Photo: WHO Nigeria

POLIO GLOBAL ERADICATION INITIATIVE

Vaccine Safety Requirements in the Context of nOPV2 Use

EVERY LAST CHILD

Background

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, now have the option to use the novel oral polio vaccine type 2 (nOPV2), which is currently available under an Emergency Use Listing (EUL) of the World Health Organization (WHO).[1]

Countries wishing to use nOPV2 under an EUL will need to meet additional safety monitoring requirements in line with established criteria. During new vaccine rollouts, safety monitoring criteria are critical to detect rare or unexpected adverse events, particularly as nOPV2 is given to a larger number of individuals beyond the clinical trials that preceded the EUL.

Two kinds of adverse events are 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 unfavourable 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 which needs to be carefully monitored.

Routine passive surveillance for AEFI should already be in place within countries and will be ongoing before, during and after nOPV2 use to help with detecting adverse events, including unexpected and unanticipated events.

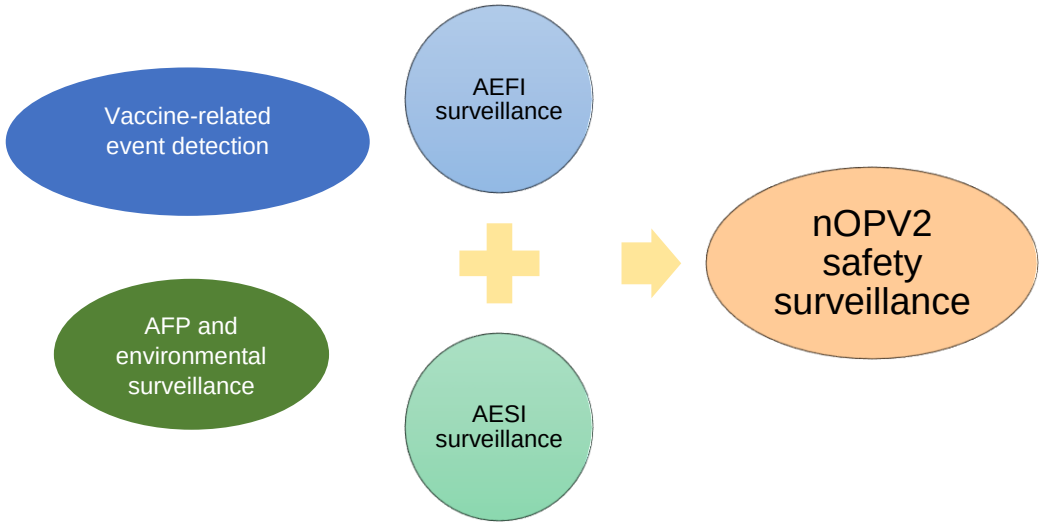
To meet the EUL requirements for nOPV2 use, time-limited active AESI surveillance will need to be implemented in order to detect more complex adverse events that may be anticipated based on what is currently known about the nOPV2 vaccine.[2] Based on summary safety data from the WHO, the conditions that are likely to be of interest for nOPV2 AESI surveillance, and therefore constitute “safety signals,” include:

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

[1] Based on a decision by the Strategic Advisory Group of Experts on Immunization (SAGE) that nOPV2 should become the vaccine of choice after the initial use period. See SAGE meeting summary, Oct 2020 (https://apps.who.int/iris/bitstream/handle/10665/337100/WER9548-eng-fre.pdf).
[2] 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 for these conditions and potentially other safety signals builds upon AFP surveillance and environmental surveillance, the existing AEFI surveillance system and the close monitoring of vaccine-related events (VREs). See **Fig. 1**.

Fig 1. Surveillance systems that contribute to nOPV2 safety surveillance



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. AESI safety monitoring activities

This enhanced safety monitoring processes will facilitate rapid identification and response to safety signals, should they arise. No significant safety signals have been associated with nOPV2 to date in clinical trials. Furthermore, the Global Advisory Committee on Vaccine Safety (GACVS) has reviewed data from nOPV2 initial use for over 70 million doses administered across four countries – and concluded there were no serious safety concerns from the data.

Objective

In times of public health crises, such as cVDPV outbreaks, 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 programme, as the careful monitoring of AEFI / AESI, 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.

*The Global Polio Eradication Initiative (GPEI) has prepared this document to highlight what is **required** for all countries using nOPV2 under the EUL. This document should be read in conjunction with Preparing for nOPV2 Use: An overview on requirements for countries.*[3]

While several resources have been developed to support nOPV2 use in-country (see **Vaccine safety surveillance resources** at the end of this document), this guidance outlines the steps required to meet and implement EUL criteria for safety surveillance (see **Fig. 3**). (A complete list of all readiness requirements by category is available in **Annex A**.)

Steps toward nOPV2 use in a country

Step 1: **Getting ready for nOPV2 use** – In order for countries to use nOPV2, they must meet established readiness requirements. For safety, these requirements include: having an established system for AEFI surveillance; developing an AESI monitoring protocol, an operational plan for implementing nOPV2 safety surveillance and a series of vaccine safety trainings; and ensuring a functional Causality Assessment Committee.

Step 2: **Conducting nOPV2 campaigns** - Before launching an nOPV2 response, each country must review a checklist of activities to ensure all requirements are met and all systems and processes that were created to support nOPV2 readiness are followed through, implemented and upheld.

Step 3: **Implementing post-campaign activities** - Once nOPV2 has been used in a country, a series of ongoing safety surveillance activities related to data analysis and interpretation, reporting and data sharing are required. Data requirements and timelines for submission are explained later in this document.

[3] Preparing for nOPV2 Use: An overview on requirements for countries. Geneva: World Health Organization; 2021 (http://polioeradication.org/wp-content/uploads/2021/10/nOPV2-Requirements-Overview-for-Countries.pdf.) All documents and guidance on nOPV2 can be found at http://polioeradication.org/nOPV2.

Fig 3. Steps toward nOPV2 readiness verification, use and implementation

Step 1: Getting ready for nOPV2 use

Four vaccine safety criteria are required for countries to verify readiness for nOPV2 use under EUL commitments (see **Table 1**).

Table 1. Summary of safety-related readiness requirements for in-country nOPV2 use

Req #	Requirement	What needs to be submitted
F1	Confirmation of nOPV2 safety surveillance monitoring activities, including: (1) an active AESI safety monitoring protocol for nOPV2; and (2) a national AEFI surveillance manual or abridged guide and key forms.	• Existing national AEFI surveillance manual or abridged guide, including AEFI reporting form and AEFI investigation form • nOPV2 AESI active search guide/protocol
F2	An operational plan for implementing nOPV2 safety surveillance, which includes plans for implementing AEFI and AESI surveillance, along with plans for managing a vaccine-related event (VRE) and confirmation of data-sharing processes and timelines.	• Operational plan for implementing nOPV2 safety surveillance activities • Key components of the VRE response plan • Data-sharing process and timelines for sharing of data with WHO country office / GPEI, globally and with other countries
F3	Key nOPV2-related safety trainings have been completed or are planned.	• Completed training status template, which covers trainings already conducted and outlines those planned
F4	Causality Assessment Committee terms of reference (TORs) along with a list of members (noting their specialty), training plans and, if applicable, previous meeting minutes.	• TORs for the committee • List of expert committee members and their specialties • Training reports: details on dates, facilitators and agenda on general refresher and nOPV2-specific training • If the committee is already functional, the minutes of the last expert committee meeting should be included. If the committee is newly established, certificates demonstrating all members have completed the trainings should be provided prior to the start of the campaign.

Each requirement is detailed below as part of "Step 1: Getting ready for nOPV2 use." In preparation of their documentation, countries should adapt all materials to suit the local country context.

Before submission for nOPV2 readiness verification, countries should confirm their documentation matches all criteria and circulate it for review by the relevant in-country partners. Support is available from regional and global teams. Country teams are welcomed and encouraged to reach out directly to technical focal points who can be found through the WHO regional office or by emailing nOPV2@who.int.

F1. Confirmation of nOPV2 safety surveillance monitoring

Requirement: Confirmation of nOPV2 safety surveillance monitoring activities, including: (1) an active AESI safety monitoring protocol for nOPV2; and (2) a national AEFI surveillance manual or abridged guide and key forms.

Meeting this requirement helps identify the already-existing systems for AEFI surveillance and complements them by developing an active AESI safety monitoring protocol for nOPV2 use.

The AESI safety monitoring protocol should 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.

The protocol provides the active safety surveillance system for conditions of interest for AESI following nOPV2 use, and as such should include the following components:

- case definitions;
- country-specific surveillance processes;
- data flow;
- country-specific forms; and
- defined roles and responsibilities.

To support the active search for AESI conditions, countries should plan to:

- draft and validate a protocol for AESI active case search; and
- print the screening tool for AESI active case search for district disease surveillance officers (two per week).

An existing national AEFI manual for passive safety surveillance should already be in place. To meet the requirement, the AEFI surveillance manual should be submitted in its entirety or as an abridged guide developed to support implementation by frontline health workers.

Resources to support countries

Forms and Guides

- nOPV2 AESI surveillance guide includes forms for AESI reporting, line listing, case ascertainment and data abstraction
- AEFI reporting form and AEFI investigation form
- Overview of safety surveillance and response (video)

nOPV2 examples

- AEFI national surveillance guides
- AEFI abridged guides

To support the implementation of AEFI surveillance, countries should plan to:

- draft, validate, print and disseminate to subnational levels a national manual for AEFI surveillance; or
- draft, validate, print and disseminate to subnational levels an abridged version of the AEFI surveillance manual.

Please note that if a country-specific AEFI manual or abridged AEFI guide already exists, then the drafting and validation steps described above may not be necessary.

Required

1. ***Existing AEFI surveillance manual or abridged guide. If submitting abridged guide, also submit the AEFI reporting form and AEFI investigation form.***
2. ***nOPV2 AESI active search guide or protocol.***

F2. An operational plan for implementing nOPV2 safety surveillance

Requirement: An operational plan for implementing nOPV2 safety surveillance is developed which details plans for implementing AEFI and AESI surveillance, along with plans for managing a vaccine-related event (VRE) and confirmation of data-sharing processes and timelines.

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, the operational plan summarizes key activities to enable sufficient safety monitoring of nOPV2 use.

The 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 defines 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 timeframe in which activities should be initiated and completed. Development of the safety budget will be done in coordination with the GPEI Outbreak Response and Preparedness Group (ORPG); nOPV2 safety focal points should liaise with the ORPG to understand the requirements for nOPV2 safety budget development.

Components of the safety surveillance operational plan

- Reporting
- Investigation
- Causality assessment
- Data analysis
- Crisis and risk communication
- Vaccine-related event response

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

Vaccine-related events (VREs) include a range of possible events related to vaccines that can negatively affect an immunization programme, of which an AEFI is one possible event. By proactively preparing for VREs, countries safeguard their immunization programme'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.[4]

Data flow is a third aspect of this requirement, as it supports timely detection and ensures information is available for action. To support the global review of safety data, an independent, nOPV2-specific subcommittee has been established under the Global Advisory Committee for Vaccine Safety (GACVS) to assess any safety signals associated with nOPV2 use. Data and timelines for submission to the GACVS subcommittee on nOPV2 are explained in **Step 3** below (see **Tables 3 and 4**). Some of the data may be submitted in summarized table form; these tables are included in **Annex C**. The operational plan should include the processes and timelines for data collection, reporting and analysis to support reporting to the Secretariat of the GACVS subcommittee on nOPV2.

Developing the operational plan will 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. AESI data may be owned and managed by the country's polio eradication programme, Expanded Programme on Immunization (EPI) or National Regulatory Authority (NRA) programme, and data should be shared between these programmes.

To meet the full requirement, countries should:

- draft an operational plan for AEFI surveillance and AESI active case search;
- complete the VRE tables in **Annex B**; and
- plan for data harmonization meetings to be held monthly with relevant staff at the subnational and quarterly with stakeholders at the national level.

Resources to support countries

Templates

- Operational plan tables
- VRE tables

Safety training materials

- Sample country trainings
- VRE guidance document

Required

1. Operational plan for implementing nOPV2 safety surveillance activities.
2. Key components of the VRE response plan.
3. Data-sharing process and timelines for sharing of data globally and with other countries.

[4] 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).

F3. Key nOPV2-related safety trainings

Requirement: Key nOPV2-related safety trainings have been completed or are planned, with the following details provided: (1) the title of the training, the date of the training, an agenda and a list of participants; (2) the title and role of each participant in the safety system; and (3) the requisite training areas: case investigation, reports management and processing for entry in data systems and AESI active case search.

The rollout of a new vaccine and related protocols to implement AESI surveillance requires rigorous training to ensure that the right people are well-equipped to conduct all necessary activities for nOPV2 safety surveillance. It also requires the training of trainers (ToT) so facilitators are up-to-date on the latest methods and approaches to AEFI monitoring, AESI surveillance and VRE response.

To meet the full requirement, countries should:

a. arrange 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;
b. ensure that every disease surveillance officer has completed three online courses on vaccine safety: (1) vaccine safety basics, (2) investigating AEFI, and (3) immunization safety;
c. organize a one-day training on AEFI / AESI for disease surveillance officers, which can be added to their surveillance training agenda; and
d. identify facilitators, list of participants and schedule trainings for later face-to-face two-day trainings for disease surveillance officers on investigation.

Resources to support countries

Template

- Training status template

Online courses

- Vaccine safety basics
- Investigating AEFI
- Immunization safety

Sample training materials

- Training agenda
- Training of trainers

Annex D provides a training status template that can be completed to meet this requirement.

Required

Completed training status template, which covers trainings already conducted and outlines those planned.

F4. Establishment of a Causality Assessment Committee

Requirement: Causality Assessment Committee terms of reference (TORs) along with list of members (noting their specialty), training plans and, if applicable, previous meeting minutes.

To ensure the Causality Assessment Committee is functional, has the right composition and can conduct nOPV2 AESI causality assessment, countries should select committee members in consideration of their specialties, and emphasis should be given to ensure the committee is trained sufficiently and briefed regularly.

To meet this requirement, countries should:

a. arrange a decree creating the national experts committee for pharmacovigilance (AEFI) and nominating the members, or submit minutes from a recent meeting to confirm the committee's existence and its current membership;
b. conduct an orientation training / refresher training for members of the Causality Assessment Committee on various tools and guides for nOPV2 safety surveillance and causality assessment; and
c. organize monthly meetings of the national experts committee during nOPV2 deployment.

Resources to support countries

Case studies

- ADEM
- AFP
- Anaphylaxis
- Aseptic meningitis
- Encephalitis
- GBS
- SIDS

Required

1. ***TORs for the Causality Assessment Committee.***
2. ***List of Causality Assessment Committee members and specialties. If specialties are not included in the official list, please add a separate document to specify specialties of members.***
3. ***Training reports: details on dates, facilitators and agenda for Causality Assessment Committee training, both a general refresher and nOPV2 specifics.***
4. ***If the Causality Assessment Committee is already functional, the minutes of the last meeting should be included. If the committee is newly established, confirmation all members have completed the trainings should be provided prior to the start of the campaign.***

Step 2: Conducting nOPV2 campaigns

As countries begin to conduct nOPV2 campaigns, nOPV2 safety readiness requirements must be upheld through the implementation of AESI surveillance activities. Routine or passive AEFI surveillance and active AFP surveillance should already be ongoing before nOPV2 use and should continue during and after nOPV2 campaigns per country-specific methods. A full pre-campaign checklist across all nOPV2 readiness categories can be found online.[5]

After readiness verification is achieved, countries will need to perform a set of safety activities pre- and post-campaign (see **Annex E**).

For safety surveillance during nOPV2 campaigns, countries must ensure:

- all trainings identified in the operational plan have been completed;
- AESI process and tools have been piloted and updated to reflect the country context;
- health facilities are equipped with AEFI surveillance manuals (full or abridged), outpatient department (OPD) 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., monthly district data harmonization meeting, quarterly national data harmonization meeting, monthly Causality Assessment Committee meeting);
- national safety team templates 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 nOPV2@who.int.

The *Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine Type 2 (nOPV2) Use* outlines different potential staff cadres and reporting structures based on whether AFP surveillance officers may be positioned to implement AESI surveillance – or whether a standalone AESI system should be established. [6]

All countries using nOPV2 under an EUL should consider enlisting a vaccine safety coordinator at the national or subnational level, depending on the scope of nOPV2 campaigns, who will collaborate with the MoH, the WHO and other partners to oversee and coordinate nOPV2 safety surveillance activities. Because active surveillance may generate numerous events, a designated person responsible for the management and coordination of AEFI / AESI information will be critical to the success of the safety surveillance and monitoring.

[5] nOPV2 pre-campaign checklist: Activities to complete prior to launch of nOPV2 response. (https://bit.ly/nOPV2-pre-campaign-checklist).
[6] Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine Type 2 (nOPV2) Use. Last updated: October 2021. (http://polioeradication.org/wp-content/uploads/2021/10/nOPV2-AESI-surveillance.pdf).

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 2**). A checklist for post-nOPV2 campaign activities across all categories can be found online.[7]

Table 2. 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 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 should enter the data into Vigiflow (or equivalent e-reporting tool). National safety team or NRA should simultaneously send notification of any SAE to nOPV2@who.int (can be an export of Vigiflow reporting or separate report).
Weekly until timeline noted below	*AEFI surveillance* ❒ Ensure AEFI investigations are completed in one week and AEFI reports filed in open data kit (ODK) or other platform. ❒ Ensure AEFI investigation reports are entered into Vigiflow (or equivalent e-reporting tool) and ensure they are submitted and received. *AESI surveillance* ❒ District surveillance officers line-list AFP and AESI cases and upload to ODK or other 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.) ❒ Coordinate prompt certification of results by MoH and submission of Causality Assessment Committee reports and investigation reports (in English) to nOPV2@who.int. *Safety data* ❒ Coordinate prompt MoH sign-off on release of AESI and AEFI data to ensure submission of data to nOPV2@who.int to comply with GACVS safety data requirements and timelines (see country safety data requirements). ❒ Submit all required data to allow for the regional office to review databases, including identifying silent reporting districts, completeness of forms, etc.

[7] nOPV2 post-campaign checklist: Activities to complete after an nOPV2 response. (https://bit.ly/nOPV2-post-campaign-checklist).

Table 2 (continued). Post-campaign checklist for safety surveillance

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 to monitor anaphylactic reactions, aseptic meningitis / encephalitis, ADEM, GBS / Miller Foster Syndrome, myelitis / transverse myelitis, AFP due to VDPV or VAPP, and unexplained death. ❒ Causality Assessment Committee meetings are held to review any nOPV2-related AEFI/AESI data.
For 6 months following the last round of nOPV2	❒ Systematic contact sampling of AFP cases (at least 3 contacts per case) for 6 months after last round of nOPV2.

Table 3. Data requirements by expected submission date following the first round (R1) of nOPV2 campaign use

Weeks after R1	Data category	Required items	Format of data
+ 6 weeks	**Preliminary data**	Any preliminary data available 6 weeks after R1 should be submitted (in English). REMINDER that personal identifying information (PII) must be redacted in line-listed and individual-level case data	As below
+ 11 weeks	**SIA data**	Summary of SIA R1 campaign (coverage, dates, number of doses) by national and regional levels	See template in Annex C. Complete Table C1 of target denominator, doses administered and coverage at the national and regional levels.
		Summary of surveillance indicators by national and regional levels	See templates in Annex C. Complete Tables C2-C5 with number and type of healthcare facility where AESIs present/are captured by national and regional levels. Number of areas with documented AEFI reporting, and AEFI reporting rate.
	AFP	Line-listed AFP case data, including review of the AFP data to confirm the categorization of each case, including provisional. PII must be redacted	Line listing – suspected and confirmed diagnoses, patient demographics (exclude patient identifiers)
	AESI	AESI line listing, including provisional and/or confirmed. Confirm matches other sources of data inputs, including AESI reporting form, AESI case ascertainment form and condition-specific data abstraction forms. PII must be redacted.	Line listing – minimum information of age, sex, province, date(s) of nOPV2, date(s) of AESI symptom onset, AESI diagnosis (provisional and/or confirmed), AESI outcome (or severity description), relevant investigations including any pending/awaited, relevant medical history, whether case was also listed as an AEFI (exclude patient identifiers).
		Abstracted data from AESI cases' clinical records	Case narrative, including test results and diagnostic certainty
	AEFI	AEFI line listing, including provisional and/or confirmed. Confirm line listing matches other sources of data inputs, including AEFI reporting form and AEFI investigation. PII must be redacted.	Line listing – minimum information of age, sex, province, date(s) of nOPV2, date(s) of AEFI symptom onset, AEFI diagnosis (provisional and/or confirmed), AEFI outcome (or severity description), relevant investigations inc. any pending/awaited, relevant medical history (exclude patient identifiers)
		Investigation reports of serious AEFIs with PII redacted	Investigation reports with PII redacted and/or submitted as an export from Vigiflow where used
	Causality	Causality Assessment Committee reports (in English), including information on the interim and final classification of cases	Full details of the clinical characteristics of each case considered and the rationale of the committee's classification, details of pending investigations of any case, information on the diagnostic certainty according to available case definition (e.g., Brighton Collaboration)
+ 19 weeks	**VAPP**	Suspected VAPP 60-day follow-up exam outcome	Case narratives including test results and diagnostic certainty
	Causality	Causality Assessment Committee reports (in English) for VAPP cases	Case narratives including test results and diagnostic certainty

Table 4. Data requirements by expected submission date following the second round (R2) of nOPV2 campaign use

Weeks after R2	Data category	Required items	Format of Data
+ 11 weeks	**SIA data**	Summary of SIA R2 campaign (coverage, dates, number of doses) by national and regional levels	See template in Annex C. Complete Table C1 of target denominator, doses administered and coverage at national and regional levels.
		Summary of surveillance indicators by national and regional levels	See templates in Annex C. Complete Tables C2-C5 with number and type of healthcare facility where AESIs present are captured by national and regional levels. Number of areas with documented AEFI reporting and AEFI reporting rate.
	AFP	Line-listed AFP case data, including review of the AFP data to confirm the categorization of each case, including provisional. PII must be redacted.	Line listing – suspected and confirmed diagnoses, patient demographics (exclude patient identifiers)
	AESI	AESI line listing, including provisional and/or confirmed. Confirm matches other sources of data inputs, including AESI reporting form, AESI case ascertainment form and condition-specific data abstraction forms. PII must be redacted.	Line listing – minimum information of age, sex, province, date(s) of nOPV2, date(s) of AESI symptom onset, AESI diagnosis (provisional and/or confirmed), AESI outcome (or severity description), relevant investigations, including any pending/awaited, relevant medical history, whether case was also listed as an AEFI (exclude patient identifiers)
		Abstracted data from AESI cases' clinical records	Case narrative including test results and diagnostic certainty
	AEFI	AEFI line listing including provisional and/or confirmed. Confirm matches other sources of data inputs including AEFI reporting form and AEFI investigation. PII must be redacted.	Line listing – minimum information of age, sex, province, date(s) of nOPV2, date(s) of AEFI symptom onset, AEFI diagnosis (provisional and/or confirmed), AEFI outcome (or severity description), relevant investigations inc. any pending/awaited, relevant medical history (exclude patient identifiers)
		Investigation reports of serious AEFIs with PII redacted.	Investigation reports with PII redacted and/or submitted as an export from Vigiflow, where used.
	Causality	Causality Assessment Committee reports (in English), including information on the interim and final classification of cases	Full details of the clinical characteristics of each case considered and the rationale of the Committee's classification, details of pending investigations of any case, information on the diagnostic certainty according to available case definition (e.g., Brighton Collaboration)
R2 + 19 weeks	**VAPP**	Suspected VAPP 60-day follow-up exam outcome	Case narratives including test results and diagnostic certainty
	Causality	Causality Assessment Committee reports (in English) for VAPP cases	Case narratives including test results and diagnostic certainty

Annex A: Readiness requirements

For further guidance and details, see: *Preparing for nOPV2 Use: an overview on requirements for countries*

Category	Ref #	Requirement
Coordination	A1	Confirmation that a national coordinating mechanism/body has been created and technical committees have been established to oversee preparations for nOPV2 across the following critical areas: a) cold chain, logistics and vaccine management; b) safety/causality; c) advocacy, communications and social mobilization; d) surveillance; and e) laboratory.
Approvals	B1	Official documentation (letter, meeting minutes) confirming national decision by the relevant national immunization body to use nOPV2 for outbreak response.
	B2	Documentation from the NRA confirming approval for the import and use of nOPV2.
Cold Chain / Vx Mgmt	C1	National logistics plan is updated to include a) cold chain equipment inventory and gap analysis, b) updated vaccine management tools for nOPV2 (50 dose vial), and c) vaccine management plans, outlining how vial tracking and disposal will be handled.
Surveillance	D1	National surveillance guidelines and supporting documents are updated to include: a) plans for active case search at priority sites; b) plans confirming 60-day follow-up for all AFP cases with nOPV2 detected in stool samples; and c) plan for collecting vaccination coverage data from community members around AFP VDPV2 cases.
	D2	Provide evidence that the CIF has been adapted (if needed) and records polio routine and SIA doses by submitting 3 filled in CIFs.
	D3	A primary immunodeficiency disorder (PID) diagnostic capacity checklist has been completed.
Safety	F1	Confirmation of nOPV2 safety surveillance monitoring activities including: a) active AESI safety monitoring protocol for nOPV2; and b) national AEFI surveillance manual or abridged guide and key forms.
	F2	An operational plan for implementing nOPV2 safety surveillance is developed, which includes plans for implementing AEFI and AESI surveillance, along with plans for managing a vaccine-related event (VRE) and confirmation of data sharing processes and timelines.
	F3	Key nOPV2-related safety trainings have been completed or are planned.
	F4	Causality assessment committee is oriented on nOPV2 and equipped to conduct AEFI/AESI causality assessments as demonstrated through: a) terms of reference along with list of members (noting their specialty); b) training plans; and c) if applicable, previous meeting minutes.
Advocacy, Communi-cations and Social Mobilization (ACSM)	G1	Finalized advocacy strategy for key in-country stakeholders (e.g., medical practitioners, religious and community leaders).
	G2	C4D action plan that includes: a) nOPV2 communications and messaging adapted to the local context; b) key actors, including frontline workers, have been trained or plans are detailed to provide training; c) all stakeholders have been mapped and plans for sensitization outlined; d) concrete plans for digital platforms have been developed; e) all necessary messaging, tools and products and f) the outline of how the country will meet the communication-specific EUL commitments.
	G3	A crisis communications plan that addresses possible VREs and possible public controversy. Detailed digital and misinformation management plan and implementation structure description. The plan should include tailored social listening approaches, content to respond to misinformation on-line and offline, and plan on how crisis communications training was/will be conducted.
Lab	H1	A plan has been developed to prepare the national lab for nOPV2 use, including updating the isolation algorithms and stocking/ training on the ITD testing kits for both AFP and ES along with modifications to the reporting mechanism.
	H2	Relevant laboratories are prepared to ship samples to CDC or NIBSC for complete genome sequencing.

Category E, which related to environmental surveillance requirements under the initial use phase, is now a recommended but not required activity in the EUL period. No documents/data need to be submitted for verification under category E.

Annex B

Operational plan template

The operational plan submitted from countries should 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 should 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 B1: Before campaign activities for operational plan

Objective	**Key gaps** (describe briefly the existing gaps)	**Activity to be completed before the campaign starts**	**Person responsible for doing the activity prior to campaign launch**	**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 ☐Print enough forms to supply all the health facilities with		
Investigation - *Investigate all serious AEFIs to generate sufficient information for causality assessment par the experts committee*		☐Make the reporting form available to all regional health teams ☐Train regional focal point on investigation ☐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		
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 record in the planned training template (include link)		
Data analysis - *Monitor the performance of the safety surveillance* - *Monitor the safety profile of the vaccine*		☐Ensure data collection system (e.g., ODK forms) are updated and disseminated to the safety focal points		
Crisis communication		☐Orient the committee for crisis communications on AEFI and complete VRE tables below.		
Risk communication *Provide information and clear orientations that would prevent an AEFI to lead to a crisis*		☐Integrate into vaccinator training information that needs to be given to vaccinees prior to nOPV2 administration		

Table B2: During campaign activities for operational plan

Objective	**Key gaps** (describe briefly the existing gaps)	**Activity to be done during the campaign**	**Person responsible for doing this activity during the campaign**	**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*		☐ Provide vaccine safety focal points with resources for transportation and communication to collect reports from health facilities		
Investigation - *Investigate all serious AEFIs to generate sufficient information for causality assessment par the experts committee*		☐ Provide resources for ambulance referral and hospital management for serious cases, including all lab tests ☐ Provide resources for field investigation		
Causality assessment - *Classify all the cases to give a response to the community and update the safety profile of the vaccine*		☐ Hold at least monthly meetings of the Causality Assessment Committee for causality assessment of serious cases		
Data analysis - *Monitor the performance of the safety surveillance* - *Monitor the safety profile of the vaccine*		☐ Hold monthly data harmonization meeting by focal points at regional level ☐ Hold monthly data harmonization meetings by national implementation team		
Data sharing		☐ Submit data to the secretariat of the GACVS subcommittee for nOPV2 ☐ Add link to GACVS safety data specifications, timelines and forms		
Crisis communication		☐ Have a representative of the crisis committee in the Causality Assessment Committee meetings		
Risk communication *Provide information and clear orientations that would prevent an AEFI to lead to a crisis*				

Table B3: After campaign activities in the operational plan

Objective	**Key gaps** (describe briefly the existing gaps)	**Activity to be done after the campaign**	**Person responsible for doing this activity after the campaign**	**Time frame** (specify by when activity needs to start and be completed)
Reporting - *Report all AEFIs so as to rapidly detect any serious AEFI and respond effectively*				
Investigation - *Investigate all serious AEFIs to generate sufficient information for causality assessment par the experts committee*		☐ 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		
Causality assessment - *Classify all the cases to give a response to the community and update the safety profile of the vaccine*		☐ Hold meeting of the Causality Assessment Committee for causality assessment of serious cases		
Data analysis - *Monitor the performance of the safety surveillance* - *Monitor the safety profile of the vaccine*		☐ Hold monthly data harmonization meeting by focal points at regional level ☐ Hold monthly data harmonization meetings by national implementation team		
Data sharing		☐ Submit data to the secretariat of the GACVS subcommittee for nOPV2 ☐ Add link to GACVS safety data specifications, timelines and forms		
Crisis communication				
Risk communication *Provide information and clear orientations that would prevent an AEFI to lead to a crisis*				

VRE tables

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

Table B4: Assessing VRE impact

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

Table B5: Specific actions for low, medium, and high impact VRE

	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 should 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 C

Data requirement tables

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

Table C1: SIA Information by country

#	Particulars	National	Subnational level* 1	Subnational level* 2	Subnational level* 3, etc.
	Round 1 (R1) dates				
1	R1 Target population ≤ 5 years				
2	R1 Children vaccinated				
3	R1 Vaccination coverage (%)				
	Round 2 (R2) dates				
4	R2 Target population ≤ 5 years				
5	R2 Children vaccinated				
6	R2 Vaccination coverage (%)				

*subnational level = secondary administrative level (ex: province, state, county, etc.)

Table C2A: Type of health care facilities under AEFI and AESI surveillance, by country

Name of country	Name of region	Target population n (%)	Public/ government health facilities n (%)	Private/NGO/ faith-based facilities n (%)	Referral facility (do NOT include name of facility but reference by # instead)	Comments

Table C2B: AESI surveillance

Catchment area of sentinel sites						Other
Name of country	Sentinel hospital (do NOT include name of facility but reference by # instead)	Target population n (%)	Public/ government health facilities n (%)	Private/NGO/ faith-based facilities n (%)	Referral facility (do NOT include name of facility but reference by # instead)	

Table C3: Regional-level AEFI functionality and quality indicators

	# (%) Month X	# (%) Month X	# Regional-level units
Regional level units with silent AEFI reporting[a]			
Regional level units not submitting monthly AEFI reports[b]			
Regional level units with >10 AEFI reports/ 100,000 doses of all vaccines administered			

[a] Number of regional-level units where AEFI reports were zero in the month of XX / Number of regional-level units X 100

[b] Number of admin-level 2 units where AEFI reports were not received at the national level in the month of XX / Number of admin-level 2 units X 100

Note: Indicators are modeled after COVID-19 AEFI indicators. Information in SITREPS shared by month, so indicators by Round will not be presented

Table C4: National level AEFI functionality and quality indicators

	# (%) Month X	# (%) Month X	# units overall
# AEFI reports / 100,000 vaccine doses administered (for all vaccines in the same reporting period as nOPV2)			
Serious AEFI investigated (for all vaccines in the same reporting period as nOPV2)			
Serious nOPV2 AEFI investigated			
Serious AEFI cases with causality assessed (for all vaccines in the same reporting period as nOPV2)			
Serious nOPV2 AEFI cases with causality assessed			
Serious AEFI cases with causality assessed			
Serious nOPV2 AEFI cases with causality assessed			

Table C5: Percentage of population covered by active AESI surveillance facilities

# facilities in campaign area	Population < 5 years old covered by these facilities	% of population covered	# facilities with active AESI surveillance in campaign area	Population < 5 years old covered by these facilities	% of population covered	# facilities in campaign area	Population < 5 years old covered by these facilities	% of population covered	# facilities with active AESI surveillance in campaign area	Population < 5 years old covered by these facilities	% of population covered

Annex D

Training status template

Editable version of this template can be found online: Training status template

Table D1: Training status template

Training title	Target audience	Date (completed or planned)	Topics covered	List of participants (name, title/role)
Case investigation			•	•
Reports management and processing for entry in data systems			•	•
AESI active case search			•	•
			•	•
			•	•
			•	•

Annex E

Activities to implement safety surveillance (after verification achieved)

Pre-campaign

- ❒ Lead preparation for active AESI surveillance at sentinel hospitals.
  - 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 programme, 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 trainings as described in consolidated training overview document.
  - Conduct trainings 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 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 workshop 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 programme, disease surveillance, communications).

Active surveillance implementation period (during a campaign and through six weeks after the last day of the last campaign round)

- ❒ 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 become 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, FDA, others) to conduct analyses of AESI and AEFI data with support from Regional nOPV2 Safety Focal Points, P95 and nOPV2 Safety Subgroup.
  - Serve as a point person and follow schedule for sharing data with Regional nOPV2 Safety Focal Points, P95, and nOPV2 Safety Subgroup.
  - Provide technical support for AEFI and AESI investigations.

- Work with EPI, the polio eradication programme 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.
- Serve as point person for sharing data with Regional nOPV2 Safety Focal Points, P95 and nOPV2 Safety Subgroup.

❒ 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.
- Participate in weekly calls with Regional nOPV2 Safety Focal Point.

❒ 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 become 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, FDA, others) to conduct analyses of AESI and AEFI data with support from Regional nOPV2 Safety Focal Points, P95 and nOPV2 Safety Subgroup.
- Serve as a point person for sharing data on specified schedule with Regional nOPV2 Safety Focal Points, P95 and nOPV2 Safety Subgroup.

❒ Support EPI and NRA in review of data collected through passive AEFI system.
a. Support analysis and identification of signals, as needed.
b. Serve as point person for sharing data on specified schedule with Regional nOPV2 Safety Focal Points, P95 and nOPV2 Safety Subgroup.

❒ 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.
d. Participate in weekly calls with Regional nOPV2 Safety Focal Points.

❒ 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.

Vaccine safety surveillance resources

Table 5. nOPV2 vaccine safety surveillance guidance documents

Resource	Description	For more information
Guide for Surveillance of Adverse Events of Special Interest (AESI) during Novel Oral Polio Vaccine Type 2 (nOPV2) Use	Provides a comprehensive overview of AESI surveillance, case definitions for AESI, training agendas and training materials on AEFI and AESI surveillance and causality assessment, and forms to assist countries in the collection of nOPV2 AESI data, that include: (1) reporting form; (2) line listing form; (3) case ascertainment form; and (4) data abstraction form for each AESI condition.	Link
Novel Oral Polio Vaccine Type 2 (nOPV2) Vaccine Related Event (VRE) Response Plan.	Ensures surveillance for vaccine-related events and preparedness for communication are aligned and coordinated. Intended to be used by vaccine safety focal persons, such as the vaccine safety coordinator, working in conjunction with communications focal persons.	Link
Pre-campaign checklist	Details activities that should be completed across all categories of the EUL requirement or areas of work before nOPV2 use.	nOPV2 pre-campaign checklist
Post-campaign checklist	Details activities that should be completed across all categories of the EUL requirement or areas of work before nOPV2 use.	nOPV2 post-campaign checklist