
Module: Safety data management systems in countries using COVID-19 vaccines
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Abbreviations

AACVS  African Advisory Committee on Vaccine Safety
ACE  Angiotensin-converting enzyme
ADEM  Acute disseminated encephalomyelitis
ADRs  Adverse drug reactions
AEFI  Adverse event following immunization
AESI  Adverse event of special interest
ARDS  Acute respiratory distress syndrome
AVSS  Active vaccine safety surveillance
CEM  Cohort event monitoring
CEPI  Coalition for Epidemic Preparedness Innovations
CIOMS  Council for International Organizations of Medical Sciences
COVID-19  Coronavirus disease 2019
DCVMN  Developing Countries Vaccine Manufactures Network
DL  Data linkage
DNA  Deoxyribonucleic acid
EH  e-Health
EPI  Expanded programme on immunization
GACVS  Global Advisory Committee on Vaccine Safety
GBS  Guillain-Barré syndrome
GVAP  Global vaccine action plan
HCW  Health care worker
ICD  International classification of diseases
IFPMA  International Federation of Pharmaceutical Manufacturers and Associations
ISoP  International Society of Pharmacovigilance
ISRR  Immunization stress-related response
MAH  Marketing authorization holder
MedDRA  Medical dictionary for regulatory activities
MH  m-Health
MoH  Ministry of Health
mRNA  Messenger RNA
NIP  National Immunization Programme
NITAG  National Immunization Technical Advisory Group
NRA  National regulatory authority
PBRR  Periodic benefit-risk evaluation report
PHEIC  Public health emergency of international concern
PLSS  Post-licensure safety studies
PSUR  Product safety update report
PV  Pharmacovigilance
QPPV  Qualified person responsible for pharmacovigilance
RITAG  Regional Immunization Technical Advisory Groups
RMP  Risk management plan
RNA  Ribonucleic acid
SAGE  Strategic Advisory Group of Experts (for immunization)
SARS-CoV-2  Severe acute respiratory syndrome coronavirus 2
SKG  Significant knowledge gap
SIA  Supplementary immunization activities
SS  Sentinel surveillance
TGA  Therapeutic Goods Administration (Australian Ministry of Health)
VAED  Vaccine-associated enhanced disease
VLP  Virus-like particles
VDP  Vaccine preventable disease
WHO  World Health Organization
<table>
<thead>
<tr>
<th>Glossary</th>
<th>Adjuvant</th>
<th>A pharmacological or immunological agent added to a vaccine to improve its immune response.</th>
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</thead>
<tbody>
<tr>
<td>Adverse event following immunization (AEFI): general definition</td>
<td>Any untoward medical event that follows immunization and that does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.</td>
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<td></td>
<td>• AEFI by cause: coincidental events</td>
<td>• An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety.</td>
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<td></td>
<td>• AEFI by cause: immunization anxiety-related reaction</td>
<td>• An AEFI arising from anxiety about the immunization (see immunization stress related responses).</td>
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<td></td>
<td>• AEFI by cause: immunization error-related reaction</td>
<td>• An AEFI that is caused by inappropriate vaccine handling, prescribing or administration, that, therefore, is preventable.</td>
</tr>
<tr>
<td></td>
<td>• AEFI by cause: vaccine product-related reaction</td>
<td>• An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product, whether the active component or one of the other components of the vaccine (e.g. adjuvant, preservative or stabilizer).</td>
</tr>
<tr>
<td></td>
<td>• AEFI by cause: vaccine quality defect-related reaction</td>
<td>• An AEFI that is caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer.</td>
</tr>
<tr>
<td>Adverse event of special interest (AESI)</td>
<td>A preidentified and predefined medically significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies.</td>
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<tr>
<td>Causal association</td>
<td>A cause-and-effect relationship between a causative (risk) factor and an outcome. Causally-associated events are also temporally associated (i.e. they occur after vaccine administration), but events that are temporally associated may not necessarily be causally associated.</td>
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<tr>
<td>Causality assessment</td>
<td>In the context of vaccine AEFI surveillance, a systematic review of data about the AEFI case(s) to determine the likelihood of a causal association between the event and the vaccine(s) received.</td>
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<tr>
<td>Cluster</td>
<td>Two or more cases of the same or similar events related in time, geography (place), and/or vaccine administered. AEFI clusters are usually associated with a particular supplier/provider, health facility, and/or a vial of vaccine or a batch of vaccines.</td>
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<tr>
<td>Contraindication</td>
<td>A situation where a particular treatment or procedure, such as vaccination with a particular vaccine, must not be administered for safety reasons. Contraindications can be permanent (absolute), such as known severe allergies to a vaccine component, or temporary (relative), such as an acute/severe febrile illness.</td>
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<td>Immunity</td>
<td>The ability of the human body to tolerate the presence of material ‘indigenous’ to the human ‘body’ (self) and to eliminate ‘foreign’ (non-self) material. This discriminatory ability provides protection from infectious diseases since most microbes are identified as foreign material by the immune system.</td>
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<tr>
<td>Immunization</td>
<td>Immunization is the process whereby a person is made immune or resistant to an infection, typically by the administration of a vaccine. Vaccines stimulate the body’s own immune system to protect the person against subsequent infection.</td>
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<tr>
<td>Term</td>
<td>Definition</td>
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<td>-------------------------------------------</td>
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<tr>
<td>Immunization safety</td>
<td>The process of ensuring the safety of all aspects of immunization, including vaccine quality, adverse event surveillance, vaccine storage and handling, vaccine administration, disposal of sharps and management of waste.</td>
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<td>Immunization safety surveillance</td>
<td>A system for ensuring immunization safety through detecting, reporting, investigating, and responding to AEFI.</td>
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<td>Immunization stress related responses (ISRR)</td>
<td>Stress response to immunization that may manifest just prior to, during, or after immunization.</td>
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<td>Injections safety</td>
<td>The public health practices and policies dealing with various aspects of the use of injections (including adequate supply, a administration and waste disposal) so that the provider and recipient are not exposed to avoidable risks of adverse events (e.g. transmission of infective pathogens) and creation of dangerous waste is prevented. All injections, irrespective of their purpose, are covered by this term (see definition of safe injection practices).</td>
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<tr>
<td>Mass vaccination campaign</td>
<td>Mass vaccination campaigns involve administration of vaccine doses to a large population over a short period of time.</td>
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<td>Non-serious AEFI</td>
<td>An event that is not ‘serious’ and does not pose a potential risk to the health of the recipient. Non-serious AEFIs should also be carefully monitored because they may signal a potentially larger problem with the vaccine or vaccination or have an impact on the vaccination acceptability; in general.</td>
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<tr>
<td>Risk management plan (RMP)</td>
<td>A risk management plan is a document that describes the current knowledge about the safety and efficacy of a medicinal product. The RMP provides key information on plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine or vaccine. It also describes measures to be undertaken to prevent or minimise risks associated with the use of the product in patients.</td>
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<tr>
<td>Safe injection practice</td>
<td>Practices that ensure that the process of injection carries the minimum of risk, regardless of the reason for the injection or the product injected.</td>
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<tr>
<td>Serious AEFI</td>
<td>An event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to prevent one of the outcomes above may also be considered as serious.</td>
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<tr>
<td>Severe vaccine reaction</td>
<td>Vaccine reactions can be mild, moderate or severe. Severe reactions may include both serious and non-serious reactions.</td>
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<td>Signal (safety signal)</td>
<td>Information (from one or more sources) that suggests a new and potentially causal association, or a new aspect of a known association, between an intervention and an adverse event or set of related adverse events, that is judged to be of sufficient likelihood to justify verification.</td>
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<td>Surveillance</td>
<td>The continual, systematic collection of data that are analysed and disseminated to enable decision-making and action to protect the health of populations.</td>
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<td>Trigger event</td>
<td>A medical incident following immunization that stimulates a response, usually a case investigation.</td>
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<td>SAGE Values Framework</td>
<td>Values Framework, developed by WHO’s SAGE, offers guidance globally on the allocation of COVID-19 vaccines between countries, and guidance nationally on the prioritization of groups for vaccination within countries while COVID-19 vaccine supply is limited</td>
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<tr>
<td>Vaccine</td>
<td>A biological preparation that elicits immunity to a particular disease. In addition to the antigen, it can contain multiple components, such as adjuvants, preservatives, stabilizers, each of which may have specific safety implications.</td>
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<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
<td>Vaccine-associated enhanced disease (VAED)</td>
<td>Vaccine-associated enhanced diseases are modified and severe presentations of clinical infections affecting individuals exposed to a wild-type pathogen after having received a prior vaccine against the same pathogen.</td>
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<tr>
<td>Vaccine pharmacovigilance</td>
<td>The science and activities relating to the detection, assessment, understanding and communication of AEFI and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or vaccination.</td>
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<tr>
<td>Vaccination failure</td>
<td>Vaccination failure can be defined based on clinical endpoints or immunological criteria, where correlates or surrogate markers for disease protection exist. Primary failure (e.g. lack of sero-conversion or sero-protection) needs to be distinguished from secondary failure (waning immunity). Vaccination failure can be due to (i) failure to vaccinate, i.e. an indicated vaccine was not administered appropriately for any reason or (ii) because the vaccine did not produce its intended effect.</td>
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</tr>
<tr>
<td>Vaccine reaction</td>
<td>An event caused or precipitated by the active component or one of the other components of the vaccine. It may also relate to a vaccine quality defect.</td>
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<tr>
<td>Vaccine safety</td>
<td>The process that maintains the highest efficacy of, and lowest adverse reaction to, a vaccine by addressing its production, storage and handling. Vaccine safety is a part of immunization safety.</td>
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1. Introduction

WHO’s Global manual on surveillance of AEFIs\(^1\) provides guidance on the purpose of data analysis at different level. For example, who should analyse data, how it should be analysed and interpreted and its use for estimating relative and attributable risks. In the context of COVID-19 vaccine AEFI surveillance, the same principles and approaches should be applied, with some adaptation to allow for different vaccination strategies, vaccine target populations, types of vaccines and the surveillance systems available in different countries.

Guidance on vaccine safety surveillance systems and responding to AEFIs and AESIs to address the unique challenges from COVID-19 vaccine introduction is given in separate modules [link to AEFI and AESI modules to be added]. Once surveillance systems are operational, the efficiency and effectiveness of the system are determined by the outputs and outcomes from the system. First, the raw data generated by the system needs to be collated, then transmitted, processed and interpreted and, finally responded to systematically and scientifically. This module will provide guidance on how COVID-19 vaccine safety data should be processed and made actionable.

2. Sharing COVID-19 vaccine safety data

At the national level, the guarantee the integrity and validity of the COVID-19 vaccine safety data generated, data loss and duplication should be minimized. This can be achieved through data sharing between stakeholders such as national immunization programmes (NIPs) and expanded programmes for immunization (EPIs), national regulatory agencies (NRAs), pharmacovigilance centres, Ministries of Health (MoHs), AEFI committees, private sector, vaccine marketing authorization holders (MAHs).

Data in some countries will be reported through multiple channels, with programmes working on data from the same patients and sometimes via the same health care professional, but with different goals and pathways.

At regional and global levels, data sharing maximizes resources and capacity to enable efficient responses and decision-making. Also, signal detection capacity would be increased, as would the ability of detecting and analysing very rare adverse events. Data transformation is usually required to facilitate data sharing from different sources.

2.1. Rationale for data sharing

Data sharing at all levels is important to increase knowledge rapidly that can inform decisions about COVID-19 vaccine introduction and continuation strategies. Uncertainty about the frequency AEFI and clinical presentation will be expected due to the fast-track development processes for COVID-19 vaccines, with short time frames for data collection and regulatory review. The rationale for sharing data from four main sources are outlined below:

- Data from passive and enhanced passive AEFI surveillance systems: to detect signals, monitor immunization programme activities, monitor events that could be related to defective, un-registered or counterfeit COVID-19 vaccines.

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• Data from active surveillance systems: to verify and confirm the post-licensure safety profiles of COVID-19 vaccines, test hypotheses (epidemiologic associations between AEFIs and COVID-19 vaccines), detect signal with an accelerated time from reporting to detection.

• Data from COVID-19 vaccine manufacturers: bi-directional sharing\(^2\) of data with COVID-19 vaccine manufacturers will help ensure that data collection is complete and avoid double counting of events. In addition, the manufacturers may be aware of data from other countries or sources that can help in the evaluation of AEFIs.

• Data from other sources such as disease surveillance data, vaccine distribution and utilization data can help generate rapid alerts to trigger common responses from a geographical territory, know the implementation level, know the quality of surveillance at the national level to plan for improvement strategies, understand the distribution of different COVID-19 vaccines and to compare with distribution of the disease for interpreting patterns observed during data analysis.

2.2. Ethics in safety data sharing and collaboration

The key ethical considerations for data sharing include data confidentiality, data security, autonomy, sovereignty and benefits for those providing and sharing data.

2.3. Generic data sharing model

Fig 1 shows a schematic representation of the structure of a generic model for data sharing at the local, subnational, national and global levels. Each country must adapt the generic systems to their local context.

\(^2\) MAH inform the NRAs of the AEFI occurring in other parts of the world and the NRA needs to share AEFI data from their country with the MAH.
Fig 1: Schematic representation of the structure for data sharing at the local, subnational, national and global levels
2.4. Stakeholders mapping for AEFI data sharing

The potential stakeholder mapping is summarized in Table 1. It is important to consider who will be producing or managing COVID-19 vaccine AEFI data when a data sharing strategy will be developed.

Table 1: Potential stakeholder mapping of COVID-19 vaccine AEFI data sharing

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Current data mapping (variable in different contexts)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>District/Subnational level</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Health care institutions | ▪ Individual Case AEFI Reports  
▪ Case Report Form for ad-hoc studies |
| Disease surveillance offices | ▪ Investigation information to complete Individual Case AEFI report  
▪ Data on local epidemiological behaviour of infectious diseases |
| Immunization programme offices | ▪ Data on immunization activities  
▪ Individual Case AEFI reports |
| **National level** | |
| Disease surveillance Responsible | ▪ Data on infectious and non-infectious diseases  
▪ Data on AEFI surveillance |
| National Immunization Programmes / Expanded Programmes for Immunization | ▪ Data on immunization activities: Administrative data and distribution activities  
▪ Data on AEFI surveillance. |
| National Regulatory Authorities | ▪ Data on AEFI surveillance from primary health care workers and citizens  
▪ Data on AEFI surveillance from manufacturers  
▪ Data on AEFI surveillance from manufacturers  
▪ Data on AEFI surveillance from manufacturers |
| Health information systems units | ▪ Data from all sources in the country |
| Research institutions/Clinical Research Organization | ▪ Individual Case Safety (Adverse Events) Reports from clinical trials  
▪ Data on diseases considered as AESI/AEFI |
| Vaccine manufacturers or marketing authorization holders | ▪ Individual Case AEFI report |
| Clinical Research Sponsors | ▪ SUSAR from clinical trials |
| **Regional and Global Level** | |
| WHO regional offices | ▪ WHO-UNICEF JRF<sup>3</sup>  
▪ Individual case reports on infectious disease surveillance  
▪ Access to WHO UMC Global ICSR/ AEFI database<sup>4</sup> |
| WHO Headquarters | ▪ WHO-UNICEF JRF  
▪ Individual case reports on infectious disease surveillance  
▪ Access to WHO UMC Global ICSR/ AEFI database |
| WHO PIDM/VigiBase (maintained by UMC) | ▪ Individual Case AEFI report  
▪ WHO UMC Global ICSR/ AEFI database |

2.5. Data sources

There are different data sources with different data formats that can be applied to the COVID-19 pharmacovigilance. Some considerations for country capacity for data sharing include:

- timely availability of individual AEFI case reports with at least the 25 core variables;
- data centralized in a database with variables coded with a pre-defined data standard;
- completeness and accuracy of data (quality);
- technology available to implement safe data transfer;

<sup>3</sup> https://www.who.int/immunization/monitoring_surveillance/routine/reporting/en/
<sup>4</sup> https://www.who-umc.org/vigibase/vigibase/
• data governance frameworks that define rules for data sharing with external institutions.

2.5.1. Individual case safety reports (individual AEFI case reports)

Different levels of information systems exist in different countries. This information is usually collected from passive AEFI surveillance systems however, it could also be collected from active sentinel surveillance sites. Individual reports could also come from COVID-19 vaccine trials that would be assessed by a scientific committee established for the purpose. The WHO global database VigiBase, contains ICSRs and AEFS from all Member States in the WHO Programme for International Drug Monitoring. The source can be used to perform quantitative calculations at national, regional and global levels to detect signals and safety concerns.

2.5.2. Aggregated safety data from different sources

All countries routinely share aggregated safety data to help characterize vaccine safety e.g., WHO-UNICEF JRF, SITREP, IDSR, regulatory authorities’ networks reports, academic initiatives etc.

2.5.3. Ad-hoc research

Ad hoc research projects or specific studies could be performed by networks of health care institutes using data transferred to national institutes and to the data warehouse of the institute doing the final analysis. The platform selected by the study coordination and described in the study protocol will impact the database. It is necessary to perform a careful analysis of availability data for the event and its quality, and for the vaccination status of the patients to be included in the study before initiating ad-hoc studies. Patient diagnosis registration systems and vaccination registries should be available.

2.6. Data standards

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) standardises the definition of the data elements used in the electronic transmission of different types of Individual Case Safety Reports (ICSRs), regardless of source and destination. The standard adopted by the ICH for electronic transmission of ICSRs is described in the ICH E2B(R3) message standard. Additional information is available at https://www.ich.org/page/electronic-standards-estri.

Data should satisfy agreed international standards for successful data sharing, so that both the transmitter and the receiver have identical information. Multiple data standards are available for specific coding and for whole database structures and data formats. For clinical diagnosis coding, some standards have been developed e.g. Medical Dictionary for Regulatory Activities (MedDRA) and ICD. It is important to use a standard for identifying the specific vaccine that is being evaluated. Whenever available, the anatomical therapeutic chemical (ATC) standard should be used. For active surveillance systems, data standards are defined by the study protocols.

2.7. Data transformation

If the database used country does not comply with a standard as outlined above, data transformation is essential before data can be shared. The ICH E2B(R3) message standard should be used for data transformation and transmission in a standard transmission format. This requires coding as outlined in MedDRA and Identification of Medicinal Products (IDMP). Data science

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techniques should be applied for converting the source database format into the target format of the international database, using tools such as, ETL (Extract, Transform and Load). Countries are encouraged to contact WHO country offices for guidance if needed.

### 2.8. Repositories

The following are examples of repositories that are collecting and processing information on AEFI and enabling decision making at national, regional and global levels:

- examples of national databases: Vaccine Safety Datalink (US), Canadian Adverse Event Following Immunization Surveillance System (CAEFISS);
- example of regional databases: EudraVigilance;
- global databases;
  - for aggregate data: the WHO/UNICEF Joint Reporting Process; and
  - for case-based data, the WHO Vigibase, maintained by UMC.

### 2.9. Performance indicators

So that all counties can verify that their safety assessments for-19 vaccines, indicators have been adapted from existing immunization indicators where possible, but specific indicators have been developed to adapt to the current COVID-19 situation. Programme managers should take into consideration the fact that vaccine safety surveillance systems are for all vaccines, not just the COVID-19 vaccine and that routine vaccination will continue during COVID-19 deployment.

This section describes indicators obtained by extracting data on COVID-19 vaccine from pharmacovigilance monitoring and evaluation systems. The objectives of these indicators specific to COVID-19 vaccines are:

- at the national level:
  - help national AEFI committees, NRAs and NIPs/EPIs to identify any subnational programmatic issues, vaccine safety signals, crisis in a timely manner and to make decisions for correction;
  - identify if the country’s vaccine safety system is sensitive enough to identify signals and respond to them;
  - improve the quality of reporting, investigations and causality assessment; and
  - enable comparison of national safety performances with regional and global standards.
- at the subnational level:
  - help provincial governments to identify districts where surveillance is poor (low reporting);
  - identify and respond to programme and immunization errors early;
  - identify capacity gaps in specific districts, particularly those with vulnerable populations; and
  - allocate resources for building local training capacity.
- at the local level:
• Identify zones with high COVID-19 coverage but poor AEFI reporting.

Since COVID-19 vaccines are novel, it has been suggested that a separate report generated monthly for them, based upon these indicators. Three types of indicators have been proposed:

- key COVID-19 pharmacovigilance indicators include: total AEFI rate/100,000 COVID-19 vaccine doses administered/distributed; serious AEFI (SAE) rate per 100,000 doses of COVID-19 vaccine administered/distributed (Table 2);

- six indicators for monitoring the functionality of pharmacovigilance systems in the COVID-19 context include (Appendix 3.1):
  - % of districts with silent COVID-19 AEFI reporting;
  - % of districts not submitting monthly Reports;
  - % of districts with >10 COVID-19 related AEFI reports/100,000 doses of COVID vaccines doses administered;
  - % of serious AEFI after COVID-19 vaccination investigated;
  - % of serious AEFI after COVID-19 vaccination investigated within 2 days of notification;
  - Proportion of identical AEFI reports available with the NRA and the EPI (i.e. NRA reports =EPI reports).

- five indicators for monitoring the quality of pharmacovigilance systems in the COVID-19 context include (Appendix 3.2):
  - % of case based AEFI reports shared between NRA and EPI <7 days of receipt;
  - % Completeness of AEFI reporting forms with the critical variable;
  - % of AEFIs reported within 48 hours of notification;
  - % of serious AEFI cases with causality assessed within 14 days of investigation;
  - % of AEFI cases with causality assessment done where feedback was provided within 7 days of case classification.
Table 2: Key COVID-19 vaccine safety surveillance indicators

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Calculation</th>
<th>Information source</th>
<th>Measurement</th>
<th>Primary collector</th>
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</thead>
<tbody>
<tr>
<td>Total AEFI rate per 100,000 doses of COVID-19 vaccine doses administered / distributed*</td>
<td>No of AEFI reported at xx level / No of doses of COVID-19 vaccines Administered/ Distributed at the same level X 100,000</td>
<td>Numerator: Case based AEFI reports from linelist or reporting forms Denominator: Vaccination Records at the local level</td>
<td>If the reporting rate of AEFI differs from the ones available in clinical trials</td>
<td>Numerator: HW reporting AEFI Denominator: District immunization program manager</td>
</tr>
<tr>
<td>Serious AEFI rate per 100,000 doses of COVID-19 vaccines doses administered / distributed*</td>
<td>No of serious AEFI reported at xx level / No of doses of COVID-19 vaccines Administered/ Distributed at the same level X 100,000</td>
<td>Numerator: Case based serious AEFI reports from linelist or reporting forms Denominator: Vaccination Records at the local level</td>
<td>If the reporting rate of serious AEFI differs from the ones available in clinical trials</td>
<td>Numerator: HW reporting serious AEFI Denominator: District immunization program manager</td>
</tr>
</tbody>
</table>

*To consider the type of vaccine at the time of calculation.
3. Appendices
## Appendix 3.1: Indicators and targets for monitoring the functionality of pharmacovigilance systems in COVID-19 context

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Target</th>
<th>Calculation</th>
<th>Information source</th>
<th>Measure</th>
<th>Main responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of districts with silent COVID-19 AEFI reporting.</td>
<td>&lt;10%</td>
<td>Number of districts where COVID-19 related AEFI was zero in the month of XX / No of Districts X 100</td>
<td>Reports submitted with zero AEFIs. during the previous month.</td>
<td>Identification of silent districts / areas within a province</td>
<td>District immunization programme manager sending periodic reports</td>
</tr>
<tr>
<td>% of districts not submitting monthly Reports</td>
<td>&lt;10%</td>
<td>Number of districts where monthly COVID-19 related reports AEFI was not sent for a particular month / No of Districts X 100</td>
<td>Monthly (including zero) reports submitted by districts</td>
<td>Identification of delinquent reporting districts in a province</td>
<td>District immunization programme manager sending periodic reports</td>
</tr>
<tr>
<td>% of districts with &gt;10 COVID-19 related AEFI reports/100,000 doses of COVID vaccines doses administered</td>
<td>&gt;80%</td>
<td>No of districts with &gt; 10 AEFI reported for 100,000 doses of COVID-19 vaccines Administered / No of Districts X 100</td>
<td>Calculated from AEFI reporting form submitted by the districts following COVID-19 vaccination and Immunization registries</td>
<td>District performance on AEFI monitoring</td>
<td>District immunization programme manager sending AEFI reporting form and data on administered doses</td>
</tr>
<tr>
<td>% of serious AEFI after COVID-19 vaccination investigated</td>
<td>100%</td>
<td>Number serious AEFI investigated / Number of serious AEFI X 100</td>
<td>AEFI reporting form and AEFI investigation form</td>
<td>The quality of investigation of serious AEFI</td>
<td>District immunization programme manager coordinating the AEFI investigation</td>
</tr>
<tr>
<td>Parameter</td>
<td>Formula</td>
<td>Calculation</td>
<td>Measurement</td>
<td>Responsible Party</td>
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<td></td>
</tr>
<tr>
<td>% of serious AEFI after COVID-19 vaccination investigated within 2 days of notification</td>
<td>&gt;80%</td>
<td>Number serious AEFI investigated within 2 days of notification / Number of serious AEFI X 100</td>
<td>The timeliness of investigation of serious AEFI</td>
<td>District immunization programme manager coordinating the AEFI investigation</td>
<td></td>
</tr>
<tr>
<td>Proportion of identical AEFI reports available with the NRA and the EPI (i.e. NRA reports = EPI reports).</td>
<td>1 for all months.</td>
<td>No of AEFI reports with NRA in the month of XXXX / No of AEFI reports with EPI in the month of XXXX</td>
<td>Data sharing between the immunization programme and the regulators</td>
<td>Regulators and EPI programme managers</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix 3.2: Indicators and targets for monitoring the quality of pharmacovigilance systems in COVID19 context

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Target</th>
<th>Calculation</th>
<th>Source of information</th>
<th>Measure</th>
<th>Main responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of case based AEFI reports shared between NRA and EPI &lt;7 days of receipt</td>
<td>100%</td>
<td>Number AEFI reports shared between NRA and EPI within 48 hrs. of receipt / Number of AEFI reports X 100</td>
<td>AEFI reporting forms available with NRA and EPI or matching number of cases in linelist</td>
<td>Quality of data sharing</td>
<td>NRA and EPI programme managers</td>
</tr>
<tr>
<td>% Completeness of AEFI reporting forms with the critical variables</td>
<td>&gt;80%</td>
<td>Number AEFI reports with complete critical variables* / Number of AEFI reports X 100</td>
<td>AEFI reporting forms</td>
<td>Quality of AEFI data collected</td>
<td>EPI programme managers</td>
</tr>
<tr>
<td>% of AEFIs reported within 48 hours of notification</td>
<td>&gt;80%</td>
<td>Number AEFI reports sent to next level within 48 hours of notification / Number of AEFI reports X 100</td>
<td>AEFI reporting forms</td>
<td>Speed of response to AEFI notification</td>
<td>EPI programme managers</td>
</tr>
<tr>
<td>% of serious AEFI cases with causality assessed within 14 days of investigation</td>
<td>&gt;80%</td>
<td>Number serious AEFI reports with causality assessed within 14 days of investigation / Number of serious AEFI reports X 100</td>
<td>AEFI reporting forms</td>
<td>Speed of response to AEFI investigation</td>
<td>NRA and EPI programme managers</td>
</tr>
<tr>
<td>% of AEFI cases with causality assessment done where feedback was provided within 7 days of case classification</td>
<td>Number causality assessed cases with feedback provided within 7 days of case classification / Number of AEFI reports with causality assessment done X 100</td>
<td>Documentation of feedback of AEFI causality assessment</td>
<td>Speed of response to AEFI causality assessment</td>
<td>NRA and EPI programme managers</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------</td>
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<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>&gt;80%</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* Italics in reporting form