence anytime there is a need for data transfer, there must be a request from receiver. The receiver understands that one request for data by the receiver would not be used to cover all other requests.

6. RELEASE

Receiver acknowledges that any alteration or modification of the transmitted electronic data may result in adverse consequences which COUNTRY A can neither predict nor control. Receiver hereby waives, acquits and forever discharges COUNTRY A 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 receiver (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 receiver's software or hardware or both

7. PUBLICATIONS

In any case that the receiver wishes to publish all or any part of the electronic data transferred, it has to be jointly with co-authors from COUNTRY A and there has to be official consent given by COUNTRY A. In addition to seeking the official consent, the receiver 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 days' period for a proposed article or 14 days' 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. Receiver 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 COUNTRY A. In the event disclosure of such confidential information is required by law, Receiver shall provide COUNTRY A with prior written notice of such event. Such

notice shall be sent in sufficient time to enable COUNTRY A to seek any protective order or arrangement permitted by law.

9. MISCELLANOUS

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 or 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.

Country A	Receiver
_____	_____
(Signature)	(Signature)
_____	_____
(Printed Name and Title)	(Printed Name and Title)
_____	_____
(Address)	(Address)
_____	_____
(Email address)	(Email address)

ANNEX 2: nOPV2 REPORTING FORM FOR ADVERSE EVENTS OF SPECIAL INTEREST (AESI)

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: ☐ M ☐ 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 of special interest (s):**

☐ Anaphylaxis

☐ Guillain-Barré syndrome (GBS)/ Fisher's Syndrome(FS)

☐ Aseptic meningitis

☐ Myelitis/Transverse myelitis

☐ Acute disseminated encephalomyelitis

☐ Unexplained deaths

☐ Acute flaccid paralysis (VDPV)

☐ Other (Please specify)

☐ Acute flaccid paralysis (VAPP)

☐ 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 (1st, 2nd, 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*

ᵗParent/guardian's information can be provided for minors

ANNEX 3: nOPV2 AESI LINE LISTING FORM

Date: ..... District: ..... Health facility: .....

Name /ID	Age or birthdate	Sex	Address	Date onset	Initial diagnosis[a]/date Final diagnosis[a]/date	Place Hospitalized	Outcome[b]	If Vaccinated with nOPV2 Date Place	Batch Number	Reported as AEFI	Causality Assessed	Causality Assessment Result[c]
....	..... ☐ UK	☐ F ☐ M	....	.....	....	....	....	....	V ..... D	☐ Y ☐ N ☐ UK	☐ Y ☐ N ☐ UK	.....
Name /ID	Age or birthdate	Sex	Address	Date onset	Initial diagnosis[a]/date Final diagnosis[a]/date	Place Hospitalized	Outcome[b]	If Vaccinated with nOPV2 Date Place	Batch Number	Reported as AEFI	Causality Assessed	Causality Assessment Result[c]
....	..... ☐ UK	☐ F ☐ M	....	.....	....	....	....	....	V ..... D	☐ Y ☐ N ☐ UK	☐ Y ☐ N ☐ UK	.....
Name /ID	Age or birthdate	Sex	Address	Date onset	Initial diagnosis[a]/date Final diagnosis[a]/date	Place Hospitalized	Outcome[b]	If Vaccinated with nOPV2 Date Place	Batch Number	Reported as AEFI	Causality Assessed	Causality Assessment Result[c]
....	..... ☐ UK	☐ F ☐ M	....	.....	....	....	....	....	V ..... D	☐ Y ☐ N ☐ UK	☐ Y ☐ N ☐ UK	.....

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-Barre syndrome/Fisher's 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: ☐M ☐ F
***Date of birth (DD/MM/YYYY)*:** _ _/_ _/_ _ _ _ ☐UK *OR Age at onset :* ☐☐*Years* ☐☐ *Months* ☐☐☐ *Days* *OR Age Group:* ☐*< 1 Year* ☐ *1 to 5 Years* ☐ *> 5 Years*
Suspected AESI: Date & Time AESI started (DD/MM/YYYY)**:** __ __ / __ __ / __ __ __ __ ☐☐ Hr ☐ Min
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) 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) **Signs and symptoms:
Lab findings:
Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information*. Use additional sheet if needed :*
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 • 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 • 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 urticaria			
Red and itchy eyes			
Cardiovascular			
Reduced peripheral circulation as indicted by at least 2 of the following • 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	
	≥ 1major 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 *If case meets criteria for aseptic meningitis and encephalitis case definition, it should be reported as encephalitis*			
Outcome			
Full recovery to baseline status			
Recovery with residual symptoms If yes, specify			
Death			
Other outcome, specify			

Brighton 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: • > 5WBC/mm^3 in children 2 months of age or older • > 15 WBC/mm^3 in infants younger than 2 months of age AND	Pleocytosis in CSF as determined as: • > 5WBC/mm^3 in children 2 months of age or older • > 15 WBC/mm^3 in infants younger than 2 months of age AND	Presence of alternative diagnosis ***If case meets criteria for aseptic meningitis and encephalitis case definition, it should be reported as encephalitis***
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 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** Sudden death of any child under 2 years of age which remains unexplained after excluding other causes of death by:	Unexplained deaths **after clinical and final event history and autopsy** Sudden death of any child under 2 years of age which remains unexplained after excluding other causes of death by:	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:
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 UpToDate, modified Brighton Collaboration definition, medical dictionaries, or other sources
Anaphylaxis	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. Reporting criteria: Anaphylaxis diagnosed by a healthcare provider *Sources:* 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.
Acute Flaccid Paralysis	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-Barre Syndrome and transverse myelitis. Reporting criteria: Any paralytic illness described by a healthcare provider *Source:* World Health Organization. "WHO-recommended surveillance standard of poliomyelitis." http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/poliomyelitis_standards/en/. Last accessed May 21, 2018.

Aseptic meningitis	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. Reporting criteria: Aseptic meningitis as described by a healthcare provider S*ources:* BC case definition Irani DN (August 2008). *"Aseptic meningitis and viral myelitis"*. Neurologic Clinics. 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". American Family Physician. 59 (10): 2761–70. PMID *10348069*.
Encephalitis	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. Reporting criteria: Encephalitis as described by a healthcare provider Source: Brighton case definition
Acute Disseminated Encephalomyelitis (ADEM)	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. Reporting criteria: ADEM as described by a healthcare provider Source: Brighton case definition

GBS	Guillain-Barré syndrome (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 Reporting criteria: GBS as described by a healthcare provider Source: Brighton case definition
Myelitis/Transverse myelitis	Myelitis/Transverse myelitis (TM) is a rare disorder caused by inflammation of the spinal cord. *Transverse* 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. Reporting criteria: Myelitis/TM as described by a healthcare provider Sources: Brighton case definition West TW (October 2013). "Transverse myelitis--a review of the presentation, diagnosis, and initial management". Discovery Medicine. 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	Death which remains unexplained after excluding other causes of death Unexplained deaths including “Sudden Infant death syndrome” or SIDS in the first year of life, which remain unexplained after excluding other causes of death. Source: Brighton Collaboration

	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