WHO GLOBAL BENCHMARKING TOOL (GBT) FOR EVALUATION OF NATIONAL REGULATORY SYSTEM OF MEDICAL PRODUCTS

VIGILANCE (VL): INDICATORS AND FACT SHEETS

Revision VI version 1

November 2018
<table>
<thead>
<tr>
<th>Function:</th>
<th>Description:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medical products vigilance, defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medical product-related problems, is extremely important for guaranteeing that safe and effective medical products of high quality are used within the country. Vigilance activities should be established in the countries based on a risk management approach. A reporting system should be established to monitor the safety of medical products. One important activity within that function is to monitor and assess side effects and other product-related safety issues (e.g., adverse drug reactions (ADRs) for medicines, and adverse events following immunization (AEFI) for vaccines). While common side effects are likely to be detected during pre-approval clinical trials (phases I, II and III), rare events are more likely to be observed after the marketing of medical products. Other unexpected events may also be due to errors and thus could occur at any time during product development and marketing. Side effects may differ with respect to severity, causes and public health consequences. Hence, it is advised that each country establish its own vigilance system. A vigilance system, in general, monitors all kinds of patient harm potentially related to medical products, be it due to inadequate product quality, inappropriate use (e.g., medication errors) or intrinsic adverse effects. Serious effects (e.g., AEFI) often lead to public concerns and could erode the confidence in medical products and the overall regulatory and health systems. If not dealt with adequately, such concerns could have significant negative implications on the public health. A post-marketing vigilance system of medical products is therefore essential. Networking with other international bodies and regulators is a logical method for acquiring, sharing, and exchanging the relevant information on medical products safety. This information, in turn, contributes to informed science-based decisions. To facilitate networking and exchange of information with other international bodies and regulators, harmonization across countries of the vigilance systems and safety reporting requirements in accordance with internationally agreed standards, is expected.</td>
</tr>
</tbody>
</table>
### Indicator: VL01 Legal provisions, regulations and guidelines required to define regulatory framework of vigilance.

#### Objective:
The objective of this indicator is to ensure that vigilance is supported by a comprehensive set of legal provisions, regulations and guidelines which provide the necessary mandate to implement all activities related to this regulatory function. The scope and extent of the vigilance system should be clearly defined in relevant legislation, regulations and guidelines. There should be a legal basis to establish a reporting system for ADRs and AEFIs and to provide the authority for the responsible entity to take actions if needed. The legislation should also provide for adequate and proportional sanctions, penalties and prosecution of violations of the applicable legislation. (Please refer to regulatory inspection function for further information on the regulatory enforcement and compliance activities).

#### Category:
01. Legal provisions, regulations and guidelines

#### Sub Indicator: VL01.01: Legal provisions for a national vigilance system exist.

#### Maturity Level:
1

#### Description:
The assessor should identify and review the applicable legal provisions establishing the national vigilance system and assess whether these provisions have been enacted. The assessor should verify that legal provisions mandating vigilance activities in both public as well as private sectors exist and are actually implemented. In addition, legislation should support activities related to the vigilance function.

This legislation should define the duties, powers, and responsibilities of the regulatory authority to manage risks associated with the use of medical products, including collection of data on the safety of the medical products, analysis and investigation of this data, and adoption of regulatory measures by the health authority.

In general, legal provisions should designate the entities responsible for undertaking different activities pertinent to vigilance functions. Such entities may or may not lie within the National Regulatory Authority (NRA). However, in all cases, the entities responsible for vigilance functions should be independent from all interested parties (e.g., manufacturers, marketing authorization holders (MAHs), purchasers and supply divisions, including the expanded programme on immunization (EPI), distributors, and health care professionals).

#### Objective:
The objective of this sub-indicator is to ensure that legal provisions exist for establishing the national vigilance system. These legal provisions provide the mandate for the responsible entities to actually implement their activities. Without such a mandate, the relevant regulatory activities would be too fragile and could be easily challenged.
<table>
<thead>
<tr>
<th>Requirement:</th>
<th>Legal provisions establishing the national vigilance system</th>
</tr>
</thead>
</table>
| Evidence to review: | The assessor should ask for and review:  
1. Legal provisions establishing the national medical products vigilance system (e.g., defining the responsible entities as well as the roles, responsibilities, accountability, and obligations of these entities). |
| Framework: | Structure/Foundation/Input |
| Rating Scale: | NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub-indicator.  
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results yet exist.  
PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet.  
IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced. |
| Limitations and remarks: | Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Sub Indicator: | VL01.02: Legal provisions and regulations require the manufacturers and/or MAHs to set up a vigilance system of their medical products and periodically report vigilance data to the NRA. |
| Maturity Level: | 1 |
| Description: | The assessor should verify that legal provisions stipulate that manufacturers and/or MAHs have an organized vigilance system to collect, record, store, maintain, evaluate and analyze adverse events (AEs) of their medical products in order to monitor their safety profile. In addition, the legal provisions should require manufacturers and/or MAHs to set up a vigilance system during the life cycle of their medical products and periodically report such events and these data, including “zero” events (i.e., situations where no events are reported), to the NRA. Reporting of these events should be done according to established requirements and in alignment with international standards. Examples include periodic safety update reports, and periodic benefit risk evaluation reports. The assessor should verify that the "zero" events have been included systematically in routine periodic reports (i.e.,... |
include a confirmation that no reports had been received).
The assessor should also verify that legislation includes the obligation that manufacturers and/or MAHs inform the NRA of any safety signal of a product as well as any marketing or regulatory decisions taken in the country of origin or other countries where the product is marketed. In line with these legal provisions, the assessor should verify that relevant guidelines include provisions that endorse this obligation and that explain how, when and what safety issues have to be reported (e.g. recall notifications, reporting of study results from ongoing or previous studies, and information on supervision of clinical trials). A similar obligation should also be in force for the MAH for all products marketed in the country. In addition, the assessor should also confirm that the legal provisions allow the NRA to conduct inspections in order to check the existence of vigilance systems as well as the implementation of the Good Vigilance Practices at the manufacturer’s and/or MAH’s site.

Objective: The objective of this sub-indicator is to ensure the existence of legal provisions mandating that the responsible entities require the MAH to establish a vigilance system for their medical products.

Requirement: Legal provisions mandating vigilance system establishment by the MAH

Evidence to review: The assessor should ask for and review:
1. Legal provisions mandating the manufacturers and/or MAHs to establish vigilance systems for their medical products.
2. Legal provisions obligating the manufacturers and/or MAHs to report safety data to the NRA.
3. Legal provisions authorizing the NRA to conduct vigilance inspections.
4. Regulations and guidelines explaining the obligations of the manufacturers and MAHs for safety data reporting.

References:

Framework: Structure/Foundation/Input

Rating Scale:
NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub-indicator.
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results exist yet.
PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently
established and are in early implementation phase so no consolidated results exist yet.

**IMPLEMENTED (I):** There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.

**Limitations and remarks:** Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

**VL01.03:** Guidelines ensure that distributors, importers, exporters, healthcare institutions, consumers and other stakeholders are encouraged to report adverse drug reactions (ADRs) and AEs to the MAH and/or NRA.

**Maturity Level:**

1

**Description:**

The assessor should verify the existence of guidelines (including any sort of formal documentation) for encouragement of different stakeholders (e.g., importers, exporters, distributors, health care professionals and institutions, consumers and patients) to report ADRs and AEs to the MAH and/or the NRA. The regulation should ideally be widely distributed and communicated to the public community in order to be meaningful and to be implemented.

**Objective:**

The objective of this sub-indicator is to ensure reporting of vigilance events by different stakeholders as an essential block of the vigilance function which significantly contributes to its effectiveness and impact.

**Requirement:**

Guidelines encouraging different stakeholders (including importers, exporters, distributors, health care professionals and institutions, public health programmes, consumers and patients) to report vigilance events to the MAH and/or the NRA.

**Evidence to review:**

The assessor should ask for and review:

1. Guidelines or other documentation encouraging reporting of vigilance events to the MAH and/or the NRA.

**References:**


**Framework:**

Structure/Foundation/Input

**Rating Scale:**

NOT IMPLEMENTED: There are no guidelines to satisfy the requirement of the sub-indicator.
<table>
<thead>
<tr>
<th><strong>Ongoing Implementation (OI):</strong></th>
<th>The NRA is taking steps towards establishment of guidelines to satisfy the requirement of the sub-indicator; however no results exist yet.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Partially Implemented (PI):</strong></td>
<td>Guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet.</td>
</tr>
<tr>
<td><strong>Implemented (I):</strong></td>
<td>There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.</td>
</tr>
</tbody>
</table>

**Limitations and remarks:**

- Event: a specific identifiable happening or occurrence, e.g., the taking of a medicine or the experience of an adverse effect.
- Adverse event (AE): Any untoward medical occurrence that may appear during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment.
- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

| VL01.04: Legal provisions and regulations allow NRA to require manufacturers and/or MAHs to conduct specific studies on safety and effectiveness under specific conditions. |

**Maturity Level:**

- 2

**Description:**

The assessor should verify that legal provisions and regulations provide the suitable and proportionate mandate for the NRA to require the manufacturers and/or MAHs to perform specific post-authorization safety activities to further characterize the safety profile of the product. For example, these may include the conduct of additional studies on safety and effectiveness under specific conditions, establishment of registries, and specific data analyses at time points post authorization. The assessor should verify that such legislation exists and is endorsed.

**Objective:**

The objective of this sub-indicator is to ensure that legal provisions and regulations are providing the necessary mandate for the NRA to request the manufacturers and/or MAHs to conduct specific safety and effectiveness studies under specific conditions.

**Requirement:**

Legal provisions and regulations allowing the NRA to require MAHs to perform specific post-authorization safety activities to further characterize the safety profile of the product. These may include, for example, the conduct of additional studies on safety and effectiveness under specific conditions, establishment of registries, or specific data analyses at time points post authorization, etc.).
<table>
<thead>
<tr>
<th>Evidence to review:</th>
<th>The assessor should ask for and review: 1. Legal provisions and regulations authorizing the NRA to request specific post-marketing phase safety and/or effectiveness studies.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framework:</td>
<td>Structure/Foundation/Input</td>
</tr>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub-indicator. ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results exist yet. PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>Effectiveness: a measure of the chances or odds (i.e., probability) of a medicine working positively as expected for patients. Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>VL01.05: Legal provisions, regulations and guidelines require manufacturers and/or MAHs to designate an individual person to be in charge of vigilance system.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify that legal provisions require the manufacturers and/or MAHs to designate an individual to be in charge of all vigilance activities relevant to their medical products placed on the market. This person should have oversight of the vigilance system in terms of structure and performance. In addition, the assessor should check the requirements for designation of that person and the responsibilities assigned to that person. Assessors should note that the qualifications for being designated as an individual person in charge of medical products vigilance may vary from one country or region to another; however in all cases the requirements should ensure the competence of the person responsible for these assigned roles and responsibilities.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure that legal provisions and regulations provide the necessary mandate for the NRA to obligate the manufacturers and/or MAHs to designate an individual person to be in charge of medical products vigilance.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Legal provisions and regulations mandating the manufacturers and/or MAHs to designate an individual person in charge of medical products vigilance.</td>
</tr>
<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review: 1. Legal provisions and regulations obligating the manufacturers and/or MAHs to designate an individual person to be in charge of medical products vigilance. 2. Documents that define the qualifications for being designated as an individual person in charge of medical products vigilance. 3. Documents that define the responsibilities of the individual person in charge of medical products vigilance.</td>
</tr>
<tr>
<td>Framework:</td>
<td>Structure/Foundation/Input</td>
</tr>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED: There are no legal provisions, regulations or guidelines to satisfy the requirement of the sub-indicator. ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions, regulations and guidelines to satisfy the requirement of the sub-indicator; however no results exist yet. PARTIALLY IMPLEMENTED (PI): Legal provisions, regulations and guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. IMPLEMENTED (I): There are legal provisions, regulations and guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>The title of the individual person in charge of medical products vigilance may vary from one country or region to another. For example, this person may be called a Qualified Person for Pharmacovigilance in one country or region, while a different title may be used in another. Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>VL01.06: There are guidelines for planning, conducting, monitoring, and reporting of vigilance activities.</td>
</tr>
</tbody>
</table>
**Maturity Level:** 3

**Description:**
The assessor should verify that guidelines exist and are endorsed for different vigilance activities, including planning, conducting, monitoring and reporting. The assessor should verify that the guidance is in agreement with other internationally accepted guidance such as that from the World Health Organization (WHO) or International Conference on Harmonization. As a general principle, harmonization of the safety regulatory framework is expected in order to facilitate the exchange of information and experience across NRAs. When applicable, differences should be identified.

The assessor should identify and review these guidelines and make sure they include:

1. Objectives of the vigilance system;
2. List of events (ADRs and adverse events following immunization (AEFIs)) to be reported;
3. For vaccines, case definitions of events to be reported;
4. Clear definitions of terminology relevant for analysis and response (e.g., AE, adverse reaction, medication error, coincidental error, program error, serious event, and cluster event);
5. Information on how to report (i.e., who, how, where, when and to whom);
6. All medical products to be included in the reporting system (i.e., reporting is not restricted to certain products or sectors);
7. Procedures for analyzing data;
8. Procedures for providing feedback of findings to key players (e.g. reporters of complaints, informers, parents, caregivers, associations and communities) and for relevant follow-up actions;
9. Guidance for investigations and actions to be taken in case of serious events or a cluster of events;
10. Guidance on assessment of the balance between risks and benefits for medical products;
11. Guidance on crisis prevention and management;
12. Guidance on communication of vigilance information;
13. Definition of the individuals in charge;
14. Guidance on potential vigilance-related differences and particularities among different medical products (e.g. medicines versus vaccines).

**Objective:**
The objective of this sub-indicator is to ensure that the guidelines reflect the current thinking of the NRA on different vigilance activities and are facilitating and promoting Good Vigilance Practices. This significantly contributes to vigilance effectiveness and consistency.

**Requirement:**
Guidelines relevant to vigilance including planning, conducting and reporting activities.
Evidence to review: The assessor should ask for and review:
1. Guidelines for MAH and competent authorities on vigilance activities.
2. Guidelines for planning, conducting and reporting of vigilance activities. Ideally, these should include the items listed in the description section of this fact sheet.

References:

Framework: Structure/Foundation/Input

Rating Scale:
NOT IMPLEMENTED: There are no guidelines to satisfy the requirement of the sub-indicator.
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of guidelines to satisfy the requirement of the sub-indicator; however no results exist yet.
PARTIALLY IMPLEMENTED (PI): Guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet.
IMPLEMENTED (I): There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.

Limitations and remarks: Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: VL01.07: Legal provisions and regulations allow recognition and/or reliance on vigilance-related decisions, reports or information from other countries or regional or international bodies.

Maturity Level: 1

Description: The assessor should verify that legal provisions and regulations permit the application of a recognition and/or reliance regulatory model to the vigilance-related national decisions. Although there is an ultimate need to establish a national vigilance system for medical products, recognition and/or reliance on vigilance-related information and decisions from other countries or regional or international entities would significantly contribute to the safety of medical products in the country. This would, in turn contribute to the public health.

While recognition considers regulatory decisions from other sources in an automatic way with minimal sharing of information and
justification, reliance depends heavily on information-sharing, communication, and scientific rationale and reasoning. Both approaches (i.e., recognition and reliance) might be applied in passive or active modes. However, the active mode is encouraged and preferred over the passive one.

### Objective:
The objective of this sub-indicator is to ensure that legal provisions and regulations are providing the necessary mandate for the NRA to apply recognition and/or reliance regulatory model.

### Requirement:
Legal provisions and regulations authorize the NRA to recognize and/or rely on vigilance-related decisions, reports or information from other countries or regional or international entities when making national vigilance decisions.

### Evidence to review:
The assessor should ask for and review:
1. Legal provisions and regulations relevant to reliance and/or recognition as applied to vigilance.
2. Legal provisions and regulations relevant to information sharing, reliance and/or recognition as applied to vigilance.

### References:

### Framework:
Structure/Foundation/Input

### Rating Scale:
- **NOT IMPLEMENTED**: There are no legal provisions or regulations to satisfy the requirement of the sub-indicator.
- **ONGOING IMPLEMENTATION (OI)**: The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results exist yet.
- **PARTIALLY IMPLEMENTED (PI)**: Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet.
- **IMPLEMENTED (I)**: There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.

### Limitations and remarks:
In some countries, legal provisions and regulations might not support such recognition or reliance. In this case, the scoring of the sub-indicator should be **NOT APPLICABLE** provided that national vigilance system is able to respond to vigilance events elsewhere.

### Indicator:
**VL02 Arrangement for effective organization and good governance.**

### Objective:
The objective of this indicator is to ensure effective organization and good governance practices at the entities in charge of vigilance activities. Effective organization and practices in turn contribute to the effective and efficient functioning of the vigilance
<table>
<thead>
<tr>
<th>Category:</th>
<th>02. Organization and governance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub Indicator:</td>
<td>VL02.01: There is a defined organizational structure with clear responsibilities to conduct vigilance activities.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>2</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should identify the organization set in place to establish, implement or maintain the vigilance regulatory function including the defined organizational structures that undertake different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. In case of involvement of more than one entity, the assessor should check the ways and approaches by which coordination among these structures is managed.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure effective organization and good governance of vigilance activities and that these are taken over by defined structures with clear roles and responsibilities.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Roles and responsibilities of the organizational structures in charge of vigilance activities.</td>
</tr>
<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review: 1. Organization chart of the organizations responsible for the implementation of vigilance activities along with identification of the particular structures implementing the function. 2. Documentation clarifying roles and responsibilities of the structures implementing vigilance activities. This may include, for example, administrative decrees, terms of reference, and position descriptions. 3. Documentation identifying established mechanisms of coordination (e.g., committees, internal work-sharing, and workflow) among structures, if any, which take part in vigilance activities.</td>
</tr>
<tr>
<td>Framework:</td>
<td>Structure/Foundation/Input</td>
</tr>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED: There is no defined structure in charge of vigilance activities.</td>
</tr>
</tbody>
</table>
| Ongoing Implementation (OI): A mandate to establish a structure in charge of vigilance activities is available; however the structure itself is not yet established.  
| Partially Implemented (PI): Structure in charge of vigilance activities is newly established and mandated; however the regular work and practice of this structure is not yet consolidated.  
| Implemented (I): There is defined structure in charge of vigilance activities with clear, well-documented roles and responsibilities. |

**Limitations and remarks:** Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:** VL02.02: Documented procedures and mechanisms are implemented to ensure the involvement, coordination and communication among all stakeholders relevant to vigilance activities

**Maturity Level:** 3

**Description:** The assessor should verify that different stakeholders relevant to vigilance regulatory function are identified. These stakeholders would include not only the different structures (e.g., organizations, institutions, and departments) implementing the regulatory function, but also other entities (e.g., manufacturers and MAHs), governmental agencies (e.g., supply divisions, procurement divisions, and public health programmes including EPI), international organizations (e.g., WHO or the Uppsala Monitoring Centre), non-governmental organizations, professional associations, and customer representative associations. In addition, the assessor should verify the availability and implementation of agreements, memoranda of understanding (MOUs) or documented procedures ensuring the active involvement, communication and collaboration among the identified stakeholders relevant to vigilance of medical products.

**Objective:** The objective of this sub-indicator is to ensure that documented procedures and other mechanisms are implemented to ensure the involvement, coordination and communication among different organizations, institutions, and departments for appropriate organization and good governance of the function.

**Requirement:** Agreements, MOUs and procedures for ensuring involvement of and communication among stakeholders relevant to vigilance regulatory function.

**Evidence to review:** The assessor should ask for and review:
1. List of stakeholders relevant to vigilance of different medical product streams.
2. Agreements, MOUs and standard operating procedures (SOPs) defining the means of communication and collaboration among
the identified stakeholders.
3. Example records of communication and collaboration demonstrating implementation of the above-mentioned procedures.
4. Guidelines or SOPs defining procedures for external and internal communications.
5. Documentation that regular meetings and other formal or official communication among above-mentioned stakeholders take place. This documentation should provide evidence for a systematic and well-established communication process.
6. Documentation of paths of communication and reporting.
7. Platforms for information sharing and exchange.

References:

Framework: Structure/Foundation/Input

Rating Scale:
- NOT IMPLEMENTED: There are no coordination and information exchange procedures or mechanisms among different stakeholders of the vigilance function or among the central authority and the decentralized entities.
- ONGOING IMPLEMENTATION (OI): The NRA is developing a coordination and information exchange mechanism, but it is not yet ready or exchanges are being conducted without an established methodology.
- PARTIALLY IMPLEMENTED (PI): The NRA recently established a coordination and information exchange procedure and mechanism that is at the implementation stage; however, this practice is not yet consolidated.
- IMPLEMENTED (I): There are established, implemented and well-maintained coordination and information exchange procedures and mechanisms among different stakeholders of the vigilance function and among the central authority and the decentralized entities.

Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator: VL03 Human resources to perform vigilance activities.

Objective: The objective of this indicator is to ensure that all entities within a National Regulatory Authority (NRA) that are concerned with vigilance activities are adequately resourced with a trained, experienced and skilled workforce, and that this workforce has the authority to fully perform the assigned responsibilities. This will ensure that vigilance processes and activities are performed in accordance with international best practices.
This indicator is assessed through the evaluation of the human resource capacity of the entities with respect to the number of personnel, the composition, skills and experience of the personnel, and the expertise in those specific areas required to perform the vigilance function.

**Category:**
06. Resources (HR, FR, infrastructure and equipment)

**Sub Indicator:**
VL03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform vigilance activities

**Maturity Level:**
3

**Description:**
The assessor should verify that the human resources assigned to perform vigilance activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for vigilance activities and that consider the requirements for educational background, competencies, skills, experience, and training.

The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform vigilance function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.

**Objective:**
The objective of this sub-indicator is to ensure the existing human resources for vigilance is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire vigilance chain.

**Requirement:**
Sufficient number of competent human resources in charge of vigilance activities.

**Evidence to review:**
The assessor should ask for and review:
1. Evidence that the number of staff members involved in each of the documented activities along the entire vigilance process flow is adequate.
2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills.
3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that
the staff competence is appropriate for the job requirements.
4. Evidence that the professional profiles of the human resources engaged in vigilance activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the vigilance chain. Documentation should include a list of the requisite skills and training for each position.
5. Recruitment plan.

### References:


### Framework:

Structure/Foundation/Input

### Rating Scale:

<table>
<thead>
<tr>
<th>Rating Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT IMPLEMENTED:</td>
<td>The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform vigilance activities</td>
</tr>
<tr>
<td>ONGOING IMPLEMENTATION (OI):</td>
<td>The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented.</td>
</tr>
<tr>
<td>PARTIALLY IMPLEMENTED (PI):</td>
<td>The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile.</td>
</tr>
<tr>
<td>IMPLEMENTED (I):</td>
<td>The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform vigilance activities.</td>
</tr>
</tbody>
</table>

### Limitations and remarks:

Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes.

Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:

VL03.02: Duties, functions, and responsibilities of the staff in charge of vigilance activities are established and updated in the respective job descriptions

### Maturity Level:

3

### Description:

The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in vigilance activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all
staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in vigilance activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.

| Objective: | The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented. |
| Requirement: | Duties, roles and responsibilities of the staff relevant to vigilance activities. |
| Evidence to review: | The assessor should ask for and review:  
1. Procedure and guidelines that guide placement of staff members within the NRA;  
2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties;  
3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions;  
4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures;  
5. Job descriptions for designated staff. |
<table>
<thead>
<tr>
<th>Framework:</th>
<th>Structure/Foundation/Input</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating Scale:</td>
<td></td>
</tr>
<tr>
<td>NOT IMPLEMENTED:</td>
<td>There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies.</td>
</tr>
<tr>
<td>ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented.</td>
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<tr>
<td>PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date.</td>
<td></td>
</tr>
<tr>
<td>IMPLEMENTED (I):</td>
<td>The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
</tbody>
</table>

**Sub Indicator:** VL03.03: Training plan developed, implemented and updated at least once a year for staff in charge of vigilance activities.

**Maturity Level:** 3

**Description:**
The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on-the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals, and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.

**Objective:**
The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated.
annually. Through the training plan, NRA can be sure that competency of staff in charge of vigilance activities is maintained and enhanced.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Implementation of training plan</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Evidence to review</th>
<th>The assessor should ask for and review:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training.</td>
<td></td>
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<tr>
<td>2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities.</td>
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<tr>
<td>3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in relation to the respective individual job descriptions.</td>
<td></td>
</tr>
<tr>
<td>4. SOP for developing and maintaining the training plan.</td>
<td></td>
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<tr>
<td>5. Evidence that the NRA has investigated and identified training needs.</td>
<td></td>
</tr>
<tr>
<td>6. List of trainings performed.</td>
<td></td>
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<tr>
<td>7. Example records for training activities.</td>
<td></td>
</tr>
</tbody>
</table>

|------------|---------------------------------------------------------------------------------------------------|

| Framework | Process |
| Rating Scale: | NOT IMPLEMENTED: There is no systematic training program including training plan (or matrix).  
ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation.  
PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years.  
IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff. |
| Limitations and remarks: | Training plans must be updated regularly; ideally on an annual basis, but not less frequently than once every two years.  
Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine vigilance-relevant training not included in the NRA training plan.  
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Sub Indicator: | VL03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification. |
| Maturity Level: | 3 |
| Description: | The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings, and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established. |
| Objective: | The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy. |
| Requirement: | Training records |
### Evidence to review:

The assessor should ask for and review:

1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities;
2. Evaluations of training effectiveness;
3. The training inventory, and procedures for completing the inventory;
4. Examples of archived records of staff training, and procedures for the archiving system.

### References:


### Framework:

Output

### Rating Scale:

- **NOT IMPLEMENTED:** There is no evidence that the NRA generates and maintains records of staff training activities.
- **ONGOING IMPLEMENTATION (OI):** The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed.
- **PARTIALLY IMPLEMENTED (PI):** The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years.
- **IMPLEMENTED (I):** The NRA generates and maintains records of staff training activities.

### Limitations and remarks:

The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the
archiving systems in place. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

<table>
<thead>
<tr>
<th>Indicator:</th>
<th>VL04 Procedures established and implemented to perform vigilance activities.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective:</td>
<td>The objective of this indicator is to ensure that required activities of the vigilance system are implemented through standard procedures and work instructions that ensure the consistency, effectiveness, efficiency, impartiality and proportionality of the vigilance system. The NRA should have established a system which allows the regular review of safety and effectiveness aspects of the authorized products on the market, including processes to review and share relevant data between key players and to take appropriate action when necessary. There should be written procedures that define how relevant data are routinely shared among key personnel engaged in vigilance activities and how any actions taken are reviewed for appropriateness. Documented evidence to be assessed include procedures for review of safety and effectiveness aspects of medical products on the market, for review of reports of notifications, investigations, data analyses, and committee meetings, for sharing of relevant data among key players, and for taking appropriate actions.</td>
</tr>
<tr>
<td>Category:</td>
<td>07. Regulatory process</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>VL04.01: Vigilance procedures and tools are in place and implemented for collection and assessment of ADRs and AEs.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify the existence and implementation of standard procedures for different vigilance activities related to collection and assessment of ADRs and AEs including: 1. Existence of a paper-based or an electronic reporting system for ADR- and AEFI-related information that is accessible to MAHs, healthcare professionals and patients 2. Systems for detection and receipt of vigilance events and ADR reports that is complemented with reporting systems (e.g., either active or passive, and either sentinel or country- or state-wide) that have the satisfactory sensitivity to detect serious events or clusters of events. For this point, the assessor should check for the number and rates of reports within defined periods, ADRs following off-label use, and a breakdown of reports that compares district or regional reporting activities for the different products and populations that are involved in vigilance reporting.</td>
</tr>
</tbody>
</table>
3. Timely review, analysis, and causality assessment of ADRs and AEs. For this process, assessor should verify that:
   a. in 80% of cases an investigation is initiated within 48 hours following reporting (for vaccines);
   b. preliminary investigation report is available within 1 week (for vaccines);
   c. Investigation is of adequate quality, procedures are thorough, and findings are clearly-described;
   d. conclusions are scientifically justified and supported by findings.
4. Records of reported ADRs and AEFIs (for vaccines) are stored and maintained.

The assessor should verify that the above-mentioned procedures are consistent with the relevant national guidelines which in turn are in coherence with WHO or other international accepted guidance. The assessor should review records that verify the actual implementation of such procedures.
In addition, the assessor should verify that all vigilance data received are analyzed on a regular basis. The assessor should check the tools NRA is using to collect and analyze the data (e.g. calculation of incidence rates or the assessment of causality). WHO recommends the following tools:
1. A national database or similar centralized (e.g., regional, sub-regional or global) system, that is compatible with International Conference on Harmonization E2B, to code, collate, and store data and reports and to analyze vigilance data.
2. The adoption of standard case definitions for AEFIs (e.g., Brighton collaboration definitions or national case definitions).

| Objective: | The objective of this sub-indicator is to ensure consistency of different activities of the medical products vigilance system through standard procedures which are complemented by the necessary tools. |
| Requirement: | Procedures and tools necessary for effective implementation of different regulatory activities. |
| Evidence to review: | The assessor should ask for and review:
   1. Procedures and records of reporting systems including reporting forms or platforms used within the country;
   2. Codes and case definitions (for vaccines);
   3. Procedures and methods used for causality assessment;
   4. Numbers and rates of reports within defined period(s), a list of ADRs following off-label use, and a breakdown of reports that compares district or regional reporting activities for the different products and populations involved in vigilance reporting.
   5. Number of reports transmitted to WHO database along with the frequency of submission. |

#### Framework:
Process

#### Rating Scale:
- **NOT IMPLEMENTED:** No procedures exist for collection and assessment of ADRs and AEs.
- **ONGOING IMPLEMENTATION (OI):** The NRA is taking steps towards development and establishment of procedures for collection and assessment of ADRs and AEs; however no results yet exist.
- **PARTIALLY IMPLEMENTED (PI):** Procedures for collection and assessment of ADRs and AEs were recently established by the NRA and are in early implementation phase so no consolidated results exist yet.
- **IMPLEMENTED (I):** Standard procedures exist and are implemented for collection and assessment of ADRs and AEs.

#### Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

#### Sub Indicator:
**VL04.02: Vigilance procedures and tools are in place for investigation, interpretation of and response to ADRs and AEs.**

#### Maturity Level:
3

#### Description:
The assessor should verify the existence and implementation of standard procedures for different vigilance activities related to investigation and interpretation of and response to ADRs and AEs including:
1. Investigation and assessment of ADRs and AEs
2. Assessment of risk, analysis and evaluation of vigilance data, and identification of trends
3. Processes for signal detection;
4. Use of statistical tools to calculate reporting disproportionalities such as Proportional Reporting Ratio
5. Initiation of appropriate actions at the national or sub-national level when needed. For this particular process, the assessor should verify that all vigilance events are screened and triaged by staff that is qualified to assess their impact on public health and to determine the subsequent steps needed. These steps may include one or more of the following:
   - Addition to national vigilance database
   - Follow up or further analysis
   - Referral for comprehensive investigation or systematic causality assessment
   - Issue of safety alerts and/or batch or product recalls
Objective:
The objective of this sub-indicator is to ensure consistency of different activities related to investigation of, interpretation of, and response to ADRs and AEs.

Requirement:
Procedures and tools necessary for investigation, interpretation of and response to ADRs and AEs.

Evidence to review:
The assessor should ask for and review:
1. Procedures for taking action on recommendations arising from causality assessment;
2. Investigation reports;
3. Documentation of actions taken following reporting of vigilance events (ADRs, AE and AEFIs);
4. Reports of notifications, data analyses, committee meetings, and other related records;
5. Documentation regarding the number of signals detected from national, regional or linked international databases, if any;
6. Listing of the AEFIs reported (e.g., from the EPI to the NRA or vigilance center) over the last two years.

References:

Framework: Process

Rating Scale:
NOT IMPLEMENTED: No procedures exist for investigation of, interpretation of and response to ADRs and AEs.
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development and establishment of procedures for investigation of, interpretation of and response to ADRs and AEs; however no results yet exist.
**Sub Indicator:** VL04.03: Standard procedures exist and are implemented for enforcement of the national vigilance system.

**Maturity Level:** 4

**Description:** The assessor should verify the existence and enactment of standard procedures for different vigilance enforcement activities including, for example, product label changes, restrictions of use, product withdrawals or suspensions, or implementation of intensive monitoring. The assessor should confirm that, as part of these procedures, the NRA notifies manufacturers (and vice versa) of significant safety and efficacy issues and that reporting is kept up to date.

**Objective:** The objective of this sub-indicator is to ensure consistency of the vigilance function through standard procedures for enforcement activities.

**Requirement:** Standard procedures for different vigilance enforcement activities.

**Evidence to review:**

1. Standard procedures for enforcement activities relevant to vigilance system;
2. Records of vigilance inspections of MAHs and corrective actions and preventive actions issued over the last two years;
3. Records of enactment of these standard procedures (e.g., decisions communicated to manufacturers and MAHs).

**References:**

<table>
<thead>
<tr>
<th>Framework:</th>
<th>Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED: No standard procedures exist for enforcement of the national vigilance system. ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development and establishment of procedures for enforcement of the national vigilance system; however no results yet exist. PARTIALLY IMPLEMENTED (PI): Procedures for enforcement of the national vigilance system were recently established by the NRA and are in early implementation phase so no consolidated results exist yet. IMPLEMENTED (I): Standard procedures exist and are implemented for enforcement of the national vigilance system.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>VL04.04: Risk approach is considered throughout different vigilance activities, including timely response to detected signals for risks or benefits.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify that different vigilance activities are implemented with consideration of risk approach. In general, the principle of risk proportionality should be applied in the decision-making process for post-approval activities. This entails risk assessment, including identification of different risks along with their analysis and evaluation, risk control, via risk reduction, mitigation or acceptance, and regular risk review, which may include adoption of any necessary changes in the risk management process. Risk communication should also be considered across all steps of the risk management process. Those products, events, or activities of high risk should be given higher attention when establishing risk mitigation and control strategies and procedures.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure that a risk approach consideration is contributing to vigilance function efficiency and effectiveness.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Consideration of risk approach in different vigilance activities including timely response to detected signals for risks or benefits.</td>
</tr>
<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review: 1. Procedures for risk approach consideration in different vigilance activities. 2. Examples of risk management process including risk assessment, risk control and risk review. 3. Examples of risk management strategy for identified high risk products, events or activities.</td>
</tr>
</tbody>
</table>
## References:


## Framework:

<table>
<thead>
<tr>
<th>Sub Indicator:</th>
<th>VL04.05: Staff access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials) is ensured.</th>
</tr>
</thead>
</table>

## Rating Scale:

- **NOT IMPLEMENTED**: Risk approach is not considered throughout different vigilance activities.
- **ONGOING IMPLEMENTATION (OI)**: The NRA is taking steps towards consideration of risk approach for different vigilance activities; however, no results yet exist.
- **PARTIALLY IMPLEMENTED (PI)**: Consideration of risk approach for different vigilance activities was recently established and is in early implementation phase so no consolidated results exist yet.
- **IMPLEMENTED (I)**: Risk approach is considered throughout different vigilance activities.

## Limitations and remarks:

The risk approach meant herein is that related to NRA. However, employment of risk approach by manufacturers and MAHs is also of great value and should be verified by the NRA as part of its implementation and enforcement of vigilance activities.

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

## Maturity Level:

<table>
<thead>
<tr>
<th>Sub Indicator:</th>
<th>VL04.05: Staff access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials) is ensured.</th>
</tr>
</thead>
</table>

| Maturity Level: | 1 |

## Description:

The assessor should verify that staff responsible for different vigilance activities, including members of any expert committees, have access to both internal and external sources of information and reference materials, including literature and publications, to allow them to make decisions on vigilance events. Information resources include, among others, all scientific information concerning the use of medicinal products and the outcome of their use, (i.e., quality, nonclinical and clinical data, including pharmacovigilance and pharmaco-epidemiological data). Access to market information might be helpful as well (e.g. medicines utilization statistics).

## Objective:

The objective of this sub-indicator is to ensure access of the responsible staff to vigilance relevant information resources, reference materials and literature as an essential contributing factor for effective performance of the function.
<table>
<thead>
<tr>
<th>Requirement:</th>
<th>Access of vigilance staff to relevant information resources</th>
</tr>
</thead>
</table>
| Evidence to review: | The assessor should ask for and review:  
1. Subscriptions to databases of scientific literature with up-to-date studies and information on medical products safety and efficacy;  
2. A list of electronic and printed materials consulted during the vigilance event analysis and investigation (e.g., books, international guidelines, or international package inserts),  
3. Access to pre-market, preclinical and clinical trial data;  
5. Access to Periodic Safety Update Reports and Periodic Benefit Risk Evaluation Reports  
6. Access to renewal dossiers |
| Framework: | Process |
| Rating Scale: | NOT IMPLEMENTED: Staff does not have access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials).  
ONGOING IMPLEMENTATION (OI): The NRA is taking steps to guarantee staff access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials); however no results exist yet.  
PARTIALLY IMPLEMENTED (PI): Staff access to information resources relevant to vigilance processes (e.g. safety information sources and reference materials) was recently established and is in early implementation phase; however, no consolidated results exist yet.  
IMPLEMENTED (I): Staff has reasonable access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials). |
| Limitations and remarks: | Efficacy is defined as the ability of a drug to produce the purported effect as determined by scientific methods.  
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
<table>
<thead>
<tr>
<th>Sub Indicator:</th>
<th>VL04.06: The NRA has access to expert committees for review of serious emergent safety concerns, when needed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify access of the NRA to a standing advisory committee or other group of experts for the investigation, assessment and analysis of serious vigilance events (ADRs and AEFIs). The expert members of this committee might be internal or external to the NRA; however in case of external staff, the appropriate measures should be taken to ensure that relevant interests are declared and that confidentiality is maintained. The assessor should review terms of reference and written standard procedures defining conditions and processes for the election of the members and for assuring their expertise. Confidentiality, independence of the experts and prevention and handling of conflicts of interest should also be regulated. The NRA should have access to any other experts when needed. The assessor should also verify NRA access to external expertise in specific medical fields (e.g., teratology) when needed as part of this sub-indicator.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure effective investigations, assessments and analyses of serious vigilance events through the access to an expert committee (unless extensive and sufficient internal expertise is available).</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Expert committee for review of serious vigilance events</td>
</tr>
<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review: 1. Terms of reference and standard procedures for the expert committee for review of serious vigilance events. 2. Records of discussions and decisions of the expert committee for review of serious vigilance events over the last two years or the last 5 to 10 meetings. 3. Procedures for convening the expert committee when needed to provide advice and recommendations. 4. Procedures for follow-up and implementation of the expert committee recommendations, including procedures for reconvening the expert committee as needed to review progress.</td>
</tr>
</tbody>
</table>
### Framework:
Process

### Rating Scale:
- **NOT IMPLEMENTED**: The NRA does not have access to expert committees for review of serious emergent safety concerns.
- **ONGOING IMPLEMENTATION (OI)**: The NRA is taking steps towards guaranteeing access to expert committees for review of serious emergent safety concerns; however no results exist yet.
- **PARTIALLY IMPLEMENTED (PI)**: NRA access to expert committees for review of serious emergent safety concerns was recently established and is in early implementation phase, so no consolidated results exist yet.
- **IMPLEMENTED (I)**: The NRA has access to expert committees for review of serious emergent safety concerns, when needed.

### Limitations and remarks:
There might be a limitation if the expert committee is not formalized or does not meet frequently.

### Sub Indicator:
**VL04.07**: With respect to vigilance data, assessment of the risk-benefit balance of medical products is regularly conducted.

### Maturity Level:
4

### Description:
The assessor should verify that safety and/or effectiveness of medical products placed on the market are regularly evaluated through periodic assessment of the risk-benefit balance of medical products. Towards this end, the assessor should verify the availability of risk-benefit analysis tools and processes, including descriptions of their application to regulatory decision making. The assessor should also confirm that vigilance data are informing such risk-benefits assessments, and that informed, science-based decisions are taken when necessary. Risk-benefit assessment is an important regulatory tool that highlights the risk-benefit of therapeutic products. Industry (i.e., the MAH) is primarily responsible for developing risk-benefit assessments.

Product vigilance evaluation involves the ongoing assessment of the risk-benefit of a product (including, for example, data from adverse reaction reports, clinical trials, meta-analysis, and observational studies). These assessments provide the assurance that benefits outweigh the risks for a given population during clinical trials and following market authorization. The frequency of this evaluation varies significantly depending on the maturity of the national vigilance system. In addition, the assessor should verify that after the risk-benefit assessment of the medical products, the NRA is making well-justified decisions based on scientifically sound evidence and is taking necessary regulatory in response to the risks detected. The goals of the actions are to minimize risk and maintain a favorable risk-benefit profile. With the current regulatory landscape, these interventions generally fall within the following options:

- Issuance of a risk communication;
Objective: The objective of this sub-indicator is to ensure the sustained and effective evaluation of medical products safety and effectiveness, and the ongoing evaluation of their risk-benefit balance with full consideration of national and international vigilance data.

Requirement: Risk-benefit assessment of medical products with consideration of vigilance data

Evidence to review: The assessor should ask for and review:
1. Standard procedures relevant to the risk-benefit assessment of medical products;
2. Documented evidence of the consideration of the vigilance data in these processes;
3. Regulatory decisions and actions for maintaining the favorable risk-benefit balance of the medical products placed on the market.

References:

Framework: Process

Rating Scale: NOT IMPLEMENTED: Assessment of risk-benefit balance of medical products is not regularly conducted at all.
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards assessment of risk-benefit balance of medical products on regular basis; however no results exist yet.
PARTIALLY IMPLEMENTED (PI): Assessment of risk-benefit balance of medical products is regularly conducted; however consideration of vigilance data is not fully utilized or consideration of vigilance data for risk-benefit assessment was recently established and remains in early implementation phase. For these reasons, no consolidated results yet exist.
IMPLEMENTED (I): Risk-benefit balance of medical products is regularly conducted with full consideration of vigilance data.

Limitations and remarks: Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: VL04.08: Active vigilance activities, as well as proactive monitoring programmes (when needed) have been developed and implemented.

Maturity Level: 4
| Description: | The assessor should verify the existence and implementation of active surveillance systems as well as proactive vigilance systems for early detection of events. The goal is to initiate corrective actions and preventive actions to manage use of medical products of significant public health impact and medical products of potential high risk. Passive surveillance means that no active measures are taken to look for AEs other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of vigilance. It is commonly referred to as “spontaneous” or “voluntary” reporting. In some countries, this form of reporting is mandatory. Active safety surveillance, on the other hand, means that active measures are taken to detect AEs. This is managed by active follow-up after treatment and the events may be detected by asking patients directly or by screening patient records. Such follow-up is best done prospectively. Active vigilance is sometimes very descriptively referred to as, “hot pursuit”. The most comprehensive method is cohort event monitoring. Examples of this are the Intensive Medicines Monitoring Programme in New Zealand and Prescription Event Monitoring in England. Other methods used include the use of registers, record linkage and screening of laboratory results in medical laboratories. Active surveillance may entail several activities including signal detection and field research. One of the most important activities in the vigilance system is the ability to detect safety issues as quickly as possible. Safety management programs should be then established. Active surveillance might be applied to all medical products or to selected high risk medical products. Proactive approach is mainly related to and based on the assessment of pre-market data which could contribute to risk management, risk mitigation or risk minimization when necessary. |
| Objective: | The objective of this sub-indicator is to ensure that vigilance systems are implemented in active and/or proactive manners, rather than reactively, when needed for protecting public health. |
| Requirement: | Active vigilance monitoring and surveillance programme. |
| Evidence to review: | The assessor should ask for and review: 1. Standard procedures and mechanisms relevant to proactive vigilance systems; 2. Standard procedures and mechanisms relevant to active vigilance activities; 3. Risk management plans from the manufacturers. |
### Framework:
Process

### Rating Scale:
- **NOT IMPLEMENTED:** No active surveillance or proactive vigilance systems are implemented at all.
- **ONGOING IMPLEMENTATION (OI):** The NRA is taking steps towards development of procedures for active surveillance and/or proactive vigilance systems; however no results exist yet.
- **PARTIALLY IMPLEMENTED (PI):** Procedures and mechanisms for active surveillance and/or proactive vigilance system were recently established by the NRA and are in early implementation phase so no consolidated results exist yet.
- **IMPLEMENTED (I):** Active surveillance and/or proactive vigilance system are implemented based on well-established criteria.

### Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Indicator:
**VL05 Mechanism in place to monitor regulatory performance and output.**

### Objective:
The objective of this indicator is to ensure the effectiveness of the different medical-product related vigilance activities, to measure relevant advancements, and to ensure that performance indicators are established, implemented and verified on a regular basis.

### Category:
09. Monitoring progress and assessing outcomes & impact

### Sub Indicator:
**VL05.01: Vigilance information is used in timely manner to amend existing regulatory decisions or to issue new regulatory decisions or actions.**

### Maturity Level:
3

### Description:
The assessor should verify that corrective regulatory decisions and actions (e.g., suspensions, recalls, updates of product leaflet, product withdrawals or revocations of marketing authorization) are based on vigilance findings and are in accordance with national regulations and WHO recommendations. Furthermore, the assessor should verify that the regulatory actions related to the vigilance function are implemented and monitored.

### Objective:
The objective of this sub-indicator is to ensure that the vigilance function provides the scientific basis for regulatory decisions and
actions and serves to maintain a favorable risk-benefit balance for medical products placed on the market.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Regulatory decisions and actions in response to vigilance information.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence to review</td>
<td>The assessor should ask for and review: 1. List of regulatory decisions based on vigilance events in the last two years. 2. Examples of decisions and actions taken in response to vigilance events in the last two years. 3. Communications and publications of regulation decisions and actions that were provided to different entities within or outside the NRA. 4. List of investigated, detected or analyzed signals in the last two years.</td>
</tr>
<tr>
<td>Framework</td>
<td>Output</td>
</tr>
<tr>
<td>Rating Scale</td>
<td>NOT IMPLEMENTED: no evidence exists for the confirmation that vigilance information is used to amend or issue regulatory decisions and consequent actions in timely manner. ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards usage of vigilance information to amend or issue regulatory decisions; however no results exist yet. PARTIALLY IMPLEMENTED (PI): The NRA started recently to use vigilance information to amend or issue regulatory decisions; however, the practice is in the early implementation stage and not yet consolidated. IMPLEMENTED (I): Evidence exists to confirm that vigilance information is used to amend or issue regulatory decisions and consequent actions in timely manner.</td>
</tr>
<tr>
<td>Limitations and remarks</td>
<td>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator</td>
<td>VL05.02: Performance indicators for vigilance activities are established and implemented</td>
</tr>
<tr>
<td>Maturity Level</td>
<td>4</td>
</tr>
</tbody>
</table>
Description: The assessor should verify the existence and implementation of performance indicators for different activities included under the vigilance function. Specifically, the system should define key performance indicators (KPIs) along the entire vigilance activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Performance indicators for activities included under the medical products vigilance system should include:

- detection or receipt of vigilance events from within the reporting system;
- timely review, investigation and assessment of vigilance events;
- feedback on the vigilance activities to different stakeholders;
- storage and management of reported vigilance data;
- risk assessment, analysis and evaluation of vigilance data and identification of trends;
- initiation of appropriate actions at the national or sub-national level when needed; and
- risk management and risk communication plans.

Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement.

In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.

Objective: The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire vigilance chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of vigilance regulatory activities, and to making any necessary adjustments or optimizations.

Requirement: KPIs for medical products vigilance activities

Evidence to review: The assessor should ask for and review:
1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance...
indicators along the entire vigilance activity chain.
2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the vigilance function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance.
3. The current performance indicators for vigilance activities
4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities.
5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.

References:

Framework:
| Output |

Rating Scale:
| NOT IMPLEMENTED: There are no KPIs for vigilance activities. |
| ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for vigilance activities but they have not yet been reported. |
| PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for vigilance activities and has been applying them for less than two year or they have not covered all critical steps. |
| IMPLEMENTED (I): The NRA has established and implemented KPIs for vigilance activities. The indicators are reviewed regularly, and appropriate actions are taken and decisions made. |

Limitations and remarks:
When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop.
Different methodologies are used to measure the NRAs performance on vigilance activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., “SMART”). Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Indicator:
**VL06 Mechanism exists to promote transparency, accountability and communication**

### Objective:
The objective of this indicator is to ensure communication within the NRA, transparency and outreach to public, regional and international partners, and accountability of the NRA. Additionally, these contribute to mutual understanding and involvement of all stakeholders that are relevant to the vigilance system and raise the confidence in the regulatory system.

### Category:
08. Transparency, accountability and communication

### Sub Indicator:
**VL06.01: Vigilance activities and relevant feedback are appropriately communicated to the public.**

### Maturity Level:
2

### Description:
The assessor should verify that a proper mechanism is available, enacted and used to demonstrate that regular feedback and information on the vigilance system, in particular, serious events and clusters of AEs, are communicated appropriately to the public (including patients, parents and caregivers). Furthermore, guidance to the public community on ways and approaches to manage any potential risks, may contribute significantly to risk reduction or elimination. Investigation reports of public concerns and summaries of these reports should be made available to the public. Regular publications (e.g., bulletins) or awareness sessions would serve the above-mentioned communication mechanism.

In addition, considering the fact that medical professionals and the public community play a crucial role in the vigilance system, activities for raising their awareness is necessary. The assessor should verify that regular meetings, trainings, educational sessions, educational materials, and media aids are provided for a wide audience, including undergraduate, postgraduate medical, pharmacy and nursing students, staff and healthcare providers in public and private sectors, staff from immunization programs, and the general public community.

### Objective:
The objective of this sub-indicator is to ensure the implementation and effectiveness of the overall vigilance system, in particular, to ensure that the risk management and risk communication plans are regularly and systematically implemented (i.e., not on ad hoc basis).
<table>
<thead>
<tr>
<th>Requirement:</th>
<th>Communication mechanism for the public community on vigilance events, especially serious ones.</th>
</tr>
</thead>
</table>
| Evidence to review: | The assessor should ask for and review:  
1. Records of communications to the public community (e.g., social media, newsletters, and websites);  
2. Information bulletins and documentation of public awareness sessions and campaigns;  
3. Published alerts, assessments and investigation reports. |
| Framework: | Output |
| Rating Scale: | NOT IMPLEMENTED: Vigilance activities and feedback are not communicated to the public community.  
ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards sharing of vigilance activities and providing feedback to the public community, but no results yet exist.  
PARTIALLY IMPLEMENTED (PI): The NRA started recently to share vigilance activities and provide feedback to the public community; however, it has only limited experience or a limited number of documented events.  
IMPLEMENTED (I): Vigilance activities and feedback, especially for serious events and clusters of AEs, are appropriately communicated to the public community. |
| Limitations and remarks: | Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Sub Indicator: | VL06.02: Mechanism for regular feedback to all stakeholders on vigilance events exists and is complemented with a risk communication plan. |
| Maturity Level: | 3 |
| Description: | The assessor should verify that a proper mechanism is available, enacted and used to demonstrate that information on vigilance system, especially serious events and clusters of AEs, are shared among all stakeholders engaged in medical products vigilance. |
Key players include the NRA or the vigilance center, manufacturers, MAHs, purchasers and supply divisions (including the EPI in case of vaccines), distributors, and other health care professionals. The assessor should verify that the process for feedback is established, endorsed and followed down to health facility level. The assessor should note that the regularity of outreach to the stakeholders depends on the availability of data, decisions, or actions. In addition, the assessor should verify that regular formal or official communications and meetings take place among above-mentioned key players when dealing with vigilance events. The assessor should check that periodic feedback is offered from the NRA or the responsible authority to all levels country-wide, especially to medical and health professionals. Particularly for vaccines, the NRA should be informed about in-country vaccine safety and performance information including vaccine preventable diseases surveillance data, EPI coverage data, information on number of doses shipped and administered, seroprevalence study reports, outbreak investigation reports, EPI reports on vaccine supply and storage (i.e., cold chain), special instructions, and recall notifications.

**Objective:**
The objective of this sub-indicator is to ensure the implementation and effectiveness of the overall vigilance system, particularly the risk management and risk communication plans.

**Requirement:**
Risk communication plan as a part of an overall mechanism for regular feedback to all stakeholders on vigilance system.

**Evidence to review:**
The assessor should ask for and review:
1. Risk communication plan and procedures for communication with different stakeholders involved in the vigilance system.
2. Examples of shared information among those stakeholders.
3. Records of communication (e.g., social media, newsletters, websites, or publications) among the NRA and those stakeholders.
4. Records of regular meetings among the vigilance relevant stakeholders.

**References:**

**Framework:**
Output

**Rating Scale:**
NOT IMPLEMENTED: Feedback on vigilance events and activities are not communicated to all relevant stakeholders.
<table>
<thead>
<tr>
<th>ONGOING IMPLEMENTATION (OI):</th>
<th>The NRA is taking steps towards providing feedback on vigilance events and activities to all relevant stakeholders, but no risk communication plan or results yet exist.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTIALLY IMPLEMENTED (PI):</td>
<td>The NRA started recently to provide feedback on vigilance events and activities to all relevant stakeholders; however, the NRA has only limited experience or it has a limited number of documented events.</td>
</tr>
<tr>
<td>IMPLEMENTED (I):</td>
<td>Feedback on vigilance events and activities are communicated to all relevant stakeholders. These activities are based on a well-developed risk communication plan.</td>
</tr>
</tbody>
</table>

**Limitations and remarks:**

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

**VL06.03: Vigilance data and findings are shared with relevant regional and international partners.**

**Maturity Level:**

3

**Description:**

The assessor should verify that national vigilance data and findings and conclusions are shared with relevant regional and international partners (e.g. WHO Collaborating Centers). The assessor should confirm that the national vigilance staff have access to the regional and international tools (e.g., databases) and should verify that these tools facilitate information sharing and analysis. In addition, the assessor should confirm that there is two-way collaboration and interaction among the national vigilance system and relevant regional and international partners.

**Objective:**

The objective of this sub-indicator is to ensure medical products safety and efficacy through sharing of global concerns and relevant vigilance data and findings among the national and international communities; such sharing will benefit all stakeholders. This sharing also fosters regulatory convergence and harmonization.

**Requirement:**

Regional and international sharing of vigilance data and findings.

**Evidence to review:**

The assessor should ask for and review:

1. Proof of membership of the national vigilance system in relevant regional and international organizations or partnerships.
2. Proof of regular communications and interactions with those regional and international partners.
3. Proof of engagement of national vigilance system in regional or international meetings, conferences, or symposia.
4. Publication of vigilance data in scientific publications as a means of communication with international and regional partners.
5. List of serious ADRs and AEFIs submitted to WHO Collaborating Centers in the last two years.

**References:**


<table>
<thead>
<tr>
<th>Framework:</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED: Vigilance data and findings are not shared with relevant regional and international partners. ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards sharing of vigilance data and findings with other regional and international partners, but results do not yet exist. PARTIALLY IMPLEMENTED (PI): The NRA started recently to share vigilance data and findings with other regional and international partners; however, it has only limited experience or a limited number of documented events. IMPLEMENTED (): Vigilance data and findings are shared with relevant regional and international partners.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
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</table>