# COVID-19 Vaccines Safety Surveillance Guideline

**Integrated Addendum to the Third Edition of The Guideline for Surveillance and Response to Adverse Events Following Immunization, EFDA, Addis Ababa, Ethiopia, Sep 2021.**

## Contents

# Abbreviations and acronyms

| | |
|---|---|
| AEFI | Adverse Events Following Immunization |
| AEs | Adverse Events |
| AESI | Adverse Events of Special Interest |
| CA | Causality Assessment |
| COVID-19 | Corona Virus Disease Identified/Determined in 2019 |
| EFDA | Ethiopian Food and Authority |
| EPI | Expanded Program on Immunization |
| EUA | Emergency Use Authorization |
| EUL | Emergency Use Listing |
| GBS | Guillain Barre Syndrome |
| MoH | Ministry of Health |
| NPVC | National Pharmacovigilance Center |
| NSAC | National Safety Advisory Committee |
| PHEIC | Public Health Emergency of International Concern |
| PHEM | Public Health Emergency Management |
| PV | Pharmacovigilance |
| RHB | Regional Health Bureau |
| RPVC | Regional Pharmacovigilance Center |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Caused byCoronavirus type2 |
| TOR | Terms of Reference |
| TTS | Thrombosis with thrombocytopenia syndrome |
| WEO | Woreda EPI Officer |
| WHO | World Health Organization |

# 1. Background

On 30 January 2020, World Health Organization (WHO) declared the outbreak due to a novel coronavirus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), also known as COVID-19, as a public health emergency of international concern (PHEIC). It was first reported to WHO on December 31, 2019. By 12 March 2020, due to its rapid global spread, the outbreak was declared a pandemic. As of September 21, 2021, the pandemic has already caused the loss of more than 4.6 million lives. The world is employing different strategies to tackle the pandemic.

One essential strategy to control this pandemic is the rapid development of safe and effective vaccines. Unprecedented efforts are being made to develop different types of vaccines simultaneously.Within a short period of time, some COVID-19 vaccines were developed and given WHO emergency use listing. Then after, many countries have started vaccine rollout primarily for healthcare workers and those most-at-risk to mitigate the public health and economic impact of the pandemic. Similarly, onMarch 13, 2021, Ethiopia has launched COVID-19 vaccine rollout for health professionals and essential workers andothers at risk groups.

The developed COVID-19 vaccinesare expected to undergo extensive testing and review for safety, immunogenicity, and efficacy in the laboratory, in animals, and inphases of clinical trials before licensure. However, due to the pandemic nature of the diseases and rapid need of the COVID-19 vaccine, the phase III clinical trials are ongoing simultaneously with the widespread use of COVID-19 vaccines following emergency use listing by mostcountries' regulatory authority. Due to theavailability of limited safety data especially on large group of people, regulatory authoritiesshould focus on a range of surveillance options like passive (spontaneous), active surveillance and others tomonitor safety of the vaccinespost-licensure or during use.

Ensuring the functionality ofstrengthenedAdverse Events Following Immunization (AEFI)pharmacovigilance system and conducting of active surveillance during the introduction of a new vaccine, like COVID-19 in a country will help the regulatory authority detect,report, investigate,analyze and manageAEFIs. The ultimate goal of these efforts is to prevent the spread of the diseases and protect health and wellbeing of the entire population from vaccine preventable diseases.In Ethiopia, the Ethiopian Food and Drug Authority (EFDA) is legally responsible for market authorization and safety monitoring of pharmaceutical products including

vaccines.EFDA uses its pharmacovigilance system to collect any suspected adverse events (AE) including AEFIs.

AEFI is an untoward post-immunization medical incident that can cause public concern. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease. Reported adverse events can either be true adverse events resulting from the vaccine or immunization process or coincidental events that are not due to the vaccine or immunization process but are temporally associated with immunization.

Detailedinvestigation of the reported cases andconducting causality assessmentmay trigger regulatory action including, immunization programstrengthening to avoid errors, revoking the marketing authorization of a vaccine, instructing vaccine manufacturers to change their product labels, restricting the use of vaccines to specific client groups or recalling defective vaccine batches from the market. Thus, this supplementary document to the AEFI surveillance and response guideline, helps to guide safety monitoring of COVID-19 vaccines.

## 2.Objective of the Guideline

The objectives of this guideline are:

- To provide an overview of COVID-19 vaccines.
- To list the common AEFIs and Adverse events of special interest of COVID-19 vaccines.
- To describe prevention and management strategies of COVID-19 AEFIs
- To clarify reportable AEFIs
- To define the routes of reporting of AEFIs from the lower level of health care system (health centers, health posts or vaccination site) to the national pharmacovigilance center.
- To describe the currently available AEFI reporting methods and tools for COVID-19 vaccine.
- To describethe roles and responsibilities of stakeholders involved in COVID-19 vaccine safety surveillance.
- To guide on the safety communication channels and methods of COVID-19 vaccines safety and updates.

# 3.COVID-19 vaccines and AEFIs

## 3.1. COVID-19 Vaccines

The fight against COVID-19 has seen vaccine development move at record speed, with more than 170 different vaccines in trials. There are more vaccine candidates simultaneously in the pipeline for COVID-19 than ever before for an infectious disease. All of them are trying to achieve the same thing – immunity to the virus, and some might also be able to stop transmission. They do so by stimulating an immune response to an antigen, a molecule found on the virus. In the case of COVID-19, the antigen is typically the characteristic spike protein found on the surface of the virus, which it normally uses to help it invade human cells.

There are four categories of COVID-19 vaccines in clinical trials: whole virus (e.g., Sinopharm), protein subunit (e.g., Novavax, Nuvaxovid), viral vector (e.g., AstraZeneca, Janssen), and nucleic acid(e.g., Pfizer, Moderna)). Some of them try to smuggle the antigen into the body, others use the body's own cells to make the viral antigen.The COVID-19 vaccines vary based on dosage, number of doses needed, intervals between doses, and how the vaccine must be stored and handled.

There are several COVID-19 vaccines validated for use by WHO (given Emergency Use Listing/EUL). The WHO Emergency Use Listing process determines whether a product can be recommended for use based on all the available data on safety and efficacy and on its suitability in low- and middle-income countries. Vaccines are assessed to ensure they meet acceptable standards of quality, safety and efficacy using clinical trial data, manufacturing and quality control processes. The assessment weighs the threat posed by the emergency as well as the benefit that would accrue from the use of the product against any potential risks. In line with their national regulations and legislation, countries have the autonomy to issue emergency use authorizations for any health product. Domestic emergency use authorizations are issued at the discretion of countries and not subject to WHO approval. As of 12 January 2022, the following vaccines have obtained EUL:

- The Pfizer/BioNTech Comirnaty vaccine, 31 December 2020.
- The SII/COVISHIELD and AstraZeneca/AZD1222 vaccines, 16 February 2021.
- The Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson, 12 March 2021.

- The Moderna COVID-19 vaccine (mRNA 1273), 30 April 2021.
- The Sinopharm COVID-19 vaccine, 7 May 2021.
- The Sinovac-CoronaVac vaccine, 1 June 2021.
- The Bharat Biotech BBV152 COVAXIN vaccine, 3 November 2021.
- The Covovax (NVX-CoV2373) vaccine, 17 December 2021.
- The Nuvaxovid (NVX-CoV2373) vaccine, 20 December 2021

In line with the WHO recommendations, the EFDA has given emergency use authorization (EUA) for four COVID-19 vaccines namely AstraZeneca, Janssen, Pfizer and Sinopharm. Furthermore, Moderna and Sputnik are under review for EUA. Vaccine rollout has been going on using the vaccines given EUA and EFDA has been conducting safety monitoring surveillance on these vaccines to determine the type and nature of AEFIs and detect any AESIs.

## 3.2. Adverse Events Following Immunizationwith COVID-19 vaccines

**Adverse event following Immunizations**:are any untoward medical events that follow immunization, and that do not necessarily have a causal relationship with the immunization. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease. AEFIs can be classifiedbased on the possible causeas:vaccine product-related,vaccine-quality defect-related, immunization error-related, immunization anxiety-related reactions and coincidental events.

***Vaccine product-related reaction:*** An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of thevaccine product.The identification of rare (occurring in 0.01% to less than 0.1% of immunized individuals) and very rare (occurring in <0.01% of individuals) adverse eventsis insufficient at the time of COVID-19 vaccine licensure and more information will be needed for which AEFI surveillance has to be strengthened.Clearly distinguishing genuine vaccine product-related events from coincidental events or concomitant medication-related AEFIs will be a challenge.

***Vaccine quality defect-related reaction:*** An AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the vaccine manufacturer.Potential vaccine quality defects for new COVID-19 vaccine platforms might not be known at the time of authorization. Hence, vaccine safetysurveillance must be strengthened to be able to gather this knowledge.The rapid scaling up of vaccine production also poses additional potential risks and theidentification of the exact substance in the vaccine formulation causing the adverse eventwill be needed.The likelihood of AEFIs being cause by a substandard or counterfeit version of COVID-19vaccines should also be considered.

***Immunization error-related reaction:*** An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and so is preventable. It is anticipated that COVID-19 vaccines will be administered on a massive scale in a short timeinterval with minimum training and field preparation and hence,immunizationerror-related reactions are anticipated. Also, staff who are not familiar with immunization,may be asked to perform immunization duties. Multiple vaccines with different specifications for storage, administration, dose etc, may be in use in a country simultaneously.

***Immunization anxiety-related reaction****:*Itis an AEFI arising from anxiety about the immunization and is unrelated to the content of the vaccine but to fear of the injection. Individuals can react in anticipation to and as a result of an injection of any kind. A larger number of Immunization anxiety-related reactions are anticipated due to numerous factors including older age groups, the different vaccination environments, the novelty of the vaccines and their administration modalities.

***Coincidental event:*** An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety. An event happening after immunization is wrongly considered to be caused by immunization. They mostly occur after a vaccination has been given but are not caused by the vaccine or its administration.Because of real and potential underlying comorbidities in a large number of the potential vaccinees, it will be challenging to differentiate true coincidental events from COVID-19 vaccine product related reactions or drug reactions or interactions.

Regardless of the cause of AEFIs,during clinical trials of COVID-19 vaccinesmostAEFIsreported were categorized as mild and/or moderate while a few are considered as **serious AEFIs**.

**A serious AEFI** is an event that results in death, hospitalization or prolongation of an existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth defect or is life-threatening or is a medically important event or reaction. The types and characteristics of serious AEFI particularly rare and very rare adverse events that could occur following COVID-19 vaccines are currently unknown.Careful investigation of serious AEFIs including **cluster**s and conducting subsequent causality assessment will help classify the AEFIs based on the possible cause and identify **signal**s.**A cluster** is when two or more AEFIs related in time, place or by vaccine occur. Two or morecases of the same or similar events in an AEFI cluster are usually associated with a particularvaccine manufacturer, a health facility, a vaccine batch, or a vial of vaccine, when multidosepresentations are used.When vaccines are administered on a massive scale, it is important for immunizationprogrammes to anticipate and prepare for clusters of AEFI as the chances of immunizationerrors and Immunization anxiety-related reactions are much higher than that during routineimmunization. Coincidental events can also occur as clusters.**A signal** is information that arises from one or multiple sources (including observations

andexperiments) which suggests a new potentially causal association, or a new aspect of a knownassociation, between an intervention and an event or set of related events, either adverse orbeneficial, that is judged to be of sufficient likelihood to justify verification. Signal detection, verification and response is a key activity that has to be specificallyaddressed in the COVID-19 context. Signals can best be identified by pooling of data frommultiple sources and analyzing if the pooled data points to the occurrence of a new eventthat could be causally related to the vaccine.

The researchers and developers of Covid-19 vaccines identified some adverse events as **adverse events of special interest**(AESI) and recommend their detection and reporting by regulatory authorities. **An AESI** is a pre-specified 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 special studies.AESIs are usually identified through active vaccine safety surveillance systems. AESI identified for COVID-19 vaccine surveillanceinclude:

- Vaccine-associated enhanced disease
- Multisystem inflammatory syndrome in children
- Acute cardiovascular injury (microangiopathy, heart failure, stress cardiomyopathy, coronary artery disease, arrhythmia, myocarditis)
- Coagulation disorder (thromboembolism, hemorrhage)
- Acute respiratory distress syndrome
- Acute kidney injury
- Generalized convulsion
- Guillain Barré Syndrome
- Acute liver injury
- Anosmia, ageusia
- Single organ cutaneous vasculitis
- Erythema multiforme
- Anaphylaxis
- Acute aseptic arthritis
- Meningoencephalitis
- Acute disseminated encephalomyelitis

- Thrombocytopenia

3.3. CommonAdverse Effects of COVID-19 vaccines

Like any vaccine, COVID-19 vaccines can cause AEFIs, most of which are mild or moderate and go away within a few days on their own. Most COVID-19 AEFIs reported to date have been general events, such as 'flu-like conditions' illness, headache, pain at the injection site, chills, fatigue, nausea, fever, dizziness, weakness, myalgia, and tachycardia. The chances of occurrence and severity of any of these AEFIsdiffer according to the specific vaccine. These events usually occur within seven days of vaccination and are not associated with serious illnesses. Serious reactions such as allergic and anaphylactic reactions are very rare and usually occur soon after vaccination, with a sudden onset. However, even though they are very rare, clinical trials and post marketing surveillance results have shown that serious or long-lasting AEFIs are possible. The mRNA-based vaccines are associated with a higher prevalence of local side effects, while the viral vector-based vaccine is associated with a higher prevalence of systemic side effects

3.3.1. Common Adverse Effects of Specific COVID-19 vaccines

Systemic Adverse effects such as fatigue, headache, muscle aches, and chills are common following administration of mRNA vaccines (e.g., Moderna, Pfizer), but they usually resolve within a day or two. Localized adverse effects, most notably pain at the injection site, are also common, and also resolve within a day or two. The rate of severe adverse effects (severe enough to interfere with a person's daily activities) appears to be in the range of 5 to 10 percent. The rate and severity of adverse events increases with vaccine dose. The rate and severity of adverse events also appears to be greater following a second dose of vaccine than following the first.

Injection site pain, headache/fatigue, muscle pain, malaise, chills, and joint pain are among the most common adverse effects of vector based covid-19 vaccines (e.g.,AstraZeneca, Janssen). Majority of these side effects resolve within 1–3 days after vaccination. When compared with the first dose, adverse reactions reported after the second dose ofAstraZenecaCOVID-19 vaccine were milder and reported less frequently.

The most common adverse effectsreported for viral based covid-19 vaccines (e.g., Sinopharm, Sinovac) were localized pain at the injection site, muscle pain, fatigue, and headache and/or dizziness.Most of these adverse effects were mild and lasted for only about 2 days. Furthermore,

clinical trial data for thevaccines has shown that trial participants who received the Sinovac vaccine reported a lower occurrence of fever in comparison to mRNA vaccines like the Pfizer-BioNTech and Moderna vaccine.

The most common adverseeffects reported for protein based COVID-19 vaccines (e.g., Nuvaxovid) were pain or tenderness at the injection site, tiredness, headaches, muscle or joint pain and generally feeling unwell.These adverse effects usually fade away after 1–2 days. According to the European Medicine Agency, localized adverse reactions are more common after the second dose of Nuvaxovid.

Even if most adverse events reported after administration of COVID-19 vaccine were mild/moderate, rare serious adverse events after COVID-19 vaccination may occur.Timely updates should be provided on the following serious adverse events of interest:

**Anaphylaxis after COVID-19 vaccination** is rare and has occurred in approximately 5 people per one million vaccinated. Anaphylaxis, a severe type of allergic reaction, can occur after any kind of vaccination. If it happens, healthcare providers can effectively and immediately treat the reaction.

**Thrombosis with thrombocytopenia syndrome** (TTS) after COVID-19 vaccination. TTS is a rare but serious adverse event that causes blood clots in large blood vessels and low platelets (blood cells that help form clots).Women ages 30-49 years, especially, should be aware of the increased risk of this rare adverse event. TTS following COVID-19 vaccination has been reported following the administration of Johnson & Johnson's/Janssen, AstraZeneca, Moderna and Pfizer-BioNTech.

Based on available data, there is not an increased risk for TTS after mRNA COVID-19 vaccination.

**Guillain-Barré Syndrome** (GBS) in people who have received the J&J/Janssen COVID-19 vaccine is rare. GBS is a rare disorder where the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis. Most people fully recover from GBS, but some have permanent nerve damage. These cases have largely been reported about 2 weeks after vaccination and mostly in men, many in those ages 50 years and older. Analysisof the available data found no increased risk of GBS after Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines).

**Myocarditis and pericarditis**:Inflammation of the heart muscle(myocarditis), and inflammation of the outer lining of the heart (pericarditis)may rarely occur after administration of COVID-19 vaccine. Most patients with myocarditis or pericarditis after COVID-19 vaccination responded well to medicine and rest and felt better quickly.Most cases have been reported after receiving Pfizer-BioNTech or Moderna, (mRNA COVID-19 vaccines) particularly in male adolescents and young adults.

3.4. Prevention and Management of COVID-19AEFIs

3.4.1.Prevention of AEFIs

COVID-19 vaccines are very rarely contraindicated. However, the following principles should be taken into consideration to minimize the chance of an allergic reaction after being vaccinated against COVID-19 and to use the vaccines safely and effectively.

- It is important to check for contraindications to avoid serious reactions
- A vaccine is contraindicated if there is a history of anaphylaxis to a given vaccine or its components in previous vaccinations.
- People who have had known severe allergic reactions, also called anaphylaxis, to any ingredient in the COVID-19 vaccines should not receive that vaccine.
- People who have had severe allergic reaction to any vaccine or treatment that is injected should consult their health care provider about balancing the risks and benefits of vaccination.
- People with allergies to foods, animals, environmental triggers (such as pollen), latex, or medications taken by mouth, or who have family members with past severe allergic reactions should consult healthcare provider before taking COVID-19 vaccine.
- Cold chain must be maintained properly and vaccine should be administered by a well-trained and skilled health worker.
- It is also necessary to follow the manufacturer instruction and recommendations.
- It is important to double-check the product-specific emergency use authorization fact sheet or package insert, users & health care provider’s guide and recommendations prepared by the national immunization program and the regulatory authority for age indication, route, dosage, and storage and handling requirements.

3.4.2. Management of AEFIs

Responding to AEFI may involve immediate short-term activities or/and long-term follow-up activities. Follow-up activities should be based on findings of investigations, causality assessments and recommendations by the investigation/expert committees.Major follow-up actions may have an impact on the national immunization programme, as well as onregional and global programmes and planning.

It is of utmost importance to ensure that proper and early treatment is received by affected vaccinees (patients), regardless of the diagnosis. Mild symptoms such as mild fever and pain are likely to be of short duration and can be managed by assuring and educating parents during immunization. Health workers need to know how to recognize AEFI, how to treat them or refer them to a clinician/hospital, and must report AEFI as soon as possible.

It is recommended to observe all vaccineesfor15 minutesfollowing vaccine administration at vaccination center to monitor for any immediate adverse reactions such as syncope and anaphylaxis. Sudden syncope and/or anaphylaxis and other serious adverse events can occur post-vaccination. Thus, emergency medicines and equipment must be immediately at hand whenever immunizations are given. All vaccinators must be familiar with the practical steps necessary to save life following anaphylaxis. Each vaccinating center must have an emergency kit with adrenaline.

## 4. AEFI Surveillance in Context of COVID-19 Vaccines(vaccinovigilance)

The unprecedented rapid development of the COVID-19 vaccines followed by their rapid large-scaleuse, pose unique challenges in monitoring vaccine safety and mitigating any potential risks through arobust AEFI Surveillance system.The AEFI surveillance cycle (Fig 4.1) outlines the different steps in identification (detection), notification, reporting, investigation, data analysis, causality assessment and feedback following all AEFI, including that of COVID-19 vaccines.

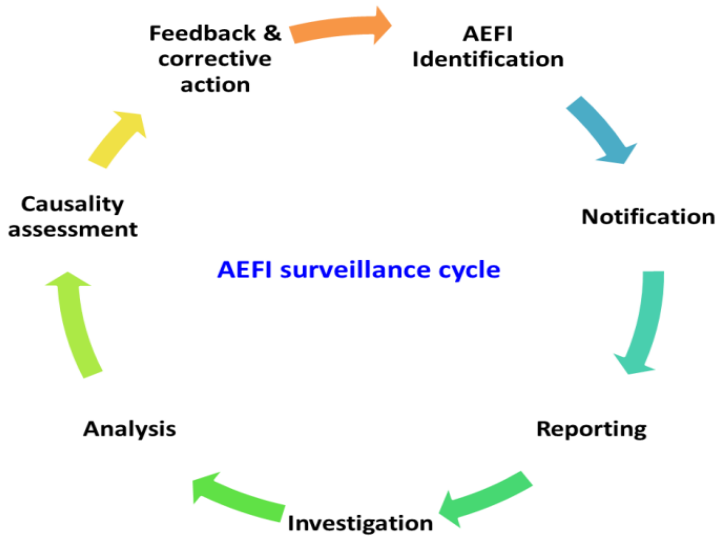



**Fig 4.1 AEFI surveillance cycle**

The key components of the AEFI surveillance system could be understood as follows:

- AEFI identification/detection: when the adverse event is first identified by the vaccine recipient.
- AEFI notification: when the event is brought to the notice of the health-care system, either by the patient or by their relative.
- AEFI reporting: when the first information of the event is obtained by a health-care worker (any person in the health-care system) and the information on the event is documented in an AEFI reporting form and is sent to the next level.
- AEFI investigation: when a detailed enquiry is made, and effort taken to collect adequate information so that the underlying cause of the event can be determined.
- AEFI Analysis: when the information of all events (minor or severe) is collated, and the data is processed to determine the occurrence of signals.

- AEFI Causality assessment: when all information about a particular case, obtained after completion of the investigation, is studied in detail, deliberated by experts and the underlying cause of the event is established.

The role of vaccine safety surveillance during COVID-19 vaccine introduction and use is to facilitate the early detection, investigation and analysis of AEFIs and AESIs to ensure an appropriate and rapid response.AEFI surveillance systems shall identify both known AEFIs seen in clinical trials as well as new events, including potential rare serious adverse reactions in all age groups, particularly adults.

## 4.1. AEFI Detection and Reporting

### 4.1.1. AEFI Detection

AEFI detection is the recognition of any unusual medical event following vaccination/immunization which can be done by vaccine recipients, parents of immunized children, health care providers and staff in immunization or health care facilities and reporting them to health care provider working within the healthcare system.AEFIscan also be detected through active surveillance, via sentinel sites or through cohort eventmonitoring. In addition, AEFIs may be detected in phase IV clinical studies of COVID-19 vaccineswhere they should be independently reported, assessed and processed, in compliance withthe study protocol and should not be reported through the passive reporting systems.

### 4.1.2. AEFI Reporting

For COVID-19 vaccines, it is essential to notify any safety concern and report all AEFIs that are brought tonotice by including all available information as accurately as possible. It should be clearly understood that, there is no need to confirm the cause of AEFIs to report them to the higher level.Health professionalsshould reportall AEFIs that occur after COVID-19 vaccine administration following appropriate channels and using one of the available reporting tools.

#### 4.1.2.1. COVID-19 vaccines AEFI Reporting Requirements and Channels

A health care provider who identifies an AEFI case after COVID-19 vaccination should completeAEFI case reporting form**(**Annex 7.1**)**and submit it to the health facility's immunization focalperson. The focalperson should prepare a copy for himself and thenshare the original report

to the woreda EPI focal person using the fastest means possibleas indicated in channels of reporting (Fig 4.2).In case of serious AEFIs, vaccine administrators should inform their supervisors and/or woreda EPIofficer immediately (over telephone) and complete the reporting form.The woreda EPI focal person should review the report;decide on whether the cases are serious or non-serious and share the report tothe zonalor regionalEPI officer (i.e., tonext higherlevel) through e-mail or fax immediately. The zonal or regional immunization officer should send the reports to EFDA within 24 hours after the occurrence of the events (Fig 4.2). Moreover, AEFI reports can be sent directly to the central EFDA' pharmacovigilance center, or to the nearest regional pharmacovigilance offices situated inthe six referral hospitals(Tikur Anbessa Specialized Hospital,Hawassa University Comprehensive Specialized Hospital, Felege Hiwot Referral Hospital,GondarUniversity Referral Hospital, Jimma University MedicalCenter andAyder Referral Hospitalor to the branch EFDA office's pharmacovigilance focal person at regions.

When the AEFI is judged to be investigated,investigation will be done in consultation with the regional/zonal/woreda focal person using standardized investigation form (Annex 7.2).In addition to reporting of AEFI using standard form, when the AEFI is judged to be serious, reporting should also include a telephone call, SMS message, email, direct conversation, or notification via an emergency letter.AEFI cases that need to be reported and investigated immediately include serious AEFIs, cluster AEFIs, AEFIs that concerns parents or community, AESIs, significant events of unexplained causeoccurring up to 1 year after COVID-19 vaccination,AEFIs as a result of potential immunization errors, events that are not listed in the product information and events with an unexpected high rate or unusual severity.Other non-serious AEFIs should be recorded on the standardized COVID-19 AEFI line list (Annex 7.3) and sent to the national level every month.

An AEFI report should contain all the necessary information regarding the vaccinee, the vaccine,reporter and the observed AEFI in order to make complete evaluation of the AEFI reports. Usually, the primary reporter, i.e., the immunization provider or health care worker, is responsible for providing most of the information required in the COVID-19 AEFI reporting form. However, vaccine recipients or their parents may complete the form by themselves and submit it to a health care provider.

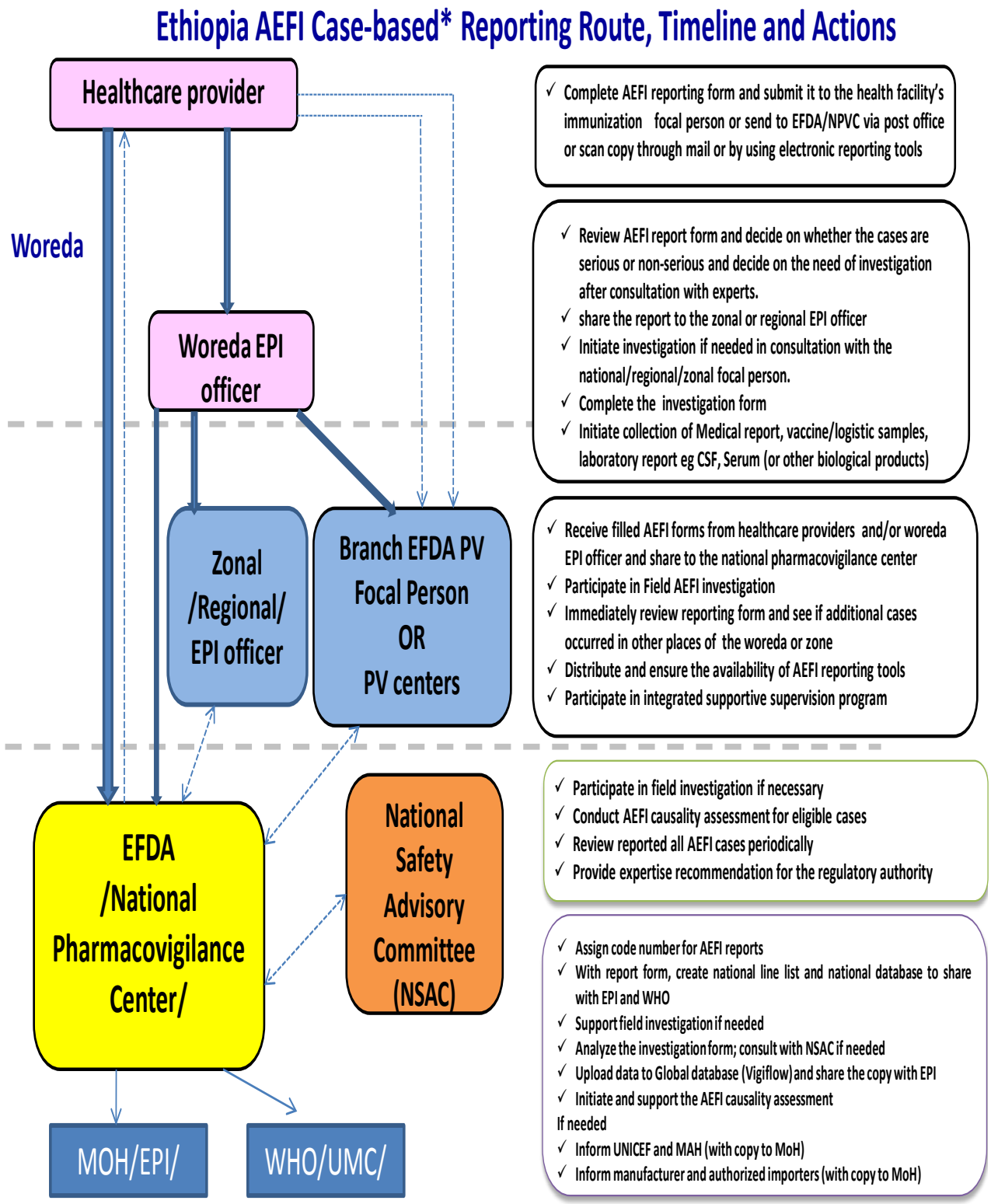



Fig. 4.2. AEFI case-based reporting routes, timeline and action at each level.

4.1.2.2. COVID-19 vaccines AEFI Reporting Tools

Currently available AEFI reportingtools/methodsin use include:

- **Standard AEFI reporting form** (yellow card):

This is aprepaid paper based AEFI reporting form on which health care providers are expected to fill necessary information clearly and completely and submit to the health facility's EPI focal person, then the filled case reporting form/ line list should be sent to EFDA following appropriate channels as described above. Alternatively,the health care providers can send the scanned copy of the filled form through mail using he addressespharmacovigilance@efda.gov.et and or viapost office directly to the regionalor national pharmacovigilance center/es.

- **Web based online reporting tools**:

These are an electronic AEFI reporting form easily available and accessible at EFDA's official websites (www.fmhaca.gov.et)↦services↦e-reporting of ADR) orhttps://med-safety.redant.cloud/login. The latter online reporting tool requests a reporter to create an account to report an AEFI. For more information see(Annex 7.4).

- **MedSafety mobile based application tool:**

This is an electronic AEFIreporting using smart phone and the application is available at google store and apps store.The reporter will be requested to create an account to report an AEFI. For more information see (Annex 7.5).

- **AEFI excel line list:**

This excel sheet is used for compiling and sending of non-serious AEFI cases regularly.

- **Toll free number 8482**

This is a free tool telephone number used for notification/reporting of AEFIsin addition to using standard case based AEFI reporting forms.

4.2. AEFI Investigation

Among the reported AEFI cases, those fulfilling the eligibility criteria will be selected for investigation. AEFI cases eligible for investigation include:

- All serious AEFI cases
- Cluster AEFIs
- Events above the expected rate and/or severity
- AESIs
- Suspected signals and/or any new events associated with the COVID-19 vaccines
- Suspected immunization error (e.g., injection site abscesses, sepsis)
- Significant events of unexpected cause within 30 days of vaccination
- Events causing significant parental and community concerns (e.g., febrile seizures, hypotonic hypo-responsive episode)

Once the reported AEFI cases are selected for investigation, detail case investigationisnecessary.For AEFIs following COVID-19 immunization, the same case selection criteria,investigationprocesses and methodology should be followed, after the relevant staffs have been trained.The purposes of AEFI investigation activities include but not limited to:

- Confirming a diagnosis and timing
- Identifying details of vaccine(s) administered (vaccine manufacturer and distributors details, vaccine transport, storage and handling),
- Reviewing and documenting vaccinated client details (concomitant medication, with indication and administration dates, past medical history),
- Evaluating vaccine administration techniques (routes of administration, diluents used, reconstitution procedures,)
- Assessing immunization session environment and organization (reviewing the operational aspects of the programme …)
- Documenting the outcome of the reported adverse events (eg: death, disability, hospitalization, sequalae…)
- Determining whether the reported event is solitary or part of a cluster

The woreda EPI officer (WEO) along with the woreda rapid response team (RRT) will carry out the investigation with expert (s) support from zonal to national levels.Close communication among all levels is important. EFDA, National PV team, National EPI, University Hospital

Pharmacovigilance Center (if available), regional AEFI task forces and zonal regulatory bodies are expected to support the investigation of the case according to their capacity at their level when necessary. Technical supports from partner organizations like WHO may be sought as needed.

Investigation should begin as soon as possible, ideally within24 hours but within a maximum of seven days of notification to the healthcare provider. Immediate investigations help to identify any immunization error(s) that might be present, to correct them before other people are exposed to the same error, and to show members of the community that their health concerns are taken seriously.However, any significant AEFI or those AEFIs which are eligible to investigation should be investigated irrespective of the time interval between vaccination and onset of symptoms.

An AEFI investigation follows standard principles and step by step approaches in accordance with standardized investigation form (Annex 7.2). The following are steps in investigating AEFIs:

I. Confirm information in the AEFI report
II. Investigate and collect data about
    a. the patient
    b. the event
    c. the suspected vaccine(s)
    d. other individuals associated with reported AEFI
III. Assess the immunization service by
    a. Making enquiries
    b. Observing the service in action
IV. Specimen collection
    a. From Patient
    b. Vaccine and logistics
V. Conclude investigation

The investigators will need to look directly at the reported reaction as well as gather information from the client/parent, healthcare providers and supervisors, and community members. The information collected (and conclusions) should be recorded on an AEFI Investigation Form.

Since, immunization related errors and coincidences are the most likely causes of adverse events,the investigator should suspect immunization errors as the cause and examine the evidence for any errors in the storage, handling, or administration of vaccines. Attention can then focus on finding out more about the particular error and taking the necessary corrective action. The investigators should seek to identify system problems rather than to find individuals to blame.

Comprehensive and complete AEFI investigation report should be prepared and send to the national pharmacovigilance center within not more than a week after the conduction of investigation.In addition to the investigation report,completed AEFI investigation form(Annex 7.2)and signed minutes containing list of participants in the investigation activity shall be prepared and send to the NPVC. The findings of investigation are used select cases for conduct causality assessment.

4.3. AEFI Causality Assessment

Causality assessment (CA) is the systematic review and evaluation of available data about an AEFI to determine the likelihood of a causal association between the event(s) and the vaccine received. CA does not necessarily establish whether or not a definite relationship exists, but generally ascertains a degree of association between the reported adverse events and the vaccine/vaccination. Nevertheless,CA is a critical part of AEFI monitoring and enhances confidence in the national immunization program and regulation of the safety and quality of the product.

The selection of AEFI cases reported from active/passive surveillance systems for causality assessment should focus on the following situations:

- Serious AEFIs in vaccinated individuals that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in persistent or significant disability/incapacity, or result in a congenital anomaly or birth defect or is a medically important event or reaction.
- The occurrence of events with an unexpected high rate or unusual severity.
- Signals generated because of individual or clustered cases.

- Significant events of unexplained cause, occurring up to 1 year after COVID-19 vaccination (and that are not listed in the product information); or
- Events causing significant parental, family, or community concerns.

For conducting of COVID-19 AEFI causality assessment, the National Safety Advisory Committee (NSAC)should consistofbroad range of experts from pediatrics, neurology,general medicine, forensic medicine, pathology, microbiology, immunology, epidemiology, pharmacology,pharmacoepidemiology, clinical pharmacy, and infectious diseaseare involved. In addition, other external specific medical experts could be includedduring the introduction of COVID-19 vaccines when itis necessary as the vaccine will be administered to individuals of all ages.

The Causality assessment of an AEFI user manual/software, the revised WHO AEFI causality assessment classification (Table 1), outlines the scientific basis for causality assessment and performing of the assessment in a four-step process. The same causality assessment principles and processes should be applied for the assessment of COVID-19 vaccine related AEFIs.

Before conducting causality, assessment investigation reports and filled AEFI investigation form should be prepared and sent to the committee. The committee perform the assessment using the information obtained during the AEFI investigation and other evidence-based data.

Causality assessment should be conducted within not more than two weeks after the investigation is carried out. However, in emergency and public or political concerns, the causality assessment shall be made within a week or less after the investigation is done and the report is ready for causality assessment. Causality assessment helps to come up with sound AEFI classification, to generate corrective and preventive actions for the immunization program and to take regulatory decisions.

4.4. AEFI communication and Feedback

No official communication or feedback on AEFI shall be made before the conduct of causality assessment without knowing the resultsof AEFI classification and recommendationsof the

NSAC. The classification of the AEFI and the recommendations of the NSAC should be communicated to the MOH/National EPI and relevant stakeholders or partners accordingly.

The MOH/National EPI will cascade the decision and recommendations made by NSAC to RHBs and healthcare facilities. In addition, EFDA and MOH may jointly give media briefing on the safety and quality of the COVID-19 vaccines andwill also send alerts for healthcare professionals on safety, efficacy, and quality of vaccine via mails and other possible channels.EFDA will also communicate to RPVC, EFDA branch office, regional regulatory bodies and to public on the safety of COVID-19 vaccines.

## 5.Roles and Responsibilities of stakeholders on vaccine safety

### 5.1. Federal Ministry of Health (FMOH)

- Ensureavailabilityoffundingfornationalstakeholderstoconductkeyactivitiestostrengthensafetymonitoringfor COVID-19vaccines
- Establish anationalcoordinationtaskforceor working groupconsistingofmulti-disciplinaryandmulti-agency representativestoensureinter-stakeholdercoordinationandcooperation
- Generatevaccinedemandandensureacceptability
- EstablishefficientcommunicationmechanismsforCOVID-19vaccinesbetweenregulatoryauthorities, immunizationprogrammes, Public Health Emergency Management (PHEM), MinistryofEducationandotherauthorities
- Beprepared to respondtorumors,mediaandcommunityconcerns
-

### 5.2. Ethiopian Food and Drug Authority (EFDA)

- Overseepreparationsforemergencyuselisting(EUL)
- Verifysubmission and review of riskmanagementplanspriortomarketingauthorizationandmakingrisk-based recommendationsforpost-authorizationsafetysurveillance
- Overseecommunicationandinformationsharingwithimmunizationprogrammes, surveillance/PHEM, pharmacovigilancecenters andotherkeyinstitutionson COVID-19vaccinessafetyupdates
- Havean authority tomandate COVID-19vaccinessafety studiesby thevaccinemanufacturersandimportersof vaccines,asrequired
- Havetheindependentauthorityto investigatepotentialsafetysignalsandassurethecontinuedpost- authorizationsafetyof COVID-19vaccines;
- OverseethemonitoringofCOVID-19vaccinesafetyby reviewing

theperiodicsafetyupdatereports (PSURs)/ periodic benefit-riskevaluationreports (PBRERs);

- Sharesafetyinformationgeneratedwith national,regional,internationaldecision-makersandvaccinemanufacturers
- Ensuretimelysubmissionof COVID-19 AEFI'sandadverseeventsofspecialinterest (AESI's)datafrom EPIs/surveillance/ PHEMand pharmacovigilancecentersacrossthecountryfor datacompilation,analysisandsignaldetection;
- Ensure that AEFI's are reported, investigated, and analyzed so thatregulatory measures are taken, and recommendations are implemented in a timely manner and the public is protected from unnecessary harmresulting from poor quality and safety COVID vaccines.
- Develop a national framework to process vaccine safety signals and determine which should be prioritized for more rigorous evaluation and risk assessment.
- Whenrecommended,conductspecificactivesurveillancestudiesforCOVID-19vaccines
- Measureandcharacterizeother AEFI'sidentifiedinactivesurveillance andsentinelsystems
- Share informationwithkeynationalstakeholdersonCOVID-19vaccinesafetyandwiththeglobalcommunity byuploadingtheinformation ontheWHOglobalpharmacovigilance database, vigibasemaintained atUppsala monitoringCentre(UMC)in Swedenunderthe WHOInternationalDrugMonitoringProgramme

5.3 Immunization program

- In collaboration with EFDA, regularly review reportssubmittedtopassivesafety surveillancesystemstoidentifyratesandunexpectedpatterns,with special attentiontoseriousoutcomes, suchasdeath,disabilities, life-threatening events,andprogrammaticerrors;
- Identifyandquantifypublicconcernssurroundingvaccinesthroughcross-sectionalsurveysand monitoring of socialmedia;
- Measureand characterize backgroundratesofmedicaloutcomesthatmay becometemporallyassociatedwithCOVID-19vaccines

- Coordinate existing active andsentinelsurveillancenationally, regionally,andgloballytoensureharmonization,avoid duplication,increasepowertodetectrareeventsandtakeadvantageofvariabilityinvaccinationpracticesandtarget population

5.4.AEFI task force members

- The AEFI task force will be established at national, regional, zonal and woreda level.
- Must use the model TOR prepared and distributed by theNPVCand prepare their own TOR to implement activitieson COVID vaccine AEFI's at their level.
  - The AEFI task force might be involved in the field investigation of AEFI cases.
  - The AEFI task force shall meet every two weeks to evaluate their plan of action.
  - The AEFI task for shall request for support from the EFDA whenever necessary

5.5.National safety advisory committee**.**

- The NSAC members are responsible for conducting causality assessment of eligible AEFI cases, reviewing and analysis of the AEFI cases.
- The NSACmembers shall meet every two weeks and when called by the EFDA to conduct causalityassessment and review the AEFI cases.
- The NSAC will accomplish their roles and responsibilities as stipulated in their TOR.

5.6. Vaccine manufacturers

- Shareriskmanagementplans andinformationondetectedsignals for COVID-19vaccineswithNRAS.
- ConductphaseIVstudiesonCOVID-19vaccinesand submitperiodicsafety updatereports(PSURs)onaregular basis tohelppolicydecisions; thefrequencyofPSURsubmissionsmay beincreased tobi-monthly/monthlyto guidequickcorrectiveactions anddecisions
- Respond tonationalrequests toimplementinnovativeriskminimizationmeasures,forexample,peel-offlabels onvaccinevials;
- Respondtonationalrequests toshareadditionalandupdatedproductinformationandclinicaltrial data
- Keepthecountriesupdatedon

allsafetyandefficacyfindingsinothercountries,particularlyfromphaseIV studies

## 6.Monitoring and Supervision System

- EFDA jointly with MOH/National EPI will conduct supportive supervision at the vaccination site.
- All the sub national level regulatory body in collaboration with their perspective EPI teams shall also conduct supportive supervision to their respective catchment facility.
- The scope of the supervision includes EPI units of the health facility, the sub national EPI offices, and mobile vaccination sites and should be supported by checklist in structured manner.
- Comprehensive and detail report should be prepared which help for improving and strengthening of the AEFI surveillance system.

# 7. Annexes

## 7.1. AEFI case reporting form

**REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)**

| | |
|---|---|
| ***Patient Name or initials*:** | ***AEFI reporting number:*** |
| ***Patient's full Address*:** | ***Reporter's Name*:** |
| | Institution: |
| Telephone: | Designation & Department: |
| Sex: ☐ M ☐ F (Pregnant ☐ Lactating ☐) | Address: |
| ***Date of birth* : _ _ / _ _ / _ _** | |
| *OR Age at onset: ☐☐ Years ☐☐ Months ☐☐☐ Days* | Telephone & E-mail: |
| *OR Age Group at onset: ☐ <1 Year ☐ 1 to 5 Years ☐ >5 Years-15 Years ☐>15 years-60 Years ☐>60 years* | Date patient notified event to health system: _ _ / _ _ / _ _ |
| | Today's date : _ _ / _ _ / _ _ |

**Health facility (place or vaccination center) name & address:**

| *Vaccine* | | | | | | | *Diluent (if applicable)* | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Name of vaccine*** | ***Brand Name incl. Name of Manufacturer*** | ***Date of vaccination*** | ***Time of vaccination*** | Dose (1st, 2nd, etc.) | ***Batch /Lot number*** | Expiry date | Name of diluent | ***Batch /Lot number*** | Expiry date | Date and time of reconstitution |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

| | |
|---|---|
| ***Adverse event(s):*** | Date AEFI started : _ _ / _ _ / _ _ |
| ☐ Severe local reaction ☐ *>3 days* ☐ *beyond nearest joint* | Time _____ |
| ☐ Seizures ☐ *febrile* ☐ *afebrile* | Describe AEFI (Signs & Symptoms): |
| ☐ Abscess<br>☐ Sepsis<br>☐ Encephalopathy<br>☐ Toxic shock syndrome<br>☐ Thrombocytopenia<br>☐ Anaphylaxis<br>☐ Fever ≥38°C<br>☐ Other (specify)..... | |

***Serious: Yes / No;*** ➔ If Yes ☐ Death ☐ Life threatening ☐ Persistent or significant disability ☐ Hospitalization ☐ Congenital anomaly ☐ Other important medical event (specify).....

***Outcome:*** ☐ Recovering ☐ Recovered ☐ Recovered with sequela ☐ Not Recovered ☐ Unknown

☐ Died If Died, date of death : _ _ / _ _ / _ _ Autopsy done: ☐Yes ☐No ☐Unknown

Past medical history(including history of similar reaction or other allergies), concomitant medication and dates of administration (exclude those used to treat reaction) other relevant information (e.g. other cases).*Use additional sheet if needed:*

*First Decision making level to complete:*

| | |
|---|---|
| Investigation needed: ☐ Yes ☐ No | If Yes, date investigation planned : _ _ / _ _ / _ _ |

*National level to complete:*

| | |
|---|---|
| Date report received at National level _ _ / _ _ / _ _ | AEFI worldwide unique ID : |
| Comments: | |

**Compulsory field*

**Email address: pharmacovigilance@efda.gov.et**

### 7.2. AEFI case Investigation Form

**AEFI Case Investigation Form**

| **Section A** | **Basic details** | | |
|---|---|---|---|
| **Region** | **Zone** | **Woreda** | **Case ID** |
| Place of vaccination ( ): Govt. health facility/Private health facility/Other (specify) _____<br>Vaccination in ( ): Campaign/Routine/Other (specify) _____ | | | |
| **Name and Address of vaccination site:** | | | |
| Type of site ( ) Fixed Mobile Outreach Other _____ | | | |

**Name of Reporting Officer:** Date of investigation: __ __ / __ __ / __ __ __ __

Date of filling this form:__ __ / __ __ / __ __ __ _

Designation/ Position:

Telephone #: Mobile: e-mail:

**Patient Name** Sex: M / F

(use a separate form for each case in a cluster)

Date of birth (DD/MM/YYYY):__ __ / __ __ / __ __ __ __***OR*** *Age at onset: __ __years __ __months __ __ __days* ***OR****Age group: < 1 year 1-5 years> 5 years*

Patient's full address with landmarks *(Kebele, Gott name, house number, locality, phone number etc.)***:**

| **Name of vaccines/diluent received by patient** | **Date of vaccination** | **Time of vaccination** | **Dose (e.g. 1st, 2nd, etc.)** | **Batch/Lot number** | **Expiry date** |
|---|---|---|---|---|---|
| | | | | Vaccine | Vaccine |
| | | | | Diluent | Diluent |
| | | | | Vaccine | Vaccine |
| | | | | Diluent | Diluent |
| | | | | Vaccine | Vaccine |
| | | | | Diluent | Diluent |
| | | | | Vaccine | Vaccine |
| | | | | Diluent | Diluent |
| | | | | Vaccine | Vaccine |
| | | | | Diluent | Diluent |

Date of first/key symptom *(DD/MM/YYYY)*:__ __ / __ __ / __ __ __ __Time of first symptom (*hh/mm):* __ __ / __ __

Date of hospitalization *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __

Date first reportedto the health authority *(DD/MM/YYYY)*:__ __ / __ __ / __ __ __ __
Statuson the date of investigation: Died () Disabled() Recovering()Recovered completely()Unknown()
If died, date and time of death *(DD/MM/YYYY)*:__ __ / __ __ / __ __ __ __ (*hh/mm):* __ __ / __ __
Autopsy done? () Yes(date)_____ No Planned on (date)_____ Time_____
Attach report (if available)

| **Section B** | **Relevant patient information prior to immunization** | |
|---|---|---|
| **Criteria** | **Finding** | **Remarks (If yes provide details)** |
| Past history of similar event | Yes / No/ Unkn | |
| Adverse event after previous vaccination(s) | Yes / No/ Unkn | |
| History of allergy to vaccine, drug or food | Yes / No/ Unkn | |
| Pre-existing illness (30 days) / congenital disorder | Yes / No/ Unkn | |
| History of hospitalization in last 30 days, with cause | Yes / No/ Unkn | |
| Patient currentlyon concomitant medication? (If yes, name the drug, indication, doses &treatment dates) | Yes / No/ Unkn | |
| Family history of any disease (relevant to AEFI) or allergy | Yes / No/ Unkn | |
| For adult women<br>• Currently pregnant?Yes (weeks) _____/ No/ Unknown<br>• Currently breastfeeding? Yes / No | | |
| For infants<br>The birth was: Full-term Pre-term___ Post-term. Birth weight:<br>Deliveryprocedure was: Normal___Caesarean___ Assisted (forceps, vacuum etc.)____<br>Withcomplication (specify)_____<br>Place of birth: Home__ Health facility_____ | | |
| **Section C** | **Details of first examination** of serious AEFI case** | |
| Source of information ( *all that apply*): **Examination by the investigator__ Documents___Verbal autopsy___ Other_____***If from verbal autopsy, please mention source (e.g. parents)*_____ | | |
| Name of the person who first examined/treated the patient:_____<br>Name of other persons treating the patient: _____<br>Other sources who provided information (specify): _____ | | |
| Signs and symptoms in chronological order from the time of vaccination: | | |

| | | |
|---|---|---|
| Name and contact information of person completing these clinical details: | Designation: | Date/time |

****Instructions – Attach copies of ALL available documents (including case sheet, discharge summary, case notes, laboratory reports and autopsy reports) and then complete additional information NOT AVAILABLE in existing documents, i.e.**

- ***If patient has receivedmedical care***attach copies of all available documents (including case sheet, discharge summary, laboratory reports and autopsy reports, if available) and write only theinformation that is not available in the attached documents below
- ***If patient has not received medical care***–obtain history, examine the patient and write down your findings below (add additional sheets if necessary)

**Provisional/Final Clinical Diagnosis:**

**Section D Details of vaccines provided at the site linked to AEFI on the corresponding day**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Number immunized for each antigen at session site. Attach record if available. | Vaccine name* | | | | | | | | | |
| | Number of doses** | | | | | | | | | |

**Write name of vaccine(s) given on the same vaccination day at the site ** Write total doses administered for each vaccine*

- When was the patient immunized? (Tick the box thebelowand respond to ALL questions)

Within the first vaccinations of the session Within the last vaccinations of the session Unknown

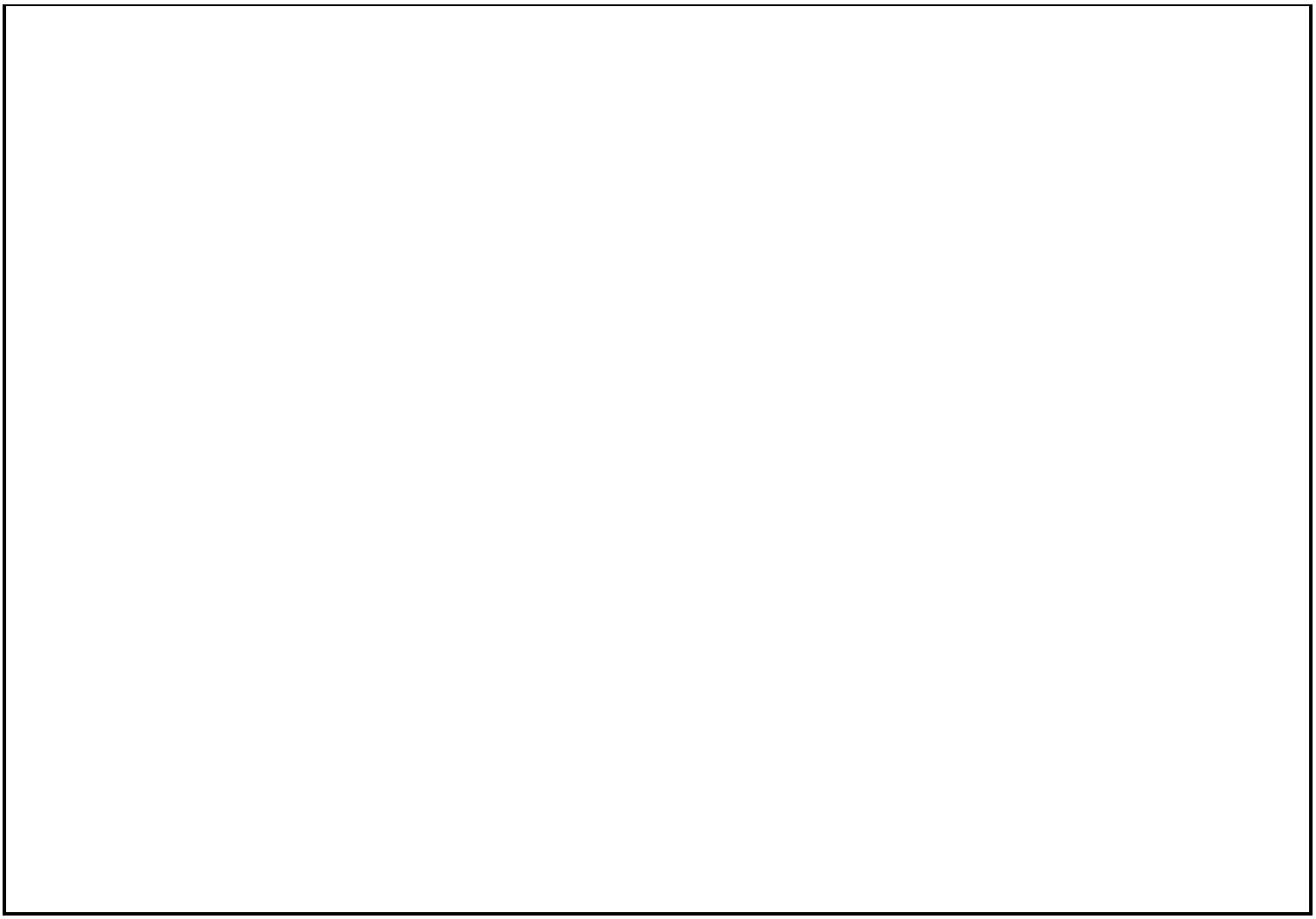
In case of multidose vials, was the vaccine givenwithin the first few doses of the vial administered? Within the last doses of the vial administered? Unknown?

| | |
|---|---|
| • Was there an error in prescribing or non-adherence to recommendations for use of this vaccine? | Yes/ No |
| • Based on your investigation, do you feel that the vaccine (ingredients) administered could have been unsterile? | Yes/ No/ Unable to assess |

| | | | |
|---|---|---|---|
| • Based on your investigation, do you feel that the vaccine's physical condition (e.g. colour, turbidity, foreign substances etc.) was abnormal at the time of administration? | Yes / No/ Unable to assess | | |
| • Based on your investigation, do you feel that there was an error in vaccine reconstitution/preparation by the vaccinator (e.g. wrong product, wrong diluent, improper mixing, improper syringe filling etc.)? | Yes / No/ Unable to assess | | |
| • Based on your investigation, do you feel that there was an error in vaccine handling (e.g.break in cold chain during transport, storage and/or immunization session etc.)? | Yes / No/ Unable to assess | | |
| • Based on your investigation, do you feel that the vaccine was administered incorrectly (e.g. wrong dose, site or route of administration, wrong needle size, not following good injection practice etc.)? | Yes / No/ Unable to assess | | |
| • Number immunized from the concerned vaccine vial/ampoule | | | |
| • Number immunized with the concerned vaccine in the same session | | | |
| • Number immunized with the concerned vaccine having the same batch number in other locations. Specify locations: _____ | | | |
| • Is this case a part of a cluster? | Yes / No/ Unkn | | |
| • If yes, how many other cases have been detected in the cluster? | | | |
| • Did all the cases in the cluster receive vaccine from the same vial? | Yes / No/ Unkn | | |
| • If no, number of vials used in the cluster (enter details separately) | | | |
| | | | |
| **Section E Immunization practices at the place(s) where concerned vaccine was used** ***(Complete this section by asking and/or observing practice)*** | | | |
| **Syringes and needles used:** | | | |
| Are AD syringes used for immunization? | Yes | No | Unkn |
| If no, specify the type of syringes used: Glass___ Disposable____ Recycled disposable_____ Other _____ | | | |
| *Specific key findings/additional observations and comments:* | | | |
| **Reconstitution: (complete only if applicable, √NA if not applicable)** | Status | | |
| Reconstitution procedure (√) | Yes | No | NA |
| Same reconstitution syringe used for multiple vials of same vaccine? | Yes | No | NA |
| Same reconstitution syringe used for reconstituting different vaccines? | Yes | No | NA |
| Separate reconstitution syringe for each vaccine vial? | Yes | No | NA |
| Separate reconstitution syringe for each vaccination? | | | |

| | | | |
|---|---|---|---|
| Are the vaccines and diluents used the same as those recommended by the manufacturer? | Yes | No | NA |
| *Specific key findings/additional observations and comments:* | | | |
| **Section F Cold chain and transport**<br>***(Complete this section by asking and/or observing practice)*** | | | |
| **Last vaccine storage point:** | | | |
| • Is the temperature of the vaccine storage refrigerator monitored? | Yes | No | Unkn |
| oIf "yes", was there any deviation outside of 2−8° C after the vaccine was placed inside? | | | |
| oIf "yes", provide details of monitoring separately. | | | |
| • Was the correct procedure for storing vaccines, diluents and syringes followed? | Yes | No | Unkn |
| • Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer? | Yes | No | Unkn |
| • Were any partially used reconstituted vaccines in the refrigerator? | Yes | No | Unkn |
| • Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator? | Yes | No | Unkn |
| • Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store? | Yes | No | Unkn |
| **Last vaccine storage point:** | | | |
| • Is the temperature of the vaccine storage refrigerator monitored? | Yes/No | | |
| oIf "yes", was there any deviation outside of 2−8° C after the vaccine was placed inside? | Yes / No | | |
| oIf "yes", provide details of monitoring separately. | | | |
| Was the correct procedure for storing vaccines, diluents and syringes followed? | Yes | No | Unkn |
| • Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer? | Yes | No | Unkn |
| • Were any partially used reconstituted vaccines in the refrigerator? | Yes | No | Unkn |
| • Were any unusable vaccines (expired, no label, VVM at stages 3 or 4, frozen) in the refrigerator? | Yes | No | Unkn |

| | | | |
|---|---|---|---|
| • Were any unusable diluents (expired, manufacturer not matched, cracked, dirty ampoule) in the store? | Yes | No | Unkn |
| *Specific key findings/additional observations and comments:* | | | |
| **Vaccine transportation:** | | | |
| • Type of vaccine carrier used | Yes | No | Unkn |
| • Was the vaccine carrier sent to the site on the same day as vaccination? | Yes | No | Unkn |
| • Was the vaccine carrier returned from the site on the same day as vaccination? | Yes | No | Unkn |
| • Was a conditioned ice-pack used? | Yes | No | Unkn |
| *Specific key findings/additional observations and comments:* | | | |
| Was the correct procedure for storing vaccines, diluents and syringes followed? | Yes | No | Unkn |
| • Was any other item (other than EPI vaccines and diluents) in the refrigerator or freezer? | Yes | No | Unkn |
| • Were any partially used reconstituted vaccines in the refrigerator? | Yes | No | Unkn |
| | | | |
| **Section G Community investigation (Please visit locality and interview parents/others)** | | | |
| Were any similar events reported within a time period similar to when the adverse event occurred and in the same locality?<br><br>If yes, describe: | Yes | No | Unkn |
| If yes, how many events/episodes?_____ | | | |
| Of those effected, how many are<br>• Vaccinated:_____<br>• Not vaccinated:_____<br>• Unknown:_____ | | | |
| Other comments: | | | |
| **Section H: Other findings/observations/comments** | | | |



7.3.AEFI Line List

AEFI line listing form for compilation at woredas/zonal /regional/ and national level to identify trends and clusters of AEFI.

**Year: _____: _____**

| Name/ID of an | Kebele(write name | Woreda (write | Zone(write name | Region | Date of | Date of | Reaction type | Outcome(1)(Recov | Suspected | Vaccine batch/Lot | Diluent batch | Onset time interval | Date reporting | Investigated?(If | Final diagnosis | Result of causality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | | |

(write code)

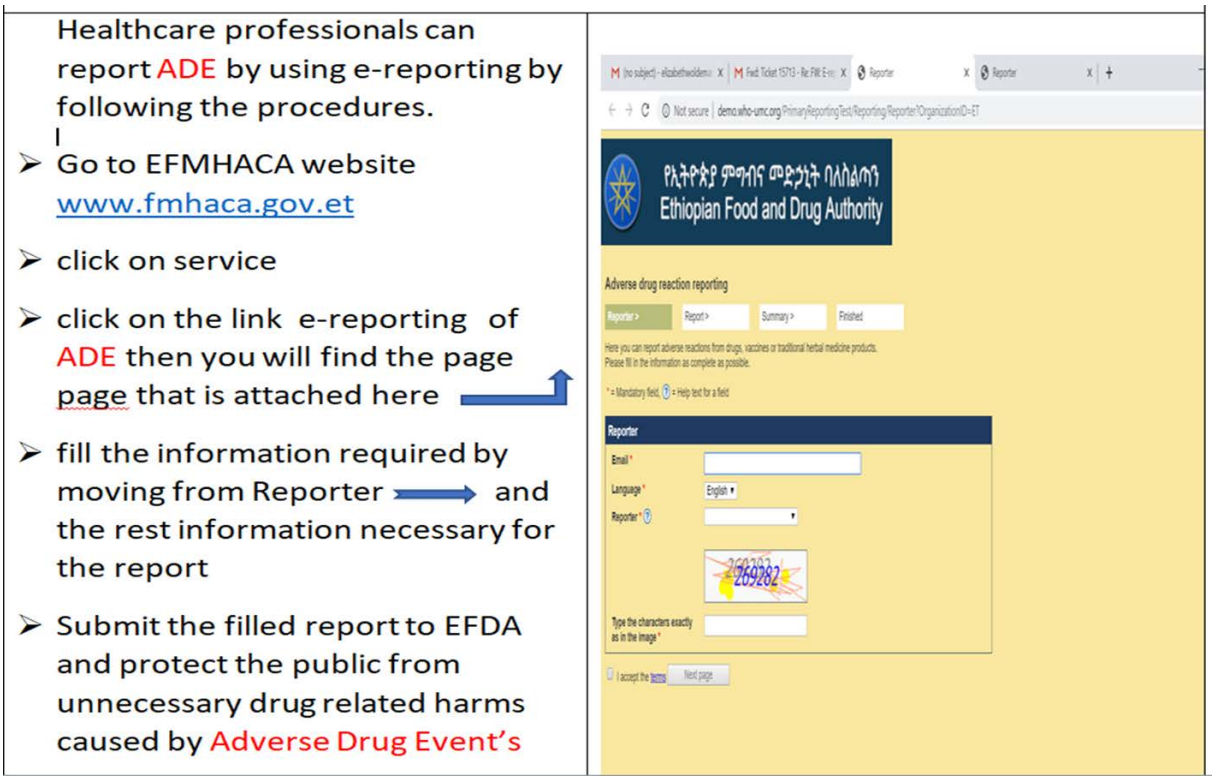
**Table 1. Final Causality Classification**

| | | | | | |
|---|---|---|---|---|---|
| [A1] Vaccine-related | [A2] Immunization error-related | [A3] Immunization anxiety-related | [B] Indeterminate | [C] Coincidental | [D] Inadequate information to classify |

**Reported by: _____Signature: _____**

**Designation: _____Date: _____**

7.4.E-reporting for ADE/AEFI/ user guide




7.5.Med Safety mobile apps ADE reporting form user guide

- Procedure and steps to access and use the Med Safety app available for free at Android-Google store and app store for I phonesmart mobiles.
- Search for Med safety in the search bar,
- Tap on the Med Safety icon app to select,tap install to install, open the App after installation,

- Select Ethiopia from the list of countries
- Create a user account to access the full features of the app
- Tap on create account and complete the required information to create your account,
- You can now access the full features of the app

7.6. Addresses and contact details of the National Pharmacovigilance Center, University Hospitals' Pharmacovigilance Centers and EFDA Branch Offices

| Ser. No. | Pharmacovigilance center/branch EFDA office | Addresses&Locations | | Contact/Focal/ Persons for pharmacovigilance activities | | |
|---|---|---|---|---|---|---|
| | | Region /city/ | Office Phone No. | Name | Mobile # | Mail |
| 1. | National pharmacovigilance center/EFDA/ | Addis Ababa City AA | +25111 | | | |
| 2. | Tikur Anbessa Specialized Hospital PVC/AAU/CHS/SOP/ | Addis Ababa City AA | +25111 | | | |
| 3 | Ayder Comprehensive Specialized Hospital PV center/MU/CHS/SOP/ | Tigray Region Mekelle | +251 | | | |
| 4 | Hiwot Fana Specialized University Hospital PV Center /HU/CHS/SOP/ | Hareri Region Harer | +251 | | | |
| 5 | Hawassa University Specialized Hospital PV Center /HU/CHS/SOP/ | SNNP Region Hawassa | +251 | | | |
| 6 | University of Gondar Specialized Referral Hospital /UOG/CHS/SOP/ | Amhara Region Gondar | +251 | | | |
| 7 | Jimma University Specialized Hospital /JU/CHS/SOP | Oromiya Region Jimma | +251 | | | |
| 8 | Xxxxx EFDA Branch | Dire Dwa City | +251 | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | DD city | | | | |
| 9 | Xxxxx EFDA Branch | Amhara Region Kombolecha | +251 | | | |
| 10 | Xxxxxx EFDA Branch | Tigray Region Mekelle | +251 | | | |
| 11 | Xxxxxx EFDA Branch | SNNP Region Hawassa | +251 | | | |
| 12 | Xxxx EFDA Branch | Amhara Region Bahir Dar | +251 | | | |
| 13 | Xxxxxx EFDA Branch | Oromiya Region Jimma | +251 | | | |

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4. Guideline for Adverse Drug Events monitoring (Pharmacovigilance) Food, Medicine and Healthcare administration and control authority of Ethiopia, third edition, 2014, Addis Ababa, Ethiopia.