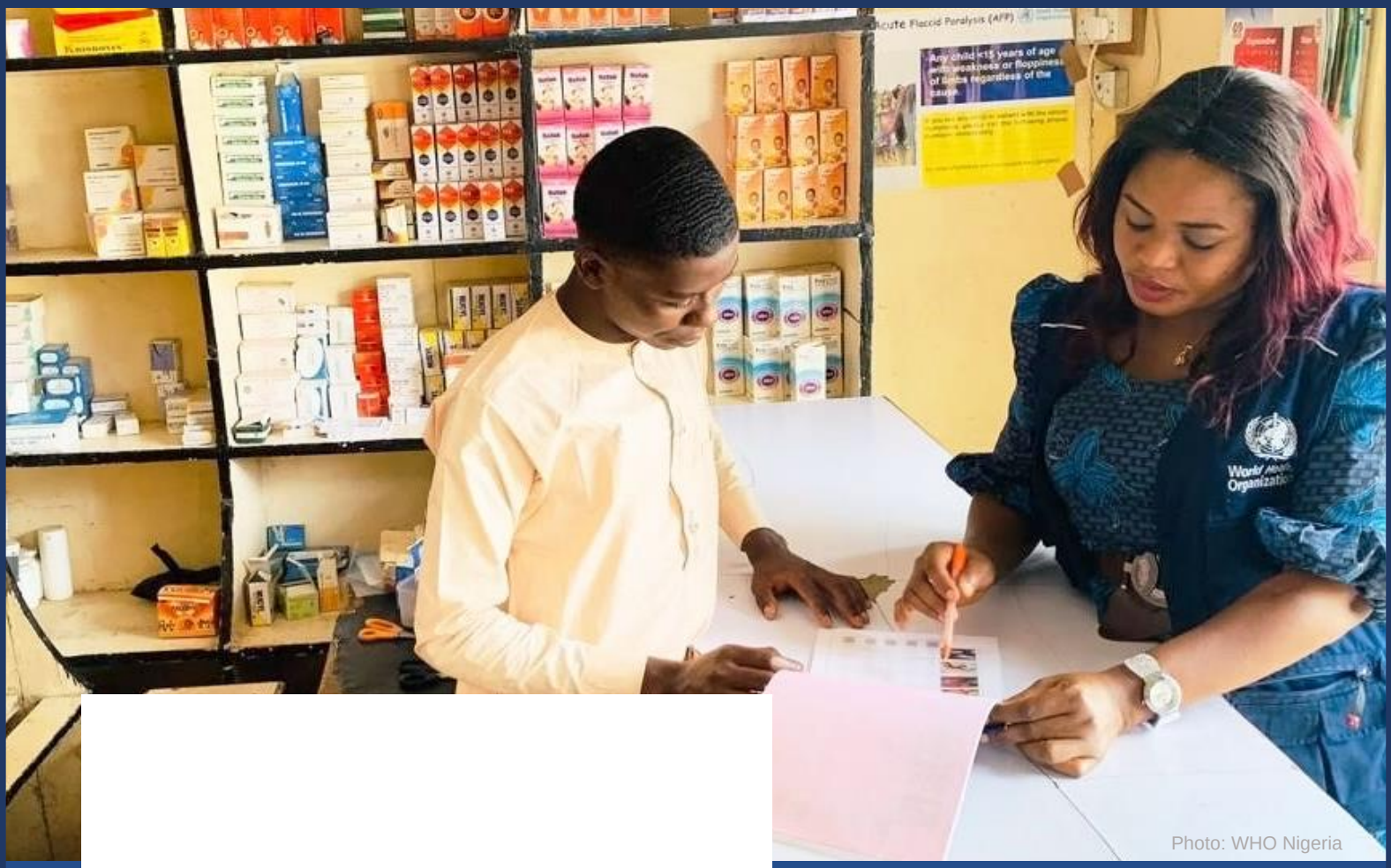

Photo: WHO Nigeria

nOPV2 Safety Monitoring Guidance Manual

August 2024 Update

EVERY LAST CHILD

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Abbreviations

ADEM	Acute demyelinating encephalitis
AEFI	Adverse event following immunization
AESI	Adverse event of special interest
AFP	Acute Flaccid Paralysis
cVDPV2	Circulating vaccine derived poliovirus type2
EPI	Expanded program on immunization
EUL	Emergency use listing authorization
GACVS	Global advisory committee on vaccine safety
GBS	Guillain-Barré syndrome
GPEI	Global polio eradication initiative
MOH	Ministry of health
nOPV2	Novel oral poliovirus vaccine type 2
NRA	National regulatory authority
ODK	Open data kit
OPV	Oral poliovirus vaccine
SAE	Serious adverse event
SOP	Standard operating procedure
VAPP	Vaccine associated paralytic polio
VRE	Vaccine related event
WHO	World Health Organization

Glossary of terms

Adverse event following immunization (AEFI)	Any untoward medical event that follows immunization and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.
Adverse event of special interest (AESI)	A pre-identified and predefined medically significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies.
Acute Flaccid Paralysis (AFP) case	An AFP case is defined as a child under 15 years presenting with sudden onset of floppy paralysis or muscle weakness due to any cause, or any person of any age with paralytic illness if poliomyelitis is suspected by a clinician.
Causality assessment	In the context of vaccine AEFI surveillance, a systematic review of data about the AEFI case(s) to determine the likelihood of a causal association between the event and the vaccine(s) received.
Circulating vaccine derived poliovirus (cVDPV)	Genetically linked vaccine derived poliovirus (VDPV) isolated: i) from at least two individuals (not necessarily AFP cases), who are not direct (i.e. household) contacts, ii) from one individual and one or more environmental surveillance (ES) samples, or iii) from two or more ES samples if they were collected at more than one distinct ES collection site (no overlapping of catchment areas), or from one site if collection was more than two months apart1.
Emergency Use Listing procedure (EUL)	A risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the aim of expediting the availability of these products to people affected by a public health emergency.
Vaccine safety	The process that maintains the highest efficacy of, and lowest adverse reaction to, a vaccine by addressing its production, storage and handling. Vaccine safety is a part of immunization safety.

Surveillance	The continual, systematic collection of data that are analyzed and disseminated to enable decision-making and action to protect the health of populations.
Serious AEFI	An event that results in death, is life-threatening, requires in patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to prevent one of the outcomes above may also be considered as serious.
Vaccine derived poliovirus (VDPV)	Oral poliovirus (OPV) strains that are > 1% divergent (or >= 10 nucleotide changes, for types 1 and 3) or > 0.6% divergent (>= 6 nucleotide changes, for type 2) from the corresponding OPV strain in the complete VP1 genomic region.
Vaccine pharmacovigilance	The science and activities relating to the detection, assessment, understanding and communication of AEFI and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or vaccination
Vaccine related event (VRE)	A range of possible events that can negatively affect a vaccination program, including: an AEFI; a new study or experimental data related to vaccines or immunization; a report in the press, or a local rumor about vaccines; temporary suspension of a vaccine; a vaccine recall; and the replacement of a vaccine.
Vigiflow	A web-based individual case safety report (ICSR) management system (E2B compatible) for medicines and vaccines, developed and maintained by Uppsala Monitoring Centre

Background

Novel oral polio vaccine type 2 (nOPV2) can be used by countries facing type 2 polio detection or outbreaks of circulating vaccine-derived poliovirus type 2 (cVDPV2), or countries looking to safeguard against a type 2 polio event.

The World Health Organization (WHO) granted nOPV2 Emergency Use Listing (EUL) approval in November 2020 and it was first rolled out for outbreak response in March 2021. Clinical trial data[1,2] and subsequent field monitoring of the vaccine during the EUL period demonstrated a favorable safety profile of the vaccine[3], contributing to its prequalification in December 2023. During the EUL period approximately 1 billion doses of nOPV2 were administered across 35 countries, providing protection to millions of children against illness and debilitating paralysis. Enhanced safety surveillance of the vaccine was implemented during the EUL period, and the Global Advisory Committee on Vaccine Safety (GACVS) and its nOPV2 sub-committee-maintained oversight on all safety related aspects of the vaccine. Summaries of the GACVS nOPV2-related meeting reports can be found on the Global Polio Eradication Initiative's (GPEI's) website.[4] Following prequalification, enhanced safety monitoring of the vaccine is no longer mandatory, however, countries must continue to implement routine processes in place for ensuring safety all vaccines. The present document provides additional resources and guidance on enhanced safety monitoring which, while no longer required for nOPV2, were valuable in the EUL period and may be helpful to countries that may opt for enhanced monitoring for all oral polio vaccines.

During new vaccine rollouts, post-authorization safety monitoring is critical to detect rare or unexpected adverse events. Two kinds of adverse events may be monitored through vaccine safety monitoring:

- *Adverse event following immunization* (AEFI) - Any untoward medical occurrence which follows immunization, and which 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. Routine passive surveillance (spontaneous reporting) for AEFIs is should already be in place within countries and will be ongoing before, during and after nOPV2 use to detect adverse events, including unexpected and unanticipated events.
- *Adverse event of special interest* (AESI) - A pre-identified and predefined medically significant event that has the potential to be causally associated with a vaccine product which needs to be carefully monitored. Based on summary safety data from the WHO, the conditions that are likely to be of interest for nOPV2 AESI surveillance, and therefore constitute "safety signals," include:

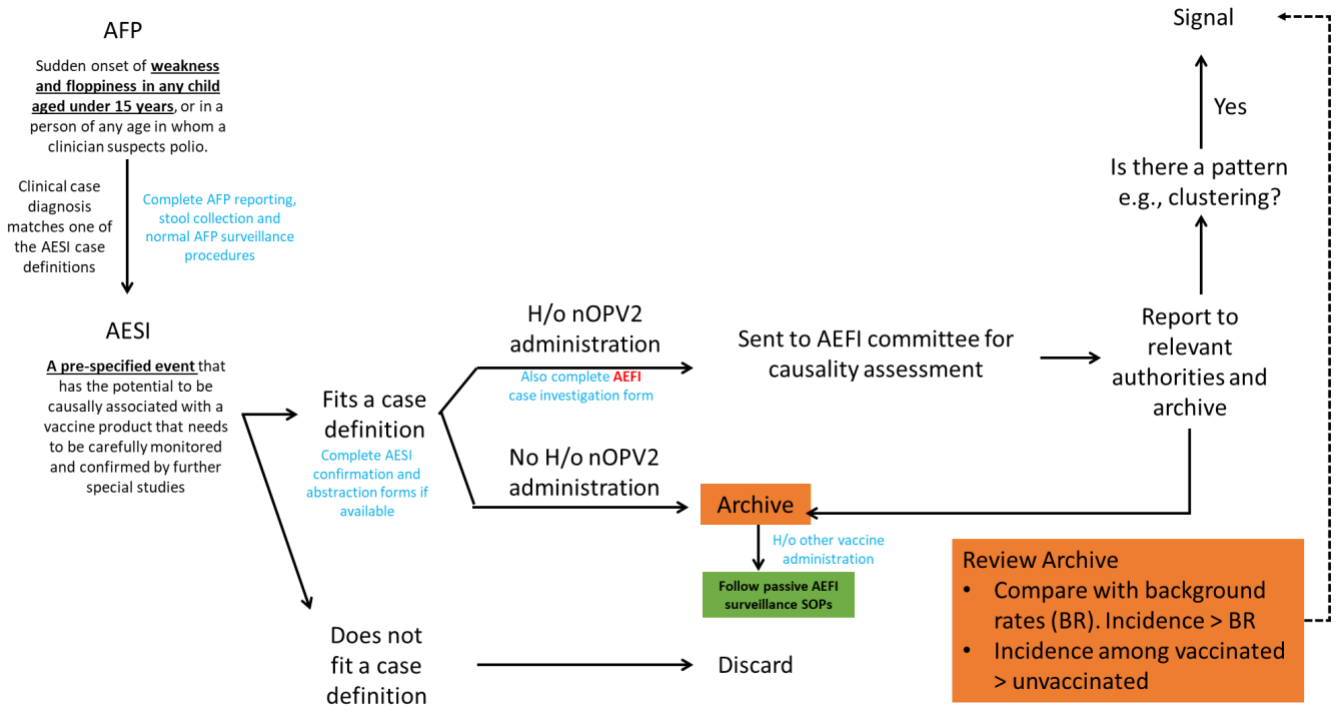
    a. Anaphylactic reactions
    b. Aseptic meningitis

[1] Rivera Mejía, Luis et al. "Safety and immunogenicity of shorter interval schedules of the novel oral poliovirus vaccine type 2 in infants: a phase 3, randomised, controlled, non-inferiority study in the Dominican Republic." *The Lancet. Infectious diseases* vol. 24,3 (2024): 275-284. doi:10.1016/S1473-3099(23)00519-4
[2] Ochoge, Magnus et al. "Safety of the novel oral poliovirus vaccine type 2 (nOPV2) in infants and young children aged 1 to <5 years and lot-to-lot consistency of the immune response to nOPV2 in infants in The Gambia: a phase 3, double-blind, randomised controlled trial." *Lancet (London, England)* vol. 403,10432 (2024): 1164-1175. doi:10.1016/S0140-6736(23)02844-1
[3] GACVS-nOPV2-sub-committee-meeting-20240718.pdf (polioeradication.org)
[4] GACVS sub-committee on novel OPV2 safety review meeting reports (https://polioeradication.org/gacvs-sub-committee-on-novel-opv2-safety/).

c. Encephalitis/ Acute disseminated encephalomyelitis (ADEM)
d. Guillain-Barré Syndrome (GBS) / Miller Fisher Syndrome ;
e. Myelitis / transverse myelitis
f. Acute flaccid paralysis (AFP) due to vaccine-derived poliovirus (VDPV) or vaccine-association paralytic paralysis (VAPP); and
g. Unexplained deaths

AFP surveillance may be leveraged for monitoring these conditions, as it captures conditions that are most likely to be related to nOPV2 AESIs[5]. Therefore, AESIs detected through the AFP surveillance systems may be reviewed and assessed by National Expert Committee's for AEFI causality assessment where possible. Additionally, countries may consider active AESI surveillance[6] for nOPV2 safety based on the availability of technical capacity and human resources to implement the active AESI protocol. AESI surveillance for these conditions and potentially other safety signals can build upon AFP surveillance and environmental surveillance, the existing AEFI surveillance system and the close monitoring of vaccine-related events (VREs). **Fig. 1** describes a suggested schematic for integration of AFP and AESI surveillance (if applicable) with ongoing passive AEFI surveillance systems.

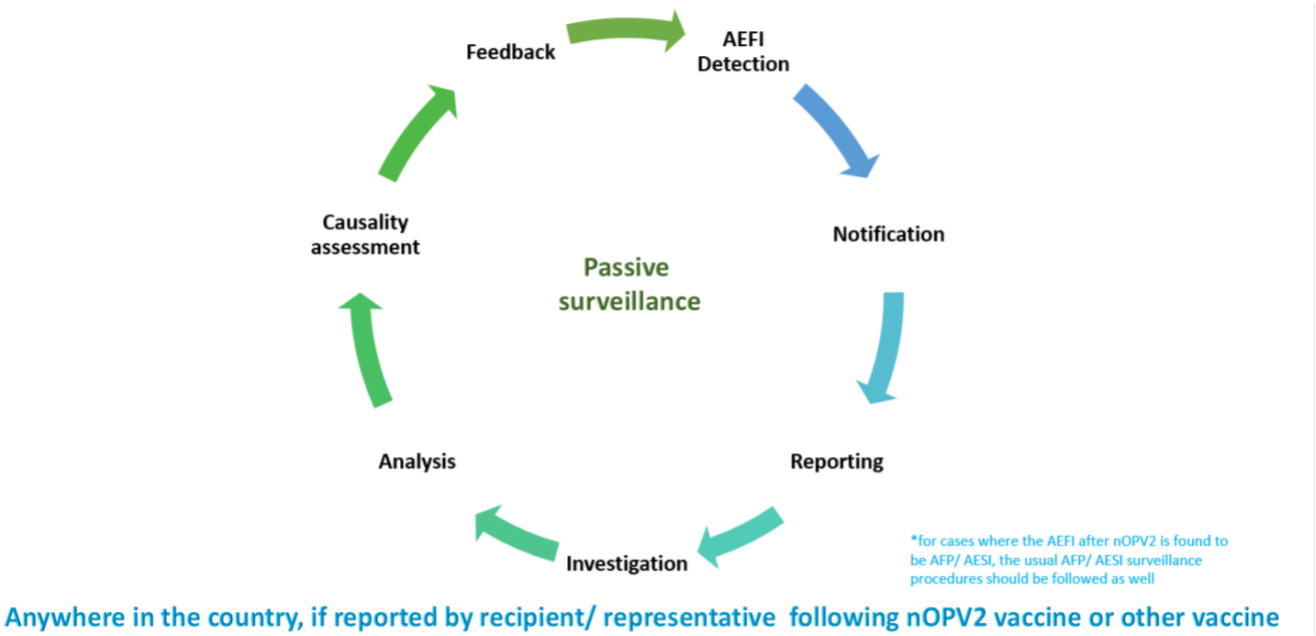
Fig 1. Surveillance systems that contribute to nOPV2 safety surveillance



[5] Global Advisory Committee on Vaccine Safety Sub-Committee on nOPV2 Safety. Summary Note for the Record (21 February 2022). https://polioeradication.org/wp-content/uploads/2022/03/GACVS-sub-committee-on-nOPV2-Report-20220221.pdf
[6] Global Polio Eradication Initiative (GPEI). Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine Type 2 (nOPV2) Use. Last updated: October 2021. (https://polioeradication.org/wp-content/uploads/2020/11/EN-nOPV-AESI-surveillance-guide.pdf).

AESI surveillance follows the traditional AEFI surveillance cycle, as described by the WHO (see **Fig. 2**). AESI surveillance is a similar process, with activities including detection, reporting, case ascertainment/verification, abstraction of medical information in relation to Brighton Collaboration case definitions, and investigation and causality assessment, if the AESI follows vaccination.

Fig. 2. AEFI safety monitoring activities



Objective

In times of public health crises, such as cVDPV2 outbreaks initiating the introduction of a new vaccine , enhanced vaccine safety surveillance can effectively and efficiently provide high-quality data for public health decision-making. It can also help ensure public trust in the immunization program, as the careful monitoring of AEFIs / AESIs, combined with advanced planning and vaccine-related event (VRE) preparedness and response, collectively ensure that AEFIs / AESIs are detected, reported, investigated and causally assessed, when appropriate, and communicated about in a way that promotes awareness and public trust.

For countries planning to use nOPV2, the present document aims to provide guidance regarding:

- Activities that may be undertaken before, during and after an nOPV2 campaign to monitor vaccine safety and support public confidence in the vaccine.
- Leveraging and enhancing vaccine safety surveillance systems in the context of nOPV2 use in countries.
- Managing a VRE which are a range of possible events, including AEFIs which may negatively affect an immunization program.

In addition to this guidance document, several resources have been developed to support nOPV2 use in-country (see **vaccine safety surveillance resources** at the end of this document).

Suggested steps for safety monitoring of nOPV2

The WHO global vaccine safety blueprints 1.0 and 2.0[7] discusses the concepts of enhanced capacity for vaccine safety assessment in countries that introduce newly developed vaccines, that introduce vaccines in settings with novel characteristics, or that both manufactured and used prequalified vaccines. In line with global guidance, countries may consider the following activities prior to, during, and after an nOPV2 campaign, depending on existing vaccine pharmacovigilance capacity and resource availability.

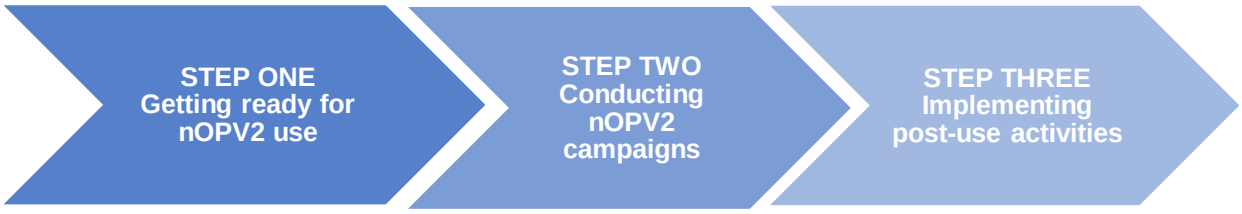
Step 1: **Activities that can be done before nOPV2 campaign** – to effectively monitor the safety of nOPV2 post authorization, countries may consider the following activities:

- take steps to update and improve established systems for AFP and AEFI surveillance
- develop protocol and train focal persons for AESI surveillance, should the country decide to implement this activity.
- develop an operational plan for implementing nOPV2 safety surveillance
- conduct a series of vaccine safety trainings for polio and routine immunization health workforce
- ensure a functional AEFI Causality Assessment Committee is established, trained and sensitized for introduction of nOPV2

Step 2: **Activities that can be done during nOPV2 campaigns** - Before launching an nOPV2 response, each country may review a suggested checklist of activities to ensure all systems and processes relevant to nOPV2 safety monitoring are in place.

Step 3: **Activities that may be conducted post campaign** - Once nOPV2 has been used in a country, a series of ongoing safety surveillance activities related to data analysis and interpretation, reporting and assessment may be conducted.

Fig 3. Steps toward nOPV2 enhanced safety surveillance



[7] Global vaccine safety blueprint 2.0 (GVSB2.0) 2021-2023 (who.int).

Step 1: Getting ready for nOPV2 use

Key considerations at this stage include:

Develop and/or update guidelines for nOPV2 safety monitoring

As recommended for all vaccines, a well-established and functional national passive AEFI surveillance network forms the cornerstone for post-licensure and post-authorization vaccine pharmacovigilance[8]. An existing national AEFI manual for passive safety surveillance should already be in place. To support the implementation of AEFI surveillance, countries can draft (if needed), validate, print and disseminate to subnational levels a national manual for AEFI surveillance or its abridged version. Countries may refer to the existing WHO Global manual for surveillance of Adverse Events Following Immunization (AEFIs), 2016 for preparation of the national AEFI surveillance manuals[8]. Assistance is also available by contacting the respective WHO Country or Regional offices for assistance

Similarly, to support the active search for AESI conditions, countries implementing AESI surveillance can:

- draft and validate a protocol for AESI active case search; and
- print the forms for district disease surveillance officers as required.

The AESI safety surveillance protocol would describe the process for identifying conditions of interest through active monitoring at selected health facilities, as well as the process that will be followed by disease surveillance officers and other safety surveillance staff to implement AESI detection, notification, investigation, analysis, causality assessment and feedback and response. An example protocol (developed for guidance to countries during EUL phase) may be accessed here.

Operational plan for implementing nOPV2 safety surveillance

Country capacity for pharmacovigilance varies considerably: while some countries may have existing systems that are well-functioning, others may be in earlier phases of establishing systems. For all countries independent of their current capacities, an operational plan for implementing nOPV2 safety surveillance needs to be developed summarizing key activities to enable sufficient safety monitoring of nOPV2 use.

A safety surveillance operational plan supports the implementation of nOPV2 safety monitoring by ensuring that roles are defined to facilitate coordination across all levels and all areas of work, from surveillance to data analysis to communications. The plan should define activities that need to take place before, during and after nOPV2 campaigns and identifies the role, person or group tasked with fulfilling each activity, as well as the resources allocated and timeframe in which activities should be initiated and completed.

Suggested components of the safety surveillance operational plan

- Reporting
- Investigation
- Data analysis

[8] World Health Organization. (2014). Global manual on surveillance of adverse events following immunization, 2016 update. World Health Organization. https://iris.who.int/handle/10665/206144

- Causality assessment
- Crisis and risk communication
- Vaccine-related event response

Annex A provides sample activity tables that form the basis of the operational plan.

VREs include a range of possible events related to vaccines that can negatively affect an immunization program, of which an AEFI is one possible event. By proactively preparing for VREs, countries safeguard their immunization program's reputation, thereby ensuring public trust and confidence in vaccines and in Ministries of Health (MoHs). VRE preparedness ensures that information reaches affected people and communities quickly, and that coordinating mechanisms within government and among stakeholders work smoothly to offer a united response, delivering on the government's promise to offer safe, effective vaccines for all who need them.[9] Detailed guidance on vaccine related event response plans may be accessed here, while WHO's step-by-step guidance for vaccine crisis communication may be accessed here. Annex table 1 and Annex table 2 provide VRE tables that may be adapted by countries in preparation of nOPV2 introduction. Developing the operational plan would require commitment from all vaccine safety stakeholders to share and reconcile the data across separate databases so that signals can be detected effectively and efficiently. All nOPV2 safety data may be owned and managed by relevant national authority, including the country's polio eradication program, Expanded Program on Immunization (EPI) or National Regulatory Authority (NRA) program, and data may be shared between these programs for reconciliation and analysis from a safety perspective.

Key nOPV2-related safety trainings

The rollout of a new vaccine and related protocols to implement safety surveillance can be supported by rigorous training to ensure that the right people are well-equipped to conduct all necessary activities for nOPV2 safety surveillance. Oftentimes, this includes the training of trainers (ToT) so facilitators are up-to-date on the latest methods and approaches to AEFI monitoring, AESI surveillance (if applicable) and VRE response. To ensure all relevant stakeholders are fully sensitized to the introduction of nOPV2 and countries may consider:

a. Arranging messaging from the chief medical officer formalizing the role of provincial and district disease surveillance officers to collect data from the AEFI reports of frontline healthcare workers and perform AESI active case search in hospital registers (if applicable).

Resources

Guidance documents:

- Global manual for AEFI surveillance
- Causality assessment of AEFIs
- VRE guidance document
- AFP surveillance manual
- AESI surveillance manual for nOPV2 during EUL

Templates

- Operational plan tables
- VRE tables

Safety training materials

- Sample country trainings
- Causality assessment aide memoire

Online trainings

- Vaccine safety basics
- Investigating AEFI
- Immunization safety

Sample training materials

- Training AEFI agenda; Training AESI agenda
- Training of trainers

[9] GPEI. Novel Oral Polio Vaccine Type 2 (nOPV2) Vaccine Related Event (VRE) Response Plan (https://polioeradication.org/wp-content/uploads/2020/11/EN-VRE-plan-draft-nOPV2.pdf). Guidance note for the Novel Oral Polio Vaccine Type 2 (nOPV2) National Vaccine-Related Event (VRE) Plan (https://polioeradication.org/wp-content/uploads/2021/02/VRE-development-guidance-note-for-countries-20210217-EN.pdf).

b. Ensuring that every disease surveillance officer has completed three online courses on vaccine safety: (1) vaccine safety basics, (2) investigating AEFI, and (3) immunization safety and AEFI data management that can be accessed here.
c. Organizing a one-day training on AEFI surveillance (and AESI surveillance if applicable) for disease surveillance officers, including for AFP surveillance officers which can be added to their surveillance training agenda; and
d. Identifying facilitators, list of participants and schedule training for later face-to-face two-day training for disease surveillance officers on investigation.

Establishment and/or sensitization of national Causality Assessment Committee

Causality assessment is the systematic evaluation of the information obtained about an AEFI following its investigation to determine the likelihood that the event might have been caused by the vaccine/s received [10]. It is a critical part of vaccine safety monitoring for ensuring confidence in immunization programs. Countries may refer to the user manual for the revised WHO causality assessment methodology for detailed guidance on the approaches, processes and tools available for conducting causality assessment.

Causality assessments should ideally be performed by National AEFI causality assessment committees which are pluri-disciplinary, including experts from diverse fields such as pediatrics, neurology, general medicine, forensic medicine, pathology, immunology, and epidemiology etc. and independent from both government and industry. Committees may invite external experts for review of specific cases.

Countries with existing AEFI causality assessment committees may consider sensitizing its members prior to use of nOPV2 regarding the vaccine, and the implementation plan, and various tools for case reporting, investigation and evaluation. The agenda for such refresher training may include a review of standardized case definitions for AESIs identified above. Countries which do not have existing AEFI causality assessment committees should aim to establish one prior to nOPV2 use to ensure adequate time for training. Therefore, countries may consider the following steps:

a. If no causality assessment committee exists, arrange a decree creating the national experts committee for pharmacovigilance (AEFI) and nominating the members
b. Conduct an orientation training / refresher training for members of the Causality Assessment Committee on AEFI surveillance, AEFI causality assessment methodology[10], case definitions, as well as AFP surveillance.
c. Organize monthly meetings of the national experts committee during nOPV2 deployment for ensuring timely review of serious AEFIs and AESIs (if applicable).

Resources

Case definitions:

- VAPP
- cVDPV
- Encephalitis and ADEM
- AFP
- Anaphylaxis
- Aseptic meningitis
- Encephalitis
- GBS
- Unexplained death
- Myelitis and transverse myelitis

Case studies

- ADEM
- AFP
- Anaphylaxis
- Aseptic meningitis
- Encephalitis

[10] Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification, 2nd ed., 2019 update

A suggested list of optional activities countries may for consider augmenting vaccine safety monitoring capacity while planning for nOPV2 use are listed in Annex B

Step 2: During nOPV2 campaigns

Routine or passive AEFI surveillance and active AFP surveillance may already be ongoing before nOPV2 use and should continue during and after nOPV2 campaigns. To support enhanced safety surveillance during nOPV2 campaigns, countries may consider:

- Confirming all trainings identified in the operational plan have been completed
- AESI process (if applicable) and tools have been piloted and updated to reflect the country context for countries undertaking AESI active surveillance
- Health facilities are equipped with AEFI surveillance manuals (full or abridged), outpatient department registers, AEFI / AESI reporting and line listing forms and AEFI investigation forms
- Safety data flow processes are agreed upon, communicated and reinforced: health facility, district and national teams should be aware of what should be reported, how often and to whom
- Relevant ongoing meetings are organized (e.g., district data harmonization meeting, national data harmonization meeting, Causality Assessment Committee meeting)
- National safety teams are in place to collate and analyze district data
- Data is shared with district, national and regional teams, in accordance with the data flow outlined in the operational plan and submitted as available to relevant authorities at national level. As per the standard operating procedures in place for other vaccines, countries may also report serious adverse events to digital platforms such as Vigiflow. A detailed list of activities pre- and post-campaign activities is provided for reference in.

As with all new vaccine introductions, countries should anticipate an increase in reporting of AEFIs and AESIs immediately following the introduction of nOPV2, and countries will benefit from allocating adequate resources to ensure identification, reporting, investigation and causality assessment of all adverse events in a timely manner.

Step 3: Implementing post-use activities

Monitoring for AEFI / AESI in the weeks and months following nOPV2 use will be necessary to ensure safety signals are detected, investigated and causally assessed (see Table 1). An example checklist for post-nOPV2 campaign safety surveillance activities is presented below:

Table 1:Example post-campaign checklist for safety surveillance

When to start	Safety activities
Immediately after nOPV2 campaign begins until timeline noted below	*AEFI surveillance* ❒ Ensure health workers in the selected facilities are recording patient symptoms in registers as cases present. ❒ Ensure health workers fill out AEFI reporting form immediately when an AEFI is detected and within 24-48 hours of case notification. ❒ Confirm that disease surveillance officer / facility focal point collects AEFI forms and sends them to central district within 24-48 hours after the forms are filled out.

	Serious adverse events ❒ Serious adverse events (SAEs) must be immediately reported through the NRA as soon as possible. NRAs may enter the data into Vigiflow (or equivalent e-reporting tool).
Weekly until timeline noted below	*AEFI surveillance* ❒ Ensure AEFI investigations are completed in one week and AEFI reports filed in an open data kit (ODK) or another e-platform. ❒ Ensure AEFI investigation reports are entered into Vigiflow (or equivalent e-reporting tool) and ensure they are submitted and received. *AESI surveillance (if applicable)* ❒ District surveillance officers' line-list AFP and AESI cases and upload to ODK or another platform. *Safety data* ❒ AEFI secretariat completes data reconciliation and submits analysis of data to Causality Assessment Committee.
Monthly until timeline noted below	*Causality Assessment Committee* ❒ Ensure the Causality Assessment Committee regularly reviews data, completes its analysis and submits reports in a timely manner to the MoH. (Ad hoc meetings may be required in the event of serious AEFI or cluster of AEFIs.)
Continue for…	**Safety activities**
6 weeks after the first use of nOPV2	❒ Retrospective case searches for AFP in all priority sites in each geographic area where nOPV2 was used, within 6 weeks following nOPV2 use in that area.
For 3 months following the last nOPV2 use	❒ Active AESI surveillance (if applicable) to monitor anaphylactic reactions, aseptic meningitis / encephalitis, ADEM, GBS / Miller Foster Syndrome, myelitis / transverse myelitis, AFP due to VDPV or VAPP, and unexplained death (for countries implementing active AESI surveillance as recommended). ❒ Causality Assessment Committee meetings are held to review any nOPV2-related AEFI/AESI data.

Annex

Annex A

Operational plan template

The operational plan may incorporate a cover page and detailed activity plan, both detailed below.

Cover page example

Ministry of Health for [Country]

The Operational Plan for
Safety Surveillance of nOPV2
in [Country]

October 2021

The cover page may indicate:

- the name of the country;
- the name of the document; and
- the date.

Activity plan

The activity plan details three categories of activities: (1) before campaign activities; during campaign activities; and (3) after campaign activities.

Editable versions of the tables below can be found online (see Operational plan tables)

Table 2:Campaign activities (before, during and after campaign) for operational plan

Objective	**Key gaps** (describe briefly the existing gaps)	**Activities to be completed to fill identified gaps** (some illustrative activities have been provided below. Please use a new row for a new activity)	**When the activity will be completed**	**Person responsible for doing the activity**	**Time frame** (specify by when the activity needs to start and be completed)
Reporting - *Report all AEFIs so as to rapidly detect any serious AEFI and respond effectively*		Train subnational focal points on processing AEFI reports	Before campaign		
		Print enough forms to supply all the health facilities	Before campaign		
		Provide vaccine safety focal points with resources for transportation and communication to collect reports from health facilities	During campaign		
		Insert a new activity under reporting here (if any) otherwise delete the row	After campaign		
Investigation - *Investigate all serious AEFIs to generate sufficient information for causality assessment par the experts committee*		Make the Investigation form available to all regional health teams	Before campaign		

		Train regional focal point on investigation	Before campaign		
		Make a formal agreement with hospitals on providing post-paid care to serious cases referred to them with submission of the bill and clinical records to EPI	Before campaign		
		Provide resources for ambulance referral and hospital management for serious cases, including all lab tests	During campaign		
		Provide resources for field investigation	During campaign		
		Active AESI surveillance* to monitor anaphylactic reactions, aseptic meningitis / encephalitis, ADEM, GBS / Miller Foster Syndrome, myelitis / transverse myelitis, AFP due to VDPV or VAPP, and unexplained death	After campaign		
		Insert a new activity under investigation here (if any) otherwise delete the row			
Causality assessment - *Classify all the cases to give a response to the community and update the safety profile of the vaccine*		Ensure all trainings are completed and recorded in the planned training template	Before campaign		
		Hold at least monthly meetings of the Causality Assessment Committee for causality assessment of serious cases	During and After campaign		

		Insert a new activity under causality assessment here (if any) otherwise delete the row			
Data analysis - *Monitor the performance of the safety surveillance* - *Monitor the safety profile of the vaccine*		Ensure data collection system that the country is using are updated and disseminated to the safety focal points (if applicable)	Before campaign		
		Hold monthly data harmonization meeting by focal points at regional level	During and After campaign		
		Hold monthly data harmonization meetings by national implementation team	During and After campaign		
		Insert a new activity under data analysis here (if any) otherwise delete the row			
Crisis communication		Orient the committee for crisis communications on AEFI and complete VRE tables in annex B	Before campaign		
		Have a representative of the crisis committee in the Causality Assessment Committee meetings	During and After campaign		
		Insert a new activity under Crisis communication here (if any) otherwise delete the row			
Risk communication *Provide information and clear guidance to prevent an AEFI from becoming a crisis*		Ensure information that needs to be given to vaccinees prior to nOPV2 administration is integrated into vaccinator training.			

Annex B

Optional activities to implement enhanced safety surveillance

Pre-campaign

- ❒ Lead preparation for active AESI surveillance at sentinel hospitals (if applicable).
  - Conduct preparatory activities for site selection and data collection.
  - Conduct meetings with in-country stakeholders to establish roles and responsibilities at all levels (e.g., EPI, NRA, polio program, disease surveillance).
  - Review and refine AESI surveillance protocol, if needed.
  - Establish criteria for sentinel sites and conduct site assessments to finalize list of included sites.
  - Verify relevant staff can access records from surveillance sites.
  - Conduct any necessary training as described in the consolidated training overview document.
  - Conduct training for hospital staff at sentinel sites and other target groups.
  - Pilot AESI data collection tools and processes to support their refinement.
- ❒ Ensure establishment and functionality of AEFI and AESI data systems.
  - Develop data management plan, including schedule of data sharing and reporting based on campaign dates.
  - Establish standard operating procedures (SOP) for integration of AESI data into AEFI reporting systems.
  - Conduct any necessary trainings on data processes.
- ❒ Support functionality of Causality Assessment Committee.
  - Organize trainings on nOPV2 and causality assessment processes as described in Causality Assessment Committee training plan.
- ❒ Support country VRE preparedness and response.
  - Organize and lead workshops with key stakeholders to orient them on the VRE response plan and establish roles and responsibilities at all levels (e.g., EPI, NRA, polio eradication program, disease surveillance, communications).

Active surveillance implementation period (during a campaign and through six weeks after the last day of the last campaign round) for countries implementing active AESI surveillance only

- ❒ Coordinate and lead implementation for active AESI surveillance at sentinel hospitals.
- ❒ Oversee data collection, management and analysis of AESI data for identification of safety signals.
  - Supervise AESI data collection, entry and management.
  - Update AESI database as new information becomes available from investigations and causality assessments.
  - Ensure completeness of AESI reporting and investigation of AESI cases and access to supplemental materials if needed to complete causality assessment.
  - Ensure quality data through supportive supervision, data quality checks and cleaning of data.
  - Work with in-country partners (EPI, NRA and WHO pharmacovigilance team) to conduct analyses of AESI and AEFI data.
  - Provide technical support for AEFI and AESI investigations.
  - Work with EPI, the polio eradication program and regulatory groups in-country to conduct supportive supervisory visits of surveillance officers and clinician associates

in the field to ensure they are equipped with the knowledge, skills, capacity and support required to operationalize AESI surveillance.

- ❒ Support EPI and NRA in review of data collected through passive AEFI system.
  - Support analysis and identification of signals, as needed.
- ❒ Support the functionality of the Causality Assessment Committee.
  - Facilitate communication of relevant AEFI and AESI data to the committee to ensure timely causality assessment determinations.
  - Facilitating external support for causality assessment as needed by the committee.
- ❒ Facilitate communication and alignment between stakeholders on AEFI and AESI data
  - Coordinate between MOH (EPI/NRA) and WHO for AEFI and AESI surveillance.
  - Communicate regularly with the relevant stakeholders as necessary to clarify issues and provide progress updates.
- ❒ Support implementation of VRE response plan if/when a vaccine-related event occurs.

Post-active surveillance implementation phase (one month after the end of the six-week active surveillance follow-up)

- ❒ Oversee management and analysis of AESI data for identification of safety signals.
  - Supervise AESI data entry and management.
  - Update AESI database as new information becomes available from investigations and causality assessments.
  - Ensure quality data through supportive supervision, data quality checks and cleaning of data.
  - Work with in-country partners (EPI, NRA, others) to conduct analyses of AESI and AEFI data
- ❒ Support EPI and NRA in review of data collected through passive AEFI system.
  a. Support analysis and identification of signals, as needed.
- ❒ Facilitate communication and alignment between stakeholders on AEFI and AESI data.
  a. Coordinate between MOH (EPI/NRA) and WHO for AEFI and AESI surveillance.
  b. Communicate regularly with the relevant stakeholders, as necessary, to clarify issues and provide progress updates.
  c. Provide final country-specific AESI reports to MoHs and GPEI partners.
- ❒ Support functionality of Causality Assessment Committee.
  a. Facilitate communication of relevant AEFI and AESI data to the committee to ensure timely causality assessment determinations.
  b. Facilitate external support for causality assessment as requested by the committee.
- ❒ Support implementation of VRE response plan, if/when a vaccine-related event occurs.

Annex C

Vaccine Related Event tables

Editable version of these tables can be found online: download VRE tables.

Increasing public attention to event and increasing impact on public trust

	Potential Negative Impact on the Vaccination Programme (and Type of Response Required)		
Type of Event	**Low**	**Medium**	**High**
Vaccine reaction (AEFI or AESI)	- Reaction is not serious or dramatic - Reaction is serious but not relevant to the public (e.g. in another country with a vaccine not used in our programme)	- Serious reaction in my country - Serious reaction with some relevance to public (e.g. in another country with a vaccine used in our programme) - Anticipated media attention - Reaction among children, teenagers, pregnant people	- Actual media attention - Serious reaction(s) with unknown cause - Reaction that is dreaded, memorable, or dramatic - Serious reaction during a mass campaign - Serious reactions with a new vaccine, especially unexplained death
Study or new experimental data published	- Research has low credibility - Research is unlikely to receive public attention	- Research receives some public attention	- Research receives significant public attention - Source has high credibility or influence - The research is relevant (e.g. mass immunization programme, new vaccine)
Media report or local rumor (including social media)	- Story receives little to no public attention - Story does not play upon emotions and/ or fears - Story is not believable - Story is limited to a small geographic area, community or platform	- Story receives some public attention - Story triggers some emotional fears - Story is plausible - Story has spread beyond initial geographic area, community or platforms	- Story receives significant public attention; taps into emotional fears - Source has high readership/viewership - Source is credible and influential - Story is relevant - Story is reported from multiple sources and constituencies, and may have evolved and combined with other sociopolitical concerns
Temporary suspension of a vaccine	N/A	- Any suspension that is not in my country	- Any suspension in my country
Recall of a vaccine	N/A	- Any recall of a vaccine not used in my country	- Any recall of a vaccine we use
Vaccine replacement	N/A	Always	- Replacement was the result of an adverse event following immunization

Annex table 1:Assessing VRE impact

	Low		Medium		High	
ACTION	**AEFI or AESI**	**non-AEFI or AESI**	**AEFI or AESI**	**non-AEFI or AESI**	**AEFI or AESI**	**non-AEFI or AESI**
Feedback, corrective action, supervision, and training for health staff if needed, and communicating findings and actions to affected vaccinees and caregivers	x	n/a	x	n/a	x	n/a
Routine ongoing communication with all vaccinees and caregivers	x	x	x	x	x	x
Monitoring in case public concerns emerge	x	x	x	x	n/a	n/a
Plans for addressing the VRE may be shared with internal and external partners	x	x	x	x	x	x
Be prepared in case the situation rapidly escalates into a high-impact VRE	x	x	x	x	n/a	n/a
Implement precautionary, passive actions	n/a	n/a	x	x	n/a	n/a
Determine if the VRE necessitates the need for communication actions	n/a	n/a	x	x	n/a	n/a
If decision is made to communicate, activate the crisis communication plan	n/a	n/a	x	x	n/a	n/a
Consider local suspension of vaccine	n/a	n/a	n/a	n/a	x	x
Causality assessment	n/a	n/a	n/a	n/a	x	n/a
Activate crisis communication plan	n/a	n/a	n/a	n/a	x	x

Annex table 2: Specific actions for low, medium, and high impact VRE

Annex D

Consensus GPEI case definitions for Vaccine Associated Paralytic Polio

Vaccine-associated paralytic polio (VAPP) occurs in approximately 1 in 2.7 million doses of OPV administered, usually at the first dose. There are no secondary cases or outbreaks associated with VAPP[11]. A consensus case definition of VAPP, used routinely investigating and confirming potential VAPP cases as identified during AFP surveillance is provided below, and may be implemented as part of AESI surveillance, or for assessing causality of suspected VAPP cases by respective national expert committees.

- AFP with residual paralysis (compatible with paralytic polio) lasting at least 60 days, and
- Paralysis onset between 4 and 40 days after the dose of OPV for vaccine recipients and up to 60 days for close contacts or individuals in areas of campaigns (60 days in some countries), and
- Isolation of vaccine like poliovirus from any stool samples (always collected after paralysis.

[11] Global-AFP-guidelines-pre-publiucation-version-2023.pdf (polioeradication.org)