This document provides interim procedural guidance and general considerations related to the evaluation and listing of a regulatory authority as a WHO Listed Authority (WLA). WHO foresees further amendment of this guidance based on experience gained from the initial piloting of the WLA Framework in 2022.
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## List of acronyms

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<th>Description</th>
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<tbody>
<tr>
<td>ADG</td>
<td>WHO Assistant Director-General</td>
</tr>
<tr>
<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
</tr>
<tr>
<td>CT</td>
<td>Clinical Trial, Clinical Trials Oversight</td>
</tr>
<tr>
<td>EC</td>
<td>Ethic Committee</td>
</tr>
<tr>
<td>EOI</td>
<td>Expression of Interest</td>
</tr>
<tr>
<td>FP</td>
<td>Finished Product</td>
</tr>
<tr>
<td>GBT</td>
<td>Global Benchmarking Tool</td>
</tr>
<tr>
<td>GCP</td>
<td>Good Clinical Practices</td>
</tr>
<tr>
<td>GDP</td>
<td>Good Distribution Practices</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practices</td>
</tr>
<tr>
<td>GRP</td>
<td>Good Regulatory Practices</td>
</tr>
<tr>
<td>GRelP</td>
<td>Good Reliance Practices</td>
</tr>
<tr>
<td>GVP</td>
<td>Good Vigilance Practices</td>
</tr>
<tr>
<td>LI</td>
<td>Licensing Establishments</td>
</tr>
<tr>
<td>LR</td>
<td>Lot Release, National Lot Release</td>
</tr>
<tr>
<td>LT</td>
<td>Laboratory Testing</td>
</tr>
<tr>
<td>MA</td>
<td>Marketing Authorization</td>
</tr>
<tr>
<td>MC</td>
<td>Market Control, Market Surveillance and Control</td>
</tr>
<tr>
<td>ML</td>
<td>Maturity Level</td>
</tr>
<tr>
<td>MS</td>
<td>Member State</td>
</tr>
<tr>
<td>NOC</td>
<td>Notice of Concern</td>
</tr>
<tr>
<td>NOD</td>
<td>Notice of Delisting</td>
</tr>
<tr>
<td>NOLD</td>
<td>Notice of Listing Decision</td>
</tr>
<tr>
<td>NOLD-R</td>
<td>Notice of Listing Decision – Renewal</td>
</tr>
<tr>
<td>NOLD-Rev</td>
<td>Notice of Listing Decision -Re-evaluation</td>
</tr>
<tr>
<td>NRA</td>
<td>National Regulatory Authority</td>
</tr>
<tr>
<td>NCL</td>
<td>National Control Laboratory</td>
</tr>
<tr>
<td>OA</td>
<td>Observed Audit</td>
</tr>
<tr>
<td>PE</td>
<td>Performance Evaluation</td>
</tr>
<tr>
<td>PEP</td>
<td>Performance Evaluation Process</td>
</tr>
<tr>
<td>PMS</td>
<td>Post Market Surveillance</td>
</tr>
<tr>
<td>PQ</td>
<td>Prequalification</td>
</tr>
<tr>
<td>PV</td>
<td>Pharmacovigilance</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>QMS</td>
<td>Quality Management System</td>
</tr>
<tr>
<td>RA</td>
<td>Regulatory Authority</td>
</tr>
<tr>
<td>REG</td>
<td>Regulation and Safety Unit, WHO</td>
</tr>
<tr>
<td>RI</td>
<td>Regulatory Inspections</td>
</tr>
<tr>
<td>RPQ</td>
<td>Regulation and Prequalification Department, WHO</td>
</tr>
<tr>
<td>RRS</td>
<td>Regional Regulatory System</td>
</tr>
<tr>
<td>RSS</td>
<td>Regulatory System Strengthening</td>
</tr>
<tr>
<td>SF</td>
<td>Substandard and Falsified products</td>
</tr>
<tr>
<td>TOR</td>
<td>Terms of Reference</td>
</tr>
<tr>
<td>VL</td>
<td>Vigilance</td>
</tr>
<tr>
<td>WAG</td>
<td>WLA Advisory Group</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WLA</td>
<td>WHO Listed Authority</td>
</tr>
</tbody>
</table>
1. Introduction

The introduction of a framework for designating and publicly listing a regulatory authority as a WHO listed authority (WLA) provides a transparent and evidence-based pathway for regulatory authorities to be globally recognized as meeting WHO and other international recognized standards and practices.

While the ultimate responsibility and decision for use of the WLA list resides with the users and depends on the specific context of its intended use, the benefits of a robust, transparent, evidence-based, global system for recognizing regulatory excellence serve the interests of a variety of stakeholders that are committed to promoting access to safe, effective, and quality medical products.

This guidance, together with the following documents, constitute the WLA Framework (hereafter the Framework):

- Policy on Evaluating and publicly designating regulatory authorities as WHO listed authorities (1);
- Manual for the performance evaluation of regulatory authorities seeking the designation as WHO listed authorities (2);
- Global Benchmarking Tool (GBT) (3) and Manual (4).

The framework is underpinned by World Health Assembly (WHA) Resolution 67.20 - Regulatory system strengthening for medical products (5) and the WHO Roadmap for access to medicines, vaccines and health products 2019-2023 (6).

This guidance should also be read in conjunction with other relevant WHO guidance documents to gain a thorough understanding of the regulatory attributes WLAs are expected to exhibit, including Good regulatory practices for regulatory oversight of medical products (7), Good reliance practices in regulatory decision-making: high-level principles and recommendations (8), and The implementation of quality management systems for national regulatory authorities (9).

The guidance takes account of the work undertaken by WHO and other organizations in benchmarking and strengthening regulatory systems with the aim of ensuring sound and effective regulatory oversight of medical products.
This guidance was developed following international consultative meetings with Member States (MS) and interested stakeholders, broad public consultations, technical working group discussions on performance evaluation and a review of comments received on the draft Operational Guidance published July 2021 and subsequent consultations with Member States on transitional arrangements.

A number of important amendments have been introduced to the guidance in response to comments received. These include but are not limited to the following:

- Simplification of the performance evaluation (PE) framework, while maintaining requirements for listing, by focusing on aspects critical to ensuring that medicines and vaccines meet international standards for quality, safety and efficacy. Simplification resulted in
  - a reduction in the number of mandatory maturity level (ML) 4 sub-indicators and performance indicators, with priority given to retaining those that enable good regulatory practices related to transparency, consistency, efficiency and flexibility;
  - removal of the more prescriptive ML4 sub-indicator ‘expansions’ to allow for greater flexibility in meeting sub-indicator objectives;
  - a narrowing of focus on regulatory outputs rather than regulatory outcomes and impact.

- The introduction of transitional arrangements for regulatory authorities on the WHO Interim list of National Regulatory Authorities, including placement on a new public list of transitional WLAs (tWLAs).

- Elaboration of performance evaluation pathways and methodologies.

- Further clarification of WHO’s intent to share information related to the performance evaluations with WLAs on a secure WHO platform.

- Amendments to the terms of reference and membership criteria for the WLA Advisory Group (WAG) to better reflect the advisory nature of the group and ensure the impartiality of its recommendations.

- Publishing of the performance evaluation framework as a companion manual rather than an annex to this guidance, taking document change management and target audiences into consideration. The guidance outlines general considerations and procedural aspects related to application, evaluation and listing whereas the manual focusses on the performance evaluation process.
2. Purpose

This guidance describes the process for evaluating and publicly designating regulatory authorities and regional regulatory systems as WLAs, in accordance with the high-level operating principles defined in the corresponding Policy.

Details are provided on the steps, timelines and processes involved in evaluating and designating a WLA. The guidance also describes the process and criteria for renewal, re-evaluation and possible delisting, the role and responsibilities of the WLA Advisory Group (WAG) and the undertakings of the WHO and eligible regulatory authorities. Definitions are also provided for terms used in this document (see Glossary).

For the purpose of this document the term regulatory authority (RA), unless otherwise stated, refers to both a national regulatory authority (NRA) and a regional regulatory system (RRS).

3. Evaluating regulatory performance

According to ISO 9000 (2015), the term performance can relate to the management of activities, processes, products, services, systems or organizations and be measured in terms of quantitative or qualitative findings. For the purpose of this guidance, performance represents the degree to which regulatory inputs and processes consistently result in desired regulatory outputs in an efficient manner. While more difficult to measure, this may be extended to regulatory outcomes and ultimately, impact (Fig. 1).

![Diagram showing elements to be considered for evaluating performance of a regulatory system](image-url)

*Figure 1: Elements to be considered for evaluating performance of a regulatory system. (Please refer to acronym list)*
Performance evaluation, in this context, refers to the process of evaluating the performance of a RA in terms of specific regulatory functions and/or product categories with a focus on regulatory outputs as opposed to outcomes and impact, which often involve factors beyond the control of the regulatory authority.

The WHO benchmarking tool and methodology represent the foundation for assessing and classifying regulatory systems according to maturity level (ML). The GBT provides a robust and structured approach to analyzing the required inputs, regulatory processes and intended outputs that together determine how well a regulatory authority is configured to provide effective regulatory oversight of medical products.

The performance evaluation activity conducted for WLA listing complements the results obtained from the benchmarking exercise by providing a more comprehensive assessment of how well the regulatory system operates through the collection and review of output data related to key regulatory parameters and activities. This objective is achieved through an expanded set of measurements aimed at assessing specific elements of performance and documenting consistency in adherence to international regulatory standards and guidelines as well as Good Regulatory Practices (7).

4. Performance evaluation framework

The performance evaluation framework (PEF) is designed to promote trust and reliance in regulatory systems in the context of the international supply of medicines and vaccines. The PEF has also been designed to ensure that all available information internal and external to WHO will be taken into account before requesting additional information or undertaking further activities to document compliance with requirements for WLA listing. The performance evaluation process will therefore focus only on requirements and activities that have not been addressed through a review of prior benchmarking or other supportive evidence.

The PEF distinguishes between technical performance (e.g., scientifically sound decision-making, quality of regulatory outputs and their consistent implementation) and operational performance (e.g., time it takes to render a decision on a marketing authorization application). In addition, PE builds upon the GBT and on the well-established PE mechanisms already used
by WHO, specifically the WHO Observed Audit for GMP inspections and the WHO Vigilance Field Visit.

The PEF consists of two components (see Table 1):

- An audit against mandatory GBT ML4 sub-indicators and PE indicators.
- A comprehensive evaluation of the conduct and/or outputs of regulatory functions critical to ensuring the safety, efficacy and quality of medicines or vaccines using a set of performance evaluation tools.

The specific regulatory functions and/or product categories evaluated represent those selected by the RA for which WLA listing is sought. Regulatory functions and product categories eligible for listing are described in Table 3 and Table 4, section 7.1.

**Table 1: Components of the PEF**

<table>
<thead>
<tr>
<th>Regulatory function</th>
<th>Mandatory ML4 sub-indicators</th>
<th>PE indicators</th>
<th>II - Evaluation of selected regulatory functions using PE tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory system</td>
<td>13</td>
<td>3</td>
<td>N/A</td>
</tr>
<tr>
<td>Market surveillance and control</td>
<td>2</td>
<td>2</td>
<td>N/A</td>
</tr>
<tr>
<td>Registration and marketing authorization</td>
<td>3</td>
<td>4</td>
<td>Expert review of MAA assessment reports Off-site evaluation</td>
</tr>
<tr>
<td>Clinical trials oversight</td>
<td>2</td>
<td>4</td>
<td>Expert review of CT assessment reports Off-site evaluation</td>
</tr>
<tr>
<td>Vigilance</td>
<td>4</td>
<td>7</td>
<td>Vigilance field visit On-site evaluation</td>
</tr>
<tr>
<td>Licensing establishments</td>
<td>2</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Regulatory inspection</td>
<td>5</td>
<td>-</td>
<td>GMP/GCP observed audit On-site evaluation</td>
</tr>
<tr>
<td>Laboratory testing</td>
<td>3</td>
<td>1</td>
<td>Expert review of laboratory activities On-site evaluation</td>
</tr>
<tr>
<td>Lot release (vaccines)</td>
<td>1</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>TOTAL</td>
<td>35</td>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>

* Desktop audit, with provision for onsite evaluation.

** May also include a review of relevant ML3 sub-indicators that were not fully implemented when assigning an overall ML3 rating.
Refer to Table 3 and 4 for regulatory functions and product categories eligible for listing and to the PEF manual for details on the performance evaluation process, indicators and tools.

WHO Headquarters, Regional Offices and Country Offices, working together under a unified plan, are responsible for conducting all activities required for the designation of a regulatory authority as a WLA.

5. Considerations for regulatory authorities seeking WLA designation

Adhere to good regulatory practices (GRP) is “a hallmark of a modern, science-based, responsive regulatory system in which regulations are translated into desired outcomes. GRP provide a means of establishing and implementing sound, affordable, efficient regulation of medical products as an important part of health system performance and sustainability.” *(Good regulatory practices for regulatory oversight of medical products (7)).*

It is for this reason that GRP indicators and enablers are a primary focus of the PEF. While all GRP principles are important to ‘smart regulation’, two bear special mention within the context of the WLA Framework: 1) transparency and 2) regulatory cooperation as an enabler of efficiency (which includes effectiveness (7)).

Transparency is a critical prerequisite to building trust and confidence in the regulatory system, as noted in the above-mentioned WHO guideline: “Transparency is a key enabler to adopting new, more efficient ways of conducting regulatory operations. It is incumbent upon regulators to practice transparency in regulatory operations and decisions as a fundamental principle of Good Regulatory Practices (GRP), but also towards building trust and maximizing opportunities for cooperation and reliance as part of a shared regulatory community responsibility.”

Regulatory authorities are both audience and beneficiary of measures that promote transparency in regulation, through the publishing and sharing of regulatory information such as product assessments and site inspections. WHO supports the implementation of reliance on other regulators’ work as a general principle in order to make the best use of available resources and expertise, as noted in the WHO guideline on Good reliance practices in regulatory decision-making: high-level principles and recommendations (8).
Given its importance in building trust and enabling reliance, transparency in regulatory operations and decisions is a key focus area in evaluating candidate WLAs. RAs seeking designation as WLAs are therefore expected to make regulatory information publicly available by issuing public assessment outcomes, while respecting and protecting personal or commercially confidential information, and to engage in information-sharing with other regulatory authorities, thereby enabling greater regulatory efficiencies and more informed decision-making at the regional and global level.

Regulatory cooperation is also a hallmark of a modern regulator in an increasingly global regulatory environment – and fundamental to achieving the objectives of the Framework. Regulation cooperation covers the range of activities that lead to more informed and efficient regulatory actions and decisions, including information and work sharing, common risk assessments, convergence and harmonization, and collaborative efforts aimed at building regulatory capacity. Regulatory cooperation, like transparency, is also essential in fostering awareness, trust and reliance. WLAs are therefore expected to play an active role in regional and/or global networks to promote regulatory convergence and harmonization, exchange and other forms of collaboration, thereby contributing to the improvement of regulatory practices.

6. Transitional arrangements

The Interim list of National Regulatory Authorities published since 2019 on the WHO website was meant to serve as a public reference of regulatory designations prior to the implementation of the WLA framework. The list compiled the pre-existing lists of stringent regulatory authorities (SRAs) for medicines, highly performing regulatory authorities for vaccines, regional reference authorities for medicines in the Americas (AMRO/PAHO), regulatory authorities operating at maturity level 3 (ML3) and maturity level 4 (ML4), and vaccine producing countries with functional regulatory authorities.

WHO recognizes that regulatory authorities on the Interim list have a history of investment in regulatory system strengthening and cooperation. Furthermore, they have been recognized by WHO and other stakeholders to have achieved levels of operation necessary for effective regulation of medicines and/or vaccines. Many of these authorities are also widely recognized by the international regulatory and procurement community as leaders in regulatory science and the oversight of medical products.
Transitional arrangements outline provisions for regulatory authorities on the Interim list to transition to WLA listing. Transitional arrangements provide all regulatory authorities on the Interim list the opportunity to be placed on a time-limited, public list of transitional WLAs or tWLAs (https://www.who.int/initiatives/who-listed-authority-reg-authorities) signaling the commitment of both listed authorities and the WHO to advance the implementation of the WLA framework.

Transitional arrangements are intended to:

• recognize the achievement and work of all the authorities on the interim list;
• protect the global supply of prequalified products;
• provide a clear and transparent path forward for regulatory authorities on the interim list that wish to become WLAs;
• ensure that the processes are feasible and efficient considering the capacity of the WHO and regulatory authorities.

With the introduction of transitional arrangements, WHO has replaced the public Interim list with the tWLA list. A regulatory authority will move from the tWLA list to the permanent WLA list upon successful completion of the WLA evaluation process. At the same time, WHO will maintain a permanent public list of ML3 and ML4 RAs to recognize their achievements.

The following principles define transitional arrangements for regulatory authorities previously on the WHO Interim list.

1. Regulatory authorities previously on the Interim list have been placed on the tWLA list, with the exception of authorities that did not wish to be on the list prior to its publication.
2. A transition period of five (5) years is established from the publication of the final Operational Guidance.
3. The tWLA list will exist only for the duration of the transition period. During the transitional period, regulatory authorities on the tWLA list will be evaluated against the requirements for designation as a WLA.
4. Placement on the transitional list does not confer WLA status and furthermore, it does not alter requirements to be met for designation as a WLA.
5. Transitional arrangements will also not affect existing procedures related to the Prequalification of medicines and vaccines and hence the international supply of quality-assured products.

6. Following agreement on the proposed scope of listing (regulatory function/product stream) and plan of performance evaluation, written consent to proceed with the WLA evaluation process will be sought from the regulatory authority.

7. Consistent with the WLA Policy, WHO will adopt a risk-based approach to performance evaluation which considers available information and the uninterrupted global supply of prequalified medicines and vaccines.

8. Should an authority decide to withdraw from the WLA evaluation process or does not fulfil the requirements for designation as a WLA within the five-year transition period, it will be removed from the tWLA list without prejudice to submitting a subsequent request for WLA listing.

7. Process for applying for, evaluating and listing a WLA

The steps and general processes for applying, evaluating and listing a regulatory authority seeking WLA designation are described below. The overall process for initial listing, illustrated in figure 2, is divided into the following steps:

1. Submission of Expression of Interest (EOI);
2. Evaluation of EOI against eligibility criteria;
3. Agreement on the scope of listing and risk-based roadmap;
4. Performance evaluation; and
5. Decision on listing and publication.
**General principles and considerations**

- The decision to apply for evaluation and listing as a WLA is voluntary and as such is initiated by or on behalf of the RA.
- The RA must satisfy one of the criteria defined in section 7.1.1 to be eligible for application to become a WLA.
- A roadmap and performance evaluation plan will be developed in discussion with the RA and will be documented in the *Agreement on the conditions to be designated a WHO Listed Authority* (Annex 2).
- The overall performance evaluation process is time bound. The RA should abide by the timelines agreed to as part of the evaluation plan. The evaluation plan may be revised upon the request and mutual agreement of WHO and RA. If the RA is not in a position to complete the PE phase, it may resubmit a new EOI without prejudice at a later date.
- Requests for designation as a WLA will be prioritized based on chronology of eligible applications, availability of resources and other considerations as described in section 7.3.
- A WLA is expected to maintain comprehensive oversight of regulatory functions and related activities for the product categories relevant to the scope of WLA listing, even when reliance is applied. In other words, although the RA may rely on other recognized authorities for some regulatory activities, the decision-making process and regulatory decisions should remain under the full responsibility and control of the RA, which in turn should demonstrate that it has the regulatory and technical capacity to perform the same...
type of activities adequately and independently. As a consequence of the above, functions in which full reliance is applied cannot be considered for listing.

- Outsourcing (i.e., via agreements with third parties to perform tasks assigned to the RA) of some technical regulatory activities (e.g., laboratory testing) is considered acceptable for a WLA, provided that the regulatory oversight of these activities and consequent regulatory decisions remain under the full control and responsibility of the RA. Consult the PEF manual for further guidance.

**Timelines for evaluation, decision and listing**

The steps and associated timelines in the WLA process are outlined in Table 2. Further detail on each step is provided in the sections which follow.

*Table 2: WLA process steps and estimated timelines*

<table>
<thead>
<tr>
<th>Calendar days</th>
<th>Responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO</strong></td>
<td><strong>RA</strong></td>
</tr>
<tr>
<td>1. Evaluation of Expression of Interest</td>
<td>30</td>
</tr>
<tr>
<td>2. Agreement on scope of listing and evaluation plan</td>
<td>60</td>
</tr>
<tr>
<td>3. Performance evaluation and report</td>
<td>60 – 180*</td>
</tr>
<tr>
<td>4. WLA Advisory Group (WAG) opinion</td>
<td>60</td>
</tr>
<tr>
<td>5. Notice of Listing Decision (NOLD) and publication on WHO website</td>
<td>60</td>
</tr>
</tbody>
</table>

*Depending on the performance evaluation pathway, scope of listing and available evidence.

**7.1 Submission of Expression of Interest**

The formal WLA process is initiated by a request from a RA using the template provided in Annex 1. A RA interested in seeking recognition as a WLA is encouraged to meet with WHO in advance of the formal application to discuss the WLA evaluation and listing process. The completed EOI and covering letter should be submitted to Regulation and Safety Unit, WHO Headquarters, through the appropriate WHO Regional Office.
The request must include a completed EOI (Annex 1) signed by a person duly authorized to represent the regulatory authority (i.e.: head of the regulatory authority or his/her designate). The EOI should also identify the person responsible for filing the request and serving as the official contact for correspondence (hereafter ‘the applicant’).

7.1.1 Scope of listing

The EOI must specify the WLA listing category(ies) being sought (see Table 3 and 4), provide evidence that eligibility criteria are met, and confirm acceptance with the general provisions described in the Agreement on the conditions to be designated a WHO Listed Authority (Annex 2).

A national regulatory authority (NRA) or a regional regulatory system (RRS) (including individual member authorities) which meets the eligibility criteria in section 7.1.1 can be listed for one or more product categories (see Table 4) and/or for one or more regulatory functions (see Table 3).

Consistent with the scope of the GBT, the regulatory oversight of export-only products is not included in the WLA evaluation framework. Regulatory authorities, procurement agencies and other organizations relying on the outputs and decisions of a WLA should therefore ensure that products of interest are subject to full regulatory oversight, including through the WHO certification scheme on the quality of pharmaceutical products moving in international commerce and issue Certificate of Pharmaceutical Product (CPP).

Table 3: Functions assessed when applying for the listing of individual regulatory functions

<table>
<thead>
<tr>
<th>Eligible Regulatory Functions</th>
<th>Function(s) to be assessed for listing</th>
<th>RS</th>
<th>MA</th>
<th>VL</th>
<th>MC</th>
<th>LI</th>
<th>RI</th>
<th>CT</th>
<th>LT</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration and Marketing Authorization (MA)</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigilance (VL)</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Market Surveillance and Control (MC)</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Licensing Establishments (LI)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Table 4: Functions assessed when applying for the listing of product categories

<table>
<thead>
<tr>
<th>Eligible Product categories</th>
<th>Function(s) to be assessed for listing</th>
<th>RS</th>
<th>MA</th>
<th>VL</th>
<th>MC</th>
<th>LI</th>
<th>RI</th>
<th>CT</th>
<th>LT</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multisource (generics)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>New medicines (new chemical entities) and/or biotherapeutics and/or similar biotherapeutic products</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Vaccines</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

7.1.2 Eligibility criteria

The RA must satisfy one of the criteria below to be eligible for application to become a WLA.

- The RA is on the tWLA list.
- The RA has attained overall ML3 as determined through a formal GBT benchmarking.

According to flexible algorithm, overall ML3 can be achieved if 100% of ML1 and ML2, and 90% of ML3 sub-indicators have been met and a plan to comply with the remaining 10% ML3 has been developed. If relevant, this plan would form part of the PEF (see section 7.4).
For further details on maturity level and the scoring algorithm, consult the *Manual for benchmarking of the national regulatory system of medical products and formulation of institutional development plans*, section 5.3 - *Scoring and algorithm for determining maturity level* (4).

The RA must agree also with the general provisions and obligations described in the *Agreement on the conditions to be designated a WHO Listed Authority* (Annex 2). The Agreement covers the resources needed to complete the PEF, the commitment of senior management and staff, and transparency obligations.

### 7.1.3 Additional consideration for Regional Regulatory Systems (RRSs)

RRSs are composed of individual regulatory authorities operating under a common regulatory framework. Regional regulatory bodies may also be established to represent the RRS. The following additional considerations apply for RRSs.

- The EOI should be submitted by the regional body (where it exists) or by another institution representing the RRS, following coordination with the individual authorities that are part of the system.
- A RRS must provide evidence that the common regulatory framework ensures equivalence among the members in terms of regulatory requirements, regulatory practices and quality assurance policies. This should include a description of the organization and governance of the RRS including enforcement powers.
- A RRS must have attained overall ML3 to be eligible for listing and undergo the PEF.
- When the RRS is further underpinned by a common legal framework, it can be considered as a single entity and, as such, is eligible for listing as a WLA, together with each of the individual authorities that form the system. In this case, not only the RRS but all individual member NRAs are expected to meet ML3 requirements. The EOI should state whether WLA listing is being sought for the individual members of the RRS in addition to the regional entity.

### 7.2 Evaluation of EOI

Upon receipt, WHO evaluates the EOI for completeness and compliance with eligibility criteria. WHO will endeavour to review the EOI within 30 calendar days of receipt. The
applicant may be contacted to obtain further clarification or additional information needed to complete the review.

Based on information provided in the EOI and any subsequent responses to requests for information, the review will result in one of the following outcomes, which is formally communicated by WHO to the applicant:

a. **The RA complies with eligibility criteria for the requested WLA listing.**
   
   An estimate of the start date for the PEF is communicated. The start date is established based on a prioritization and planning schedule (see section 7.3). The RA is invited to discuss the outcome of the review and subsequent planning and coordination matters.

b. **The RA does not comply with eligibility criteria.**
   
   A rationale for the decision is provided. The RA may request a meeting to seek further clarification for the decision and how to fulfil eligibility requirements.

c. **A decision on eligibility is deferred.**
   
   The decision is deferred pending resolution of issues which, in the view of WHO, could be addressed within 90 calendar days. The RA is invited to discuss the resolution of outstanding issues. Should the RA not be able to comply within the stated time, the application will be closed, without prejudice to a future EOI filing.

### 7.3 Agreement on scope of evaluation and roadmap to listing

A RA that complies with eligibility criteria will be requested to define the scope and extent of the performance evaluation. The RA and WHO will sign the *Agreement on the conditions to be designated a WHO Listed Authority* (hereafter ‘the Agreement’), which includes a roadmap and project plan for reaching a listing decision. The Agreement should be concluded no later than 60 calendar days from the start of discussions.

The Agreement specifies the proposed scope of listing, the roles and responsibilities of the WHO and the RA, the overall PE methodology and pathway, and confidentiality provisions concerning non-public information. The Agreement identifies the senior WHO and RA officials responsible for reviewing progress, addressing issues, and making necessary adjustments to the plan. The Agreement also requires the RA’s consent to disclose a positive PE outcome in
the form of a public listing as well as and the sharing of further information with other WLAs (see section 7.5.4).

As noted above, the roadmap and project plan forms part of the overall Agreement and provides further detail on the evaluation process and methodology, timelines, milestones and decision points. These documents also specify the assigned focal point for each regulatory function subject to the PE exercise.

RAs applying for listing should be in a position to comply with the requirements for listing within agreed upon target timeframes. The roadmap and project plan may be updated to reflect progress and findings, with the mutual agreement of the WHO and candidate WLA. Should it become evident during the performance evaluation exercise that the RA is unable to meet requirements within the agreed upon timeframe, the evaluation process is terminated and the RA invited to re-apply at a later time.

In proposing a PE start date and timeline, WHO will take into consideration the following elements as part of the WLA PE prioritization and planning process. Elements are not listed in order of importance.

- Chronology and number of eligible requests
- Estimated readiness of the RA
- Anticipated level of effort required to conduct the PE exercise (e.g., RRS versus a single regulatory authority, number of functions or product categories under evaluation)
- Wide recognition of the candidate WLA as a regional or international reference authority
- Potential to enhance and expand the PQ of medical products (local manufacturing)
- Degree to which the RA actively participates in mechanisms for cooperation and strengthening other regulatory authorities or regional systems.
- A record of, or a commitment to, making regulatory assessments of products and facilities available to other regulatory authorities in the form of publicly available information or other information-sharing mechanisms.
7.4 Performance evaluation (PE)

The operational framework for evaluating regulatory performance provides flexibility in approach. While requirements must be met, the adoption of a risk-based approach means the performance evaluation plan will be customized for each RA to ensure optimal use of existing information and resources to facilitate the conduct of the exercise and the time to decision.

In practical terms, the evaluation process will take into consideration the availability and applicability of existing information from benchmarking/audit exercises or from other sources relevant to the designation being sought, including information in the public domain. The greater the amount of supporting evidence and WHO experience with the RA, the less time expected to complete the PE - irrespective of the applicable evaluation pathway.

Performance evaluation may include a mix of desk-based and on-site evaluations that ensure the robustness, timeliness and consistency and transparency of regulatory operations and outputs. In order to ensure transparency and consistency in approach, a number of pathways have been developed to evaluate regulatory performance. Evaluation pathways are divided into those applicable for tWLAs (Abridged and Streamlined) and those for all other RAs (Standard). Pathways and associated eligibility criteria and evaluation methodology are summarized in Table 5 and described below.

The target for completion of the performance evaluation process is between 60 and 180 calendar days, depending on the complexity of the regulatory system and the amount of existing information and experience that can be used to demonstrate performance. The proposed start date for the PE process will take into consideration the readiness of the RA and WHO to complete activities outlined in the PE evaluation plan within this timeframe in order to ensure effective use of resources and chances of a successful outcome. The WHO and RA may agree to a Clock Stop of up to 180 calendar days if deemed necessary to address outstanding issues.
### Table 5: Risk-based performance evaluation pathways

<table>
<thead>
<tr>
<th>Evaluation pathway</th>
<th>Eligibility</th>
<th>Evaluation methodology</th>
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</table>
| Abridged           | SRAs for medicines and highly performing NRAs for vaccines | 1. RA self-assessment against pre-selected GBT and PE indicators that primarily target GRP and QMS  
2. WHO desktop review of self-assessment report |
| Transitional arrangements (tWLAs) | ML3 and ML4 RAs (medicines and/or vaccines) | 1. RA self-assessment against pre-populated GBT, if needed, as well as PE indicators*  
2. WHO desktop review of self-assessment report  
3. WHO assessment against PEF** |
| Streamlined        | Regional reference RAs of the Americas (medicines and/or vaccines)  
Functional RAs (vaccines) | 1. RA self-assessment against pre-populated GBT as well as PE indicators  
2.WHO desktop review of self-assessment and may involve an audit against selected GBT indicators to verify findings.  
3. WHO assessment against PEF |
| Routine arrangements (All other authorities) | Overall ML3 or ML4 RAs (medicines and/or vaccines) through GBT benchmarking | 1. RA self-assessment against PEF indicators (GBT ML4 + PE)  
2. WHO desktop review of self-assessment report  
3. WHO assessment against PEF |

* The need for self-assessment against pre-populated GBT is dependent on outcome and validity of the earlier benchmarking.
** PEF consists of an audit of mandatory ML4 + PE indicators + evaluation of selected regulatory functions using PE tools (see Table 1).

### 7.4.1 Performance evaluation pathways

**Abridged pathway**

The Abridged pathway will be used to evaluate RAs eligible for WHO abridged prequalification procedure, that is, stringent regulatory authorities (for medicines) and highly performing regulatory authorities (for vaccines). The evaluation process, which involves a self-assessment and subsequent WHO desktop review against a set of pre-selected GBT sub-indicators and PE indicators, takes into consideration the extensive knowledge gained with these authorities from engagement with the Prequalification and other WHO regulatory programmes.
Streamlined pathway

The Streamlined pathway will be used to evaluate all other RAs on the tWLA list. The precise evaluation process will vary depending on the extent of available supporting information, findings from the self-assessment, and subsequent desk review by WHO. The process may, as required, involve an onsite audit against selected indicators to verify findings. The evaluation would normally also involve a performance assessment of certain regulatory functions using a set of PE tools (see Table 1), depending on the WLA designation being sought.

Standard performance evaluation pathway

The standard pathway applies to all other RAs not subject to transitional arrangements, i.e., RAs that do not appear on the tWLA list. The process is similar to the Streamlined pathway for ML3 / ML4 RAs given that RA must first achieve overall ML3 through a formal WHO onsite benchmarking using the GBT to be eligible for application to become a WLA.

7.4.2 Evaluation methodology

While each situation is unique, the PE plan will normally include the following steps:

1. A self-assessment performed by the RA using the GBT and PE indicators. WHO will pre-populate the GBT with information on hand from previous WHO/PAHO benchmarking exercises before providing the tool to the RA for completion and possible updating. If the RA has already been benchmarked using the GBT (introduced in 2016) and information remains valid, the scope of the self-assessment would be primarily restricted to ML4 sub-indicators and PE indicators. The scope of the self-assessment would be broader when other benchmarking tools were used, and significant time has elapsed since the last benchmarking.

Once completed, the RA would upload the self-assessment report, along with any supporting information, to the secure WHO SharePoint (see section 9).

In the case of SRAs/highly performing regulatory authorities, the self-assessment involves a set of pre-selected GBT sub-indicators and PE indicators that target GRP and the quality management system.

2. WHO desktop review of information provided to confirm the completeness, relevance, and quality of self-benchmarking results and, when necessary, supporting
evidence. This could lead to dialogue with the RA to clarify aspects of the self-assessment.

3. As required, WHO onsite assessment of self-benchmarking results.

4. Subject to the WLA designation being sought, WHO desktop review and/or onsite evaluation of selected regulatory functions using PE tools as applicable (see Table 1).

*Note*: PEF related activities are conducted in English or, when appropriate, in other United Nations official languages. Whenever possible, WHO will assemble teams of assessors who have a working knowledge of the native language, including assessors from WHO Regional Offices. Translation into English should be arranged, if needed, both for relevant written documents and to enable discussions.

### 7.5 Decision and listing

#### 7.5.1 WLA Advisory Group

To ensure impartiality of the WLA process, a WLA Advisory Group (WAG) will provide an opinion to WHO on the listing or possible delisting of a RA following a review of the PE report. The WAG review process provides an additional level of assurance that due process was followed and that listing recommendations are supported by findings.

The Advisory Group is set up by WHO based on established and transparent criteria that ensure impartiality, equitable geographical representation, gender balance and professional competencies in order to provide the perspectives and practical experience from across all WHO regions. The remit and membership of the WAG is described in Annex 4.

WHO will convene meetings of the WAG and serve as secretariat. The WAG will render an opinion on whether the listing recommendation documented in the PE report are supported. The WAG opinion should be issued no later than 60 calendar days after receiving the PE report.
7.5.2 Decision on listing and Notice of Listing Decision (NOLD)

The Notice of Listing Decision (NOLD) serves as the official decision on listing. The decision on listing resides with the ADG responsible for access to medicines and health products.

The NOLD includes the following information:

- Decision on listing
- Rationale for the decision
- Scope of listing

In addition, the PE report and the WAG opinion will accompany the NOLD.

The PE decision process may result in one of three outcomes:

a. *Positive decision* when requirements for the requested scope of the listing have been met.

b. *Positive decision for reduced scope of listing (partially positive decision)* when requirements for at least one but not all categories requested for listing have been met.

c. *Negative decision* when requirements have not been met.

7.5.3 Listing

Following a positive decision to list, the RA will be listed on the WHO website ([https://www.who.int/initiatives/who-listed-authority-reg-authorities](https://www.who.int/initiatives/who-listed-authority-reg-authorities)) within a target of 60 calendar days from the issuance of the WAG opinion.

The listing consists of:

- Scope of the designation, e.g., vaccines or generic and multisource medicines in the case of product categories; or regulatory inspections and licensing establishments in the case of regulatory functions.
- Period of validity.

The listing also includes a link to a listing summary which includes the following information:

- an outline of the organizational structure and responsibilities of the RA;
- a summary of evidence reviewed, and the process undertaken to support the listing;
- steps and timelines associated with the PE and listing process;
- a link to relevant websites of the RA.
Prior to publication on the WHO website, a draft of the listing and accompanying summary report is provided to the RA to confirm the accuracy of the information.

See Annex 3 for the format and content of the public WLA list.

Note: The public tWLA list will be amended with the transition of a RA from the tWLA list to the WLA list.

WHO also intends to establish a secure, searchable platform for WLAs containing summary PE reports as well as evaluation findings related to the same set of GBT sub-indicators and PE indicators used for the Abridged performance evaluation pathway.

7.5.4 Right to appeal
The RA has the right to appeal a negative or partially positive listing decision. The rationale for contesting the decision must be based on procedural grounds and/or evidence available at the time of the PE exercise. Subsequent actions undertaken by the RA to resolve identified issues should be included in a new EOI.

The request for an appeal should be filed no later than 60 calendar days from receipt of the NOLD and addressed to the ADG responsible for access to medicines and health products. If the request is found to comply with grounds for appeal, WHO will convene an appeal panel to consider the request.

The appeal panel will be comprised of an internal group of experts not previously involved in the evaluation process, including a representation from the respective WHO Regional Office.

A meeting will be organized to review the request. The RA will be invited to present its case and respond to questions. The panel will issue a report with its decision after the meeting. This decision is final and cannot be appealed.

8. Renewal of listing and ongoing monitoring

8.1 Renewal
A listing will initially be valid for a period of five (5) years. Upon renewal, the listing is no longer subject to a validity period. The listing will, however, be subject to continuous
monitoring based on risk management principles to ensure that requirements for listing continue to be met (see section 8.2).

The WLA listing will be renewed provided that evidence reviewed by WHO continues to support the listing and that the ongoing reporting requirements described below are met.

The renewal process would normally involve a WHO desktop review of the completed Renewal Reporting Form submitted by the WLA at least two (2) months before the end of the validity period. The Renewal report should describe changes to information assessed during the performance evaluation, but do not, in the view of the WLA, warrant interim reporting (see below) or require an update to listing information. If no changes of note have taken place, the WLA would so indicate on the Form.

Supporting documents should be submitted, as necessary, with the Renewal report. A link to the relevant webpages is acceptable in lieu of submitting documents provided information on the WLA’s website is in one of the United Nations official languages.

WHO reserves the right to seek clarification of changes or conduct an on-site evaluation to assess the nature and impact of reported changes or trends.

The following renewal options are possible upon completion of the renewal evaluation process:

a. **Renewal is granted**

   The renewal of listing decision is communicated to the WLA through a *Notice of Listing Decision - Renewal* (NOLD-R) and the listing is updated on the WHO website to reflect the renewal.

b. **Renewal is granted with conditions**

   Should an issue of concern arise during the evaluation process, the listing may be renewed on condition that corrective measures being undertaken to address the concern are fully implemented and evaluated by WHO. The issue of concern, measures being implemented to address the concern, and timelines for completion are described in the NOLD-R and published on the WHO website.

c. **Renewal is deferred**
WHO may decide not to renew the listing until requested information has been provided, and that ongoing reporting requirements are met. A statement to this effect would be communicated in the NOLD-R and published on the WHO website.

d. **Renewal is not granted**

A listing may not be renewed in the event that:

- an issue of concern triggers the issuance of a Notice of Concern (see section 9.1 *Re-evaluation*);
- information requested pertinent to a renewal of listing decision has not been provided; or
- ongoing reporting requirements are not met.

See section 9.2 - *Delisting* for details.

### 8.2 Ongoing reporting and monitoring

A condition of continued listing is commitment to and compliance with ongoing reporting requirements.

#### 8.2.1 Interim reporting by WLA

The WLA is required to advise the WHO of significant changes to the regulatory framework, processes, resources, organizational structure, governance, or other parameters that could negatively impact the listing decision (for example, a major downsizing of the regulatory authority).

A description of changes and accompanying information should be uploaded on the secure WHO SharePoint. If information related to the change is available on the WLA’s website, a link to the relevant webpages is acceptable in lieu of submitting documents provided the information is in one of the United Nations official languages.

WHO may, upon review of the changes, request further clarification and/or a meeting with the WLA in order to fully evaluate the impact of the change on the listing decision.

As required, listing information is updated to reflect changes.
8.2.2 Ongoing monitoring by WHO

WHO will perform independent monitoring of regulatory performance based on information collected from different sources (e.g., concerns raised in the context of the WHO Prequalification programme, issues reported by stakeholders, or any other information suggestive of concerns with the regulatory system).

WHO reserves the right to request information on events that potentially impact the WLA listing and to undertake a formal re-evaluation should this be considered necessary.

9. Re-evaluation and delisting

9.1 Re-evaluation

WHO reserves the right to conduct a formal re-evaluation of the WLA to assess the impact of proposed or implemented changes or events of a potentially serious nature. The ‘for cause’ re-evaluation would follow prior notification of the WLA through a Notice of Concern (NOC) signed by the ADG responsible for access to medicines and health products. The NOC describes the nature of the concern and the proposed re-evaluation plan. An abbreviated version of the NOC describing the nature of concern is published on the WHO website.

Based on findings, conclusions and recommendations from the re-evaluation, WHO may decide:

a. The WLA should continue to be listed

   The decision is communicated to the WLA through a Notice of Listing Decision – Re-evaluation (NOLD-REV) together with a Re-evaluation report and a summary for publication of the concern, its resolution and listing recommendation. The WLA will review the summary prior to its publication on the WHO website.

b. The WLA should continue to be listed provided recommended corrective actions are undertaken according to agreed plan and timelines

   The decision is communicated to the WLA through a NOLD-REV together with the Re-evaluation report.

   WHO would meet with the WLA to discuss and agree with conditions for continued listing, including progress reports on corrective actions. A summary of the concern,
listing recommendation and corrective action plan is forwarded to the WLA. The WLA will review the summary prior to its publication on the WHO website.

Should agreement not be reached on the conditions for continued listing WHO may decide to convene a special meeting of the WAG to make a recommendation on delisting.

c. **Grounds for delisting the WLA exist**

The conclusion is communicated to the WLA through a NOLD-REV together with the Re-evaluation report and a description of the delisting process, which provides for the convening of the WAG and the right of appeal. The NOLD-REV is published once a final decision on listing or delisting is taken (see section 9.2).

### 9.2 Delisting

WHO reserves the right to delist a RA if, upon evaluation, WHO concludes that the basis for supporting the listing is no longer valid. This could be due to evidence of serious and persistent lapses in regulatory oversight, ineffective enforcement activities, a major downsizing or re-organization of the authority, concerns regarding the independence and integrity of the decision-making process.

Upon receipt of a Re-evaluation report and a recommendation to delist, the ADG responsible for access to medicines and health products may convene a special meeting of the WAG to render an independent opinion on delisting based on the Re-evaluation report. In exceptional circumstances, the ADG may choose to proceed with delisting the WLA without convening the WAG if concerns are of an urgent public health nature.

The decision to delist a WLA resides with the ADG. The decision is communicated to the WLA as a Notice of Delisting (NOD).

WHO will meet with the RA prior to the issuance of a NOD to explain the rationale for the decision, the delisting process and the procedure for appealing the decision. A draft of the NOD is provided to the RA in advance of the meeting, together with the Re-evaluation and WAG reports.

The NOD will be made public on the WHO website and the WLA delisted, subject to the outcome of a potential appeal.
The RA has the right to appeal a negative listing decision, as outlined in section 7.5.5. The rationale for contesting the decision must be based on procedural grounds and/or evidence available at the time of the decision to issue a NOD. The RA may reapply for listing by submitting a new EOI that includes a proposed corrective action plan.

Note: A decision to delist could also impact the ML rating of the RA and the prequalification listing of products. Actions taken in relation to prequalified products would be specified on the WHO PQ website.

10. Information management system

The PEF is also an information intensive exercise that involves the collecting, sharing, processing, analysing and storing of large amounts of information, much of which is of a confidential nature.

Electronic copies of all documents collected prior to, during or following the evaluation process, as well as all correspondence, analyses, presentations, and interim and final reports, will be stored, with restricted access, in the same secured WHO platform used for the benchmarking of RAs.

11. Glossary

Common regulatory framework
A common regulatory framework is a unified set of requirements, processes and controls used by a Regional Regulatory System and applied to the oversight of medical products. The common regulatory framework ensures equivalence among the members in terms of regulatory requirements, regulatory practices, and quality assurance policies.

Common legal framework
Unified legislation which underpins the common regulatory framework in a Regional Regulatory System. The common legal framework provides the RRS and individual members enforcement powers to ensure compliance with the common regulatory framework

Delisting
Removal of the regulatory body from the publicly available list of WHO Listed Authorities (WLAs), due to evidence of serious and persistent lapses in regulatory oversight that have an impact on the function(s) and/or product category(ies) listed.
**Effectiveness**
The extent to which a specific intervention, procedure, regimen or service, when deployed in the field in routine circumstances, does what it is intended to do for a specified population.

**Efficacy**
The extent to which a specific intervention, procedure, regimen or service, produces the intended result under ideal conditions.

**Efficiency**
The capacity to produce the maximum output for a given input.

**Export-only products**
Products not marketed nor registered in the producing country. Such products are often excluded from the remit of regulatory bodies.

**International standards and guidelines**
For the purpose of this document, the term includes relevant WHO standards and guidelines and any other relevant internationally recognized standards (e.g., ISO or pharmacopoeia standards) and guidelines (e.g., International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) or Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines).

**Listing**
Public designation, on the WHO website, of reference regulatory authorities that have successfully undergone the performance evaluation process in the context of the WHO Listed Authority (WLA) framework. Listing as a WLA includes the scope of the designation (product categories and/or regulatory functions); the evidence reviewed, and the process undertaken to support the listing. The listing also specifies the original date and the period of validity of the initial listing.

**Maturity level (ML)**
Maturity of regulatory systems is divided into four levels: (ML1) some elements of regulatory systems exist; (ML2) evolving national regulatory system that partially performs essential regulatory functions; (ML3) stable well-functioning and integrated regulatory system; and (ML4) regulatory system operating at advanced level of performance and continuous improvement.

**Performance**
The degree to which regulatory inputs and processes consistently and efficiently result in desired regulatory outputs in an efficient manner.

**Performance Evaluation Framework (PEF)**
Set of activities, specific for each regulatory function, aimed at assessing how a regulatory system operates. The process considers the nature and extent of evaluation, and it is designed to address the function(s) and/or the product category(ies) included in the Expression of Interest.

**Product category(ies)**
For the purpose of this document, refers to “medical products” which may include the following product categories: multisource (generics), new medicines (new chemical entities), biotherapeutics, similar biotherapeutic products and vaccines.

**Recognition**
Acceptance of the regulatory decision of another regulator or trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

**Regulatory Authority**
For the purpose of this document, unless otherwise specified, Regulatory Authority include both National Regulatory Authorities and Regional Regulatory Systems. See also candidate WLA

**Re-evaluation**
Assessment of the impact of proposed or implemented changes, or of events of a significant and serious nature that may impact the continued validity of listing.

**Regional regulatory system (RRS)**
A system composed of individual regulatory authorities, or a regional body composed of individual regulatory authorities, operating under a common regulatory framework including or excluding a common legal framework. The common framework must at least ensure equivalence between the members in terms of regulatory requirements, practices and quality assurance policies. The system or regional body, where it exists, may have enforcement powers to ensure compliance with the common regulatory framework. An RRS so described may be considered a single entity and therefore eligible for listing as a WLA, as well as each of the individual authorities that are part of the system. In cases where an RRS is further underpinned by a common legal framework, it should be considered as a single entity and, as such, eligible for listing as a WLA, as well as each of the individual authorities that are part of the system.

**Regulatory function**
WHO defines a national regulatory system in terms of the enabling legal system and infrastructure related to eight common regulatory functions and one non-common regulatory
function. Common regulatory functions that apply to all medical products are regulatory system (RS), registration and marketing authorization (MA), vigilance (VL), market surveillance and control (MC), licensing establishments (Li), regulatory inspection (RI), laboratory testing (LT), and clinical trials oversight (CT). National lot release (LR) for vaccines represents the non-common regulatory function.

**Reliance**
The act whereby the regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

**Renewal**
Process of re-assessment of a WLA, aimed at extending the validity of listing. Initial listing is valid for five years.

**Transparency**
Act of sharing information with citizens that is needed to let them take informed decisions. Regulatory systems are expected to be transparent; requirements and decisions should be made known, and input should be sought on regulatory proposals.

**WHO Listed Authority (WLA)**
A WHO Listed Authority (WLA) is a regulatory authority or a regional regulatory system which has been documented to comply with all the indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process.

**WLA Framework**
Set of principles, guidelines, tools and processes that provide a transparent, evidence-based and globally recognized pathway for evaluating and designating regulatory authorities as WLAs.

### 12. References

1. Policy document: Evaluating and publicly designating regulatory authorities as WHO-listed authorities ([https://www.who.int/publications/i/item/9789240023444](https://www.who.int/publications/i/item/9789240023444))
3. Global Benchmarking Tool ([https://www.who.int/publications/i/item/9789240020245](https://www.who.int/publications/i/item/9789240020245))
4. Manual for benchmarking of the national regulatory system of medical products and formulation of institutional development plans  
(https://www.who.int/publications/m/item/Benchmarking_manual_V2_09Mar2021)

5. WHA Resolution 67.20 - Regulatory system strengthening for medical products (2014)  

6. Roadmap for access to medicines, vaccines and health product 2019-2023: comprehensive support for access to medicines, vaccines and other health products  
https://apps.who.int/iris/handle/10665/330145

7. Good regulatory practices for regulatory oversight of medical products  
https://www.wto.org/english/tratop_e/trips_e/techsymp_290621/gaspar_pres2.pdf

8. Good reliance practices in regulatory decision-making: high-level principles and recommendations  

9. The implementation of quality management systems for national regulatory authorities  
https://www.who.int/publications/m/item/trs-1025-annex-13-qms-nra

13. **Annexes**

   - **Annex 1**: Expression of Interest application form
   - **Annex 2**: Agreement on the conditions to be designated a WHO Listed Authority
   - **Annex 3**: Sample listing
   - **Annex 4**: WLA Advisory Group (WAG) Terms of Reference
   - **Annex 5**: WLA Renewal Reporting Form

14. **Acknowledgments**

   Pending completion
Annex 1 – Template for Expression of Interest to be designated as WHO Listed Authority
Expression of Interest (EOI) of a regulatory authority to be listed as WHO Listed Authority (WLA)

Information contained in the completed Form is confidential

1. NRA or RRS general information

<table>
<thead>
<tr>
<th>Name of the regulatory authority applying for listing:</th>
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<td>Country or Region¹:</td>
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<td>Address of the organization:</td>
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<td>Title/position in the organization:</td>
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2. Eligibility criteria

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<thead>
<tr>
<th>NRA or RRS</th>
<th>a) Included in tWLA list:</th>
<th>Yes ☐ No ☐</th>
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<td>If yes, please indicate for which product category(ies):</td>
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<tr>
<td></td>
<td>b) benchmarked by WHO:</td>
<td>Yes ☐ No ☐</td>
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<td>If yes, please indicate for which product category:</td>
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<tr>
<td></td>
<td>Date of last benchmarking:</td>
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<tr>
<td></td>
<td>Overall ML attained:</td>
<td></td>
</tr>
<tr>
<td>Additional information related to RRS only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Member NRAs have been benchmarked by WHO:</td>
<td>Yes ☐ No ☐</td>
<td></td>
</tr>
<tr>
<td>If yes, please list all NRAs benchmarked by WHO (add rows as necessary):</td>
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<tr>
<td></td>
<td>NRA:</td>
<td></td>
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<td>Country:</td>
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<tr>
<td></td>
<td>Date of last benchmarking:</td>
<td></td>
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<tr>
<td></td>
<td>Overall ML attained:</td>
<td></td>
</tr>
</tbody>
</table>

3. Listing application²

<table>
<thead>
<tr>
<th>NRA or RRS</th>
<th>Please indicate the regulatory function(s) sought for listing (RS mandatory):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RS ☐ MA ☐ VL ☐ MC ☐ LI ☐ RI ☐ LT ☐ CT ☐ LR</td>
</tr>
</tbody>
</table>

| Please indicate the product category(ies) sought for listing: |

---

¹ For Regional Regulatory Systems indicate the region represented by the regulatory body, including the list of member NRAs.
² See Table 3 and 4 in the Operational Guidance
### 1. Product Information

- [ ] Multisource (generics)
- [ ] New medicines (new chemical entities) and/or biotherapeutics and/or similar biotherapeutic products
- [ ] Vaccines

### 2. Additional Information

**Additional information related to RRS only**

| Common legal framework exists: | Yes ☐ | No ☐ |
| RRS applying as single entity³: | Yes ☐ | No ☐ |

### 3. Additional Information

- **NRA or RRS**
- Any further information you would like to provide related to the EOI (Optional)

### 4. Further Information

- For further information on WHO listing process please visit WLA website at: [https://www.who.int/initiatives/who-listed-authority-reg-authorities](https://www.who.int/initiatives/who-listed-authority-reg-authorities)

- For further information on WHO benchmarking process please visit WHO website at: [https://www.who.int/tools/global-benchmarking-tools](https://www.who.int/tools/global-benchmarking-tools)

- If you have any questions relating to the procedure for applying to WLA, please write to WHO RSS Team at [https://www.who.int/teams/regulation-prequalification/regulation-and-safety/rss](https://www.who.int/teams/regulation-prequalification/regulation-and-safety/rss)

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³ RRS with a common legal framework are entitled to apply as single entity, and as such can be listed as WLA together with each of the individual authorities that form the system through the same evaluation process.
Annex 2 – Template for the Agreement on the conditions to be designated as WHO Listed Authority (WLA)

BACKGROUND

The WLA framework has been established to provide a transparent and evidence-based pathway for regulatory authorities operating at an advance level of performance to be globally recognized. The designation of a regulatory authority as a WLA is intended to promote the supply of safe, effective and quality medical products and the optimal use of limited resources by facilitating reliance on the work products and decisions of trusted agencies in the decision-making of regulatory authorities, the WHO Prequalification Programme, and procurement agencies.

Recognizing the importance of the above objective [name of regulatory authority] _________ of [name of country or region] _________ hereby expresses its interest to be listed as a the WLA for the following:

I - Product category (ies):

Multisource (generics) / New medicines (new chemical entities) and/or biotherapeutics and/or similar biotherapeutic products / Vaccines

and/or

II - Regulatory functions:

Marketing Authorization / Vigilance / Market Control / Licensing establishments / Regulatory Inspections / Clinical Trial Oversight / Laboratory Testing / Lot Release in addition to the overarching Regulatory System function, which provides the foundation for all regulatory activities.

UNDERTAKINGS

This template and the accompanying roadmap and project evaluation plan, once completed, serves as the Agreement on the conditions to be designated as WLA.

[Name of regulatory authority] _________ agrees to:

I. Make best efforts to comply with all the requirements for WLA listing.
II. Jointly develop a WLA roadmap and project evaluation plan with WHO. The roadmap will consider all available evidence and experience that may lessen the resources and time necessary to reach a listing decision. The roadmap will delineate the Performance Evaluation methodology and activities to be conducted per regulatory function as well as tentative timelines, milestones, and decisions points. The roadmap may be adjusted, as required, based on periodic re-evaluation of progress being made and the agreement of WHO and [name of the regulatory authority].

III. Assign sufficient resources and provide access to requested documents and designated focal points and other responsible individuals in the authority throughout the course of the WLA evaluation and listing process. Any modification to a focal point is to be promptly communicated.

IV. Respect timelines documented in the WLA roadmap and evaluation project plan jointly developed by the [name of regulatory authority] and WHO, or as amended with the consent of both parties.

V. The public disclosure of the listing information described in Annex 3 of the Operational Guidance following a positive WLA listing decision.

VI. The disclosure of additional information related to the WLA evaluation on a secure WHO regulatory platform accessible by other WLAs.

VII. Comply with post-listing reporting requirements as outlined in section 8 of the Operational Guidance.

WHO agrees to:

I. Assign sufficient resources and provide access to requested documents and designated focal points throughout the course of the WLA evaluation and listing process. Any modification to a focal point is to be promptly communicated.

II. Jointly develop a WLA roadmap and project evaluation plan with [name of regulatory authority] as described above.

III. Respect timelines documented in the WLA roadmap and project evaluation project plan jointly developed by the [name of regulatory authority] and WHO, or as amended with the consent of both parties.

IV. Hold all information pertaining to the submission of an EOI and subsequent steps preceding a positive listing decision in confidence, and thereafter disclose only
information described in Annex 3 of the Operational Guidance for the purpose of public listing and access by other WLAs on a secure WHO regulatory platform.

FOCAL POINTS:
The following focal points are established for the Performance Evaluation exercise:

<table>
<thead>
<tr>
<th>WHO</th>
<th>[Name of regulatory authority]________</th>
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<tbody>
<tr>
<td>Contact person</td>
<td>Role</td>
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Annex 3 – Sample listing

<table>
<thead>
<tr>
<th>Country</th>
<th>Regulatory Authority (RA)</th>
<th>Link to the RA and contact point</th>
<th>Listed product stream(s)¹</th>
<th>Listed function(s)²</th>
<th>Date of first listing</th>
<th>Date of renewal</th>
<th>Link to the listing summary</th>
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</tr>
</tbody>
</table>

¹ Product stream can be multisource (generics), new medicines (new chemical entities) and/or biotherapeutics and/or biosimilar products, vaccines
² RS Regulatory System (mandatory), MA Marketing Authorization, VL Vigilance, MC Market Control, LI Licensing establishments, RI Regulatory Inspections, LT Laboratory Testing, CT Clinical Trials oversight, LR Lot Release
Background

The introduction of a framework for designating and publicly listing a regulatory authority as a WHO Listed Authority (WLA) is designed to provide a transparent and evidence-based pathway for regulatory authorities to be globally recognized as meeting and applying WHO and other internationally recognized standards and guidelines, as well as good regulatory practices. The designation of a regulatory authority as a WLA is intended to promote access and the supply of safe, effective and quality medical products and the optimal use of limited resources by facilitating reliance on the work products and decisions of trusted agencies in the decision-making of regulatory authorities, the WHO Prequalification Programme, and procurement agencies.

To ensure impartiality of the WLA decision-making process, WHO will call upon a WLA Advisory Group (WAG) to render an independent opinion on the listing or possible delisting of a regulatory authority. The WAG serves to provide an additional level of assurance that due process was followed and that WHO decisions are supported by findings.

I. Role

In its capacity as an advisory body to WHO, the WAG shall render an opinion on whether:

i) the listing recommendation of the WLA Team and second level WHO review is supported by the findings from the evaluation process. The WLA Team report and second level review shall form the basis of formulating an opinion.

ii) The performance evaluation process was followed based on the WLA Operational Guidance.

The WAG may also be requested to render an opinion on a recommendation to delist a WLA based on a review of a Re-evaluation report and second-level review.

WAG opinions are advisory in nature.

II. Composition and tenure

1. The WAG shall be composed of fifteen (15) members, two each from the six (6) WHO regions plus three (3) members with global regulatory experience.

2. Members from each of the six WHO regions will be appointed by WHO from a short list of candidates proposed by the WHO Regional Offices following a call for members. Members providing a global perspective will be selected from a list of eligible candidates responding to a WHO open call.

3. Members will be selected taking the following considerations into account:
   - Widely recognized knowledge of and senior level experience in regulatory systems for medicines and vaccines, or related fields, ensuring a broad range of expertise
• Gender balance
• Geographical balance

Members to WAG will have no active role within the regulatory authority.

4. Members are expected to serve for a period of three (3) years and shall be eligible for reappointment.

5. A Chair will be selected by members for one term (3 years). The Chair will preside over meetings, facilitate discussions, help formulate WAG deliberations and opinions, ensure adherence to timelines and serve as the primary liaison with the WHO. The Chair is eligible for reappointment as a member of the WAG.

Members are expected to attend meetings. If a member misses two consecutive meetings, WHO may end his/her appointment as a member of the WAG.

III. Operation

1. The WAG shall meet at the end of the performance evaluation process. WAG meetings will be convened by WHO and will predominantly be held virtually and in closed sessions.

2. The quorum for WAG meetings shall be two thirds of the members, provided each WHO region is represented.

3. External observers may be invited to attend meetings, at the discretion of the Chair and the consent of the WAG. Observers may be invited either in their personal capacity, or as representatives from donor organizations in Official Relations with WHO, other interested UN agencies involved in the procurement and distribution of medical products, regional regulatory bodies, organizations collaborating with WHO under the Coalition of Interested Parties (CIP) Regulatory Systems Strengthening Network. Observers must complete a confidentiality undertaking and a declaration of interests form prior to attending a WAG meeting. Observers will not participate in the deliberations and decision-making process of the WAG.

4. The WLA Team Lead may be requested to attend the meeting to respond to questions the WAG may have in reaching an opinion.

5. WAG opinions should be reached by consensus. In the event consensus is not possible, dissenting views should be documented.

6. The WAG will render an opinion on whether the listing recommendation documented in the WLA Team report and subsequent second level review is supported. If not supported, the rationale for the WAG conclusion will be documented in the WAG report.

7. WAG reports should be submitted to WHO not later than 60 days after receipt of the WLA Team report and second level review.

IV. Secretariat

WHO shall provide the secretariat for and organize meetings of the WAG.

V. Impartiality and independence
6. WAG members must respect the impartiality and independence required by WHO. In performing their work, members may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of any real, potential or apparent conflicts of interest. To this end, proposed members/members shall be required to complete a declaration of interests form and their appointment, or continuation, shall be subject to the evaluation of completed forms by the WHO Secretariat.

7. WAG members have an ongoing obligation to inform the WHO of any interests real or perceived that may give raise to a real, potential or apparent conflict of interests.

8. WAG members do not receive any remuneration from the Organization for any work related to the WAG. However, when attending in-person meetings at the invitation of WHO, their travel cost and per diem shall be covered by WHO in accordance with the applicable WHO rules and policies.

VI. Information and documentation

1. Information and documentation to which members may gain access in performing WAG related activities shall be considered as confidential and proprietary to WHO and/or parties collaborating with WHO. In addition, by counter signing the letter of appointment and the accompanying terms and conditions, WAG members undertake to abide by the confidentiality obligations and also confirm that any and all rights in the work performed by them in connection with, or as a result of their WAG-related activities shall be exclusively vested in WHO.

2. WAG members and Observers shall not quote from, circulate or use WAG documents for any purpose other than in a manner consistent with their responsibilities under these Terms of Reference.
Annex 5 – Renewal Reporting Form for WHO Listed Authorities
Renewal Reporting Form for WHO Listed Authorities (WLA)

*Information contained in the completed Form is confidential*

### 1. NRA or RRS general information

<table>
<thead>
<tr>
<th>Name of the regulatory body applying for listing:</th>
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<tbody>
<tr>
<td>Country or Region¹:</td>
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<tr>
<td>Address of the organization:</td>
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<tr>
<td>Name of contact person:</td>
<td></td>
</tr>
<tr>
<td>Title/position in the organization:</td>
<td></td>
</tr>
<tr>
<td>E-mail address:</td>
<td>Tel. no:</td>
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</tbody>
</table>

### 2. Major changes²

Provide a brief description of major changes which have occurred since listing was achieved, including those already communicated in the interim reports to WHO, if any:

<table>
<thead>
<tr>
<th>Description</th>
<th>Date of the change</th>
<th>Documents provided³</th>
<th>Current status (ongoing, completed)</th>
</tr>
</thead>
<tbody>
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</table>

**Further information**

For further information on WHO listing process please visit WLA website at: [https://www.who.int/initiatives/who-listed-authority-reg-authorities](https://www.who.int/initiatives/who-listed-authority-reg-authorities)

For further information on WHO benchmarking process please visit WHO website at: [https://www.who.int/tools/global-benchmarking-tools](https://www.who.int/tools/global-benchmarking-tools)

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¹ For Regional Regulatory Systems indicate the region represented by the regulatory body, including the list of member NRAs.

² Changes to the regulatory framework, processes, resources, organizational structure and governance or other parameters which may have an impact on the listed function(s) and/or product category(ies) assessed as part of the WLA benchmarking-performance evaluation.

³ Accompanying information in electronic format should be uploaded on the WHO NRA SharePoint and the RSS Team Lead notified. If information is available on the WLA’s website, a link to the relevant webpages is acceptable in lieu of submitting documents, provided that information on the website is in English or summarized in English.