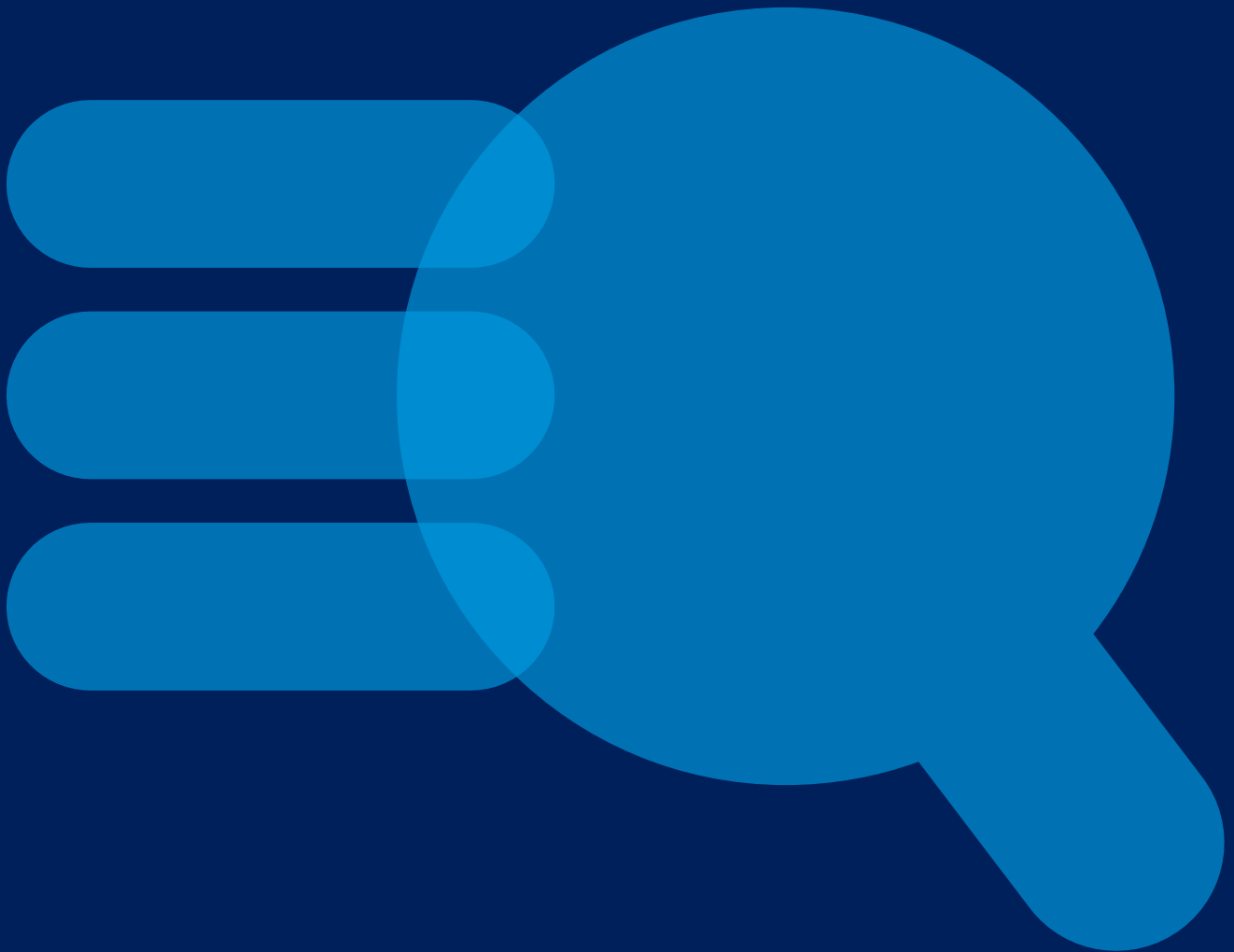


Operational guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities



World Health
Organization

**Operational guidance
for evaluating and
publicly designating
regulatory authorities
as WHO-listed
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ISBN 978-92-4-007476-7 (electronic version)

ISBN 978-92-4-007477-4 (print version)

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Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

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Design and layout: Harri Aittasalo

Contents

Acknowledgements.....	iv
Abbreviations.....	vii
1. Introduction.....	1
2. Purpose.....	2
3. Evaluating regulatory performance.....	3
4. Performance evaluation framework.....	4
5. Considerations for regulatory authorities seeking WLA designation	6
6. Transitional arrangements.....	7
7. Process for applying for, evaluating and listing a WLA.....	8
7.1 Submission of Expression of Interest.....	9
7.1.1 Scope of listing.....	9
7.1.2 Eligibility criteria.....	10
7.1.3 Additional consideration for regional regulatory systems (RRSs).....	11
7.2 Evaluation of EOI.....	11
7.3 Agreement on scope of evaluation and roadmap to listing	11
7.4 Performance evaluation (PE).....	12
7.4.1 Performance evaluation pathways	13
7.5 Decision and listing	14
7.5.1 WLA Advisory Group	14
7.5.2 Decision on listing and Notice of Listing Decision	14
7.5.3 Listing.....	14
7.5.4 Right to appeal	15
8. Renewal of listing and ongoing monitoring	16
8.1 Renewal.....	16
8.2 Ongoing reporting and monitoring	16
8.2.1 Interim reporting by WLA	16
8.2.2 Ongoing monitoring by WHO.....	17
9. Re-evaluation and delisting	18
9.1 Re-evaluation.....	18
9.2 Delisting.....	18
10. Information management system.....	19
References.....	20
Annex 1. Glossary.....	21
Annex 2. Expression of Interest (EOI) of a regulatory authority to be listed as a WHO-listed authority (WLA).....	24
Annex 3. Agreement on the conditions for being designated a WHO-listed authority (WLA)	26
Annex 4: Technical Advisory Group on WHO-listed authorities (TAG-WLA): terms of reference.....	28
Annex 5. Sample listing.....	31
Annex 6. Renewal reporting form for WHO-listed authorities (WLA).....	32

Tables

Table 1. Components of the Standard PE process.....	4
Table 2. WLA process steps and estimated timelines.....	9
Table 3. Elements assessed for the listing of eligible regulatory functions	10
Table 4. Elements assessed for the listing of eligible product categories.....	10
Table 5. Risk-based performance evaluation pathways.....	13

Figures

Figure 1. Elements to be considered for evaluating performance of a regulatory system.....	3
Figure 2. Overview of the application, evaluation and listing steps.....	8

Acknowledgements

The World Health Organization (WHO) would like to thank the Member States, technical partners, stakeholders, entities, individual experts and WHO staff who have contributed to the development of this document and the accompanying operational guidance, as well as the WHO-listed authority (WLA) framework. A list of contributors to this document and the operational guidance is included below.

Manuel Rodolfo Limeres and Mónica Bobbi, Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (National Administration of Drugs, Food and Medical Devices), Argentina; Lilit Ghazaryan, Ministry of Health and Naira Romanova, Scientific Centre of Drug and Medical Technology Expertise, **Armenia**; Paul Huleatt and Richard Hill, Therapeutic Goods Administration, **Australia**; Geneviève Waeterloos, Sciensano, **Belgium**; Sakhile Dube-Mwedzi, South African Development Conference, **Botswana**; Bernardo Luiz Moraes Moreira, Brazilian Health Regulatory Agency and Fernanda Maciel Rebelo, Fernanda Simioni Gasparotto, Patrícia Kott Tomazett, Patricia Serpa, Yane de Carvalho Guedes and Varley Dias Sousa, Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency), **Brazil**; Sea Thol, Ministry of Health, **Cambodia**; Gloria Giraldo, Amanda Jane Diniz, Maria Baca-Estrada and Richard Siggers, Health Canada, **Canada**; Andrea del Pilar Pando Seisdedos, José Miguel Crisóstomo Landeros, María Francisca Aldunate González, Nahum Vergara, Patricia Alexandra Carmona Sepúlveda and Verónica Vergara Galván, Instituto de Salud Pública de Chile (Public Health Institute of Chile), **Chile**; Blouie Po Yiu Tse, Christine Cheung, Michael Yim Tsz Kok, Raphael Yeung and Vincent Chow Wai-yan, Department of Health, Hong Kong Special Administrative Region, **China**; Carlos Rodríguez, Diana Mesa, Diego Alejandro Gutiérrez Triana, Jeannette Daza Castillo, Lilibian Silvia Patricia Álvarez Espejo, Luz Andrea Gordillo Alarcón, María Alejandra Erazo Rebolledo, Ney Callas, Yenny Marcela Suarez González and Ximena Andrea Barbosa Aguillon, Instituto Nacional de Vigilancia de Medicamentos y Alimentos (National Institute of Food and Drug Monitoring), **Colombia**; Frank Diafouka and Hrvoje Tumir, Agency for Medicinal Products and Medical Devices of Croatia, **Croatia**; Biorikys Yáñez Chamizo, Celeste Aurora Sánchez González, Danay Mora Pascual, Giset Jiménez López, Liana Figueras and Mario Alberto Díaz

García, Centro Para el Control Estatal de la Calidad de los Medicamentos (Cuba Center for State Control of Drugs), **Cuba**; Amani Hegazi, Amira Amin, Asmaa Fouad, Dalia Abouhoussein, Doaa Abd El Rady, Engy El Hosary, Heba Khalil, Ireen Habeeb, Irene Gamal Shehata and Shereen Mohamed, Egyptian Drug Authority, **Egypt**; Katrin Lambing and Marje Zernant, Estonian State Agency of Medicines, **Estonia**; Alain Alsalhani, Médecins Sans Frontières, Cristina Baccarelli, Catherine Milne, Michael Wierer and Richard Wanko, European Directorate for the Quality of Medicines and François Cano and Sylvie Morgeaux, Agence Française de Sécurité Sanitaire des Produits de Santé (National Agency for Medicines and Health Products Safety), **France**; Brigitte Mauel-Walbroel, Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices/ Benchmarking of European Medicines Agencies) and Olga Rassokhina, Paul Ehrlich Institute, Germany; Abdul-Samad Issah, Abena Asamoah-Amoakohene, Eric Karikari- Boateng, Nathaniel N. K Nkrumah and Seth Kwaku Seaneke, Food and Drugs Authority, **Ghana**; Ika Prawwahju, Elizabeth Ika P and Lucky Slamet, Badan Pengawas Obat dan Makanan (Indonesian Food and Drug Authority), **Indonesia**; Hamidreza Hozouri, Pasteur Institute, **Iran (Islamic Republic of)**; Anna Laura Salvati and Sandra Petraglia, Agenzia Italiana del Farmaco (Italian Medicines Agency), **Italy**; Eriko Fukuda, Jun Kitahara, Teruyoshi Ehara, Pharmaceuticals and Medical Devices Agency; Hirooki Tanabe and Naoyuki Yasuda, Ministry of Health, Labour and Welfare; Koji Ishii, Masaki Ochiai, National Institute of Infectious Diseases, **Japan**; Zamil Zakaria, National Pharmaceutical Regulatory Agency, **Malaysia**; Adriana Padilla Mendoza, Bertha Araceli Rodríguez Arvizu, Daniela López, Elvira Espinosa Gutiérrez, Felipe Ángel de la Sancha Mondragón, Graciela Aguilar Gil Samaniego, Imelda Rocío Guzmán Cervantes, Iris Lorena Arreola Dominguez, Karla Maricela Félix Rodríguez, María de Lourdes Rodríguez Aveleyra, Miriam Jackeline Loera Rosales, Rocio Guzman and Virginia Ramirez, Comisión Federal para la Protección contra Riesgos Sanitarios (Federal Commission for the Protection against Sanitary Risk), **Mexico**; Houda Sefiani, National Pharmacovigilance Centre, **Morocco**; Martijn Bruysters, National Institute for Public Health and the Environment and Martin Harvey Allchurch, European Medicines Agency, **Netherlands (Kingdom of the)**; Abiola Victor Olayiwola, Anthony Joseph Hotton,

Ijeoma Ukachi Nwankwo, Monica Hemben Eimunjeze and Victor Abiola Olayiwola, National Agency for Food and Drug Administration and Control, **Nigeria**; Caren Mangorangca, Pia Angelique Priagola and Jade Mae D. Biyo, Food and Drug Administration, **Philippines**; Eugenia Lopes, Infarmed/Benchmarking of European Medicines Agencies and Helena Baiao, Autoridade Nacional do Medicamento e Produtos de Saúde I.P. (National Authority of Medicines and Health Products, I.P.) **Portugal**; Eun Hye Parks, Hee Young Park, In Yeong Hwang, Jung-Ah Byun and Yu Jeong Seo, Ministry of Food and Drug Safety, Republic of Korea; Alexandru Sirbu, Independent Consultant, **Romania**; Abrar Al Musharraf, Alya Aldahash, Khalid Mohammed Al Mowaziri, Mubarak Saeed Alshahrani, Turki Abdulaziz Al Rafie, Saudi Food and Drug Authority, **Saudi Arabia**; Dragana Šmidling Koruga, Medicines and Medical Devices Agency, Serbia; Sia Chong Hock, Health Sciences Authority, **Singapore**; Deon Poovan, Portia Nkambule, Quinton Meyer, Silverani Padayachee and Tohlang Sehloho, South African Health Products Regulatory Authority (SAHPRA), **South Africa**; Johan Ellenius and Monica Plöen, Uppsala Monitoring Centre and Sten Olsson, Independent consultant, **Sweden**; Andreas Pfenninger, Gabriela Zenhäusern and Michael Gilgen, Swissmedic, Fabienne Benoist, Drugs for Neglected Diseases initiative, Daniel Brunner, Pharmaceutical Inspection Co-operation Scheme, and J Bernat, International Federation of Pharmaceutical Manufacturers Associations, **Switzerland**; Achiraya Praisuwan, Suchart Chongprasert and Supatra Phongsri, Food and Drug Administration and Supaporn Phumiamorn and Weryarmarst Jaroenkunathum, Institute of Biological Products, **Thailand**; Nihan Burul Bozkurt, Türkiye İlaç ve Tıbbi Cihaz Kurumu (Pharmaceuticals and Medical Devices Agency of Türkiye), **Türkiye**; Helen Byomire Ndagije and Helen Ndagije, National Drug Authority, Uganda; Lawrence Liberti and Prisha Patel, Centre for Innovation in Regulatory Science, **United Kingdom of Great Britain and Northern Ireland**; Sunday Kisoma, Emmanuel Alphonse Nkiligi and Felchism Apolnary, Tanzania Medicines and Medical Devices Authority, **United Republic of Tanzania**; Gopa Raychaudhuri and Theresa Mullin, US Food and Drug Administration; Jude Nwokike, United States Pharmacopeia, **United States of America**; Caroline Getrude Samatanga, Libert Chirinda and William Wekwete, Medicines Control Authority of Zimbabwe, **Zimbabwe**.

Thanks are also due to the following for their financial and technical support, including through comments, towards the development, piloting and production of this document and the accompanying performance evaluation manual:

- Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (National Administration of Drugs, Food and Medical Devices [ANMAT]), Argentina
- Agence Française de Sécurité Sanitaire des Produits de Santé (National Agency for Medicines and Health Products Safety [ANSM]), France
- Agência Nacional de Vigilância Sanitária (National Health Surveillance Agency [ANVISA]), Brazil
- Agency for Medicinal Products and Medical Devices (HALMED), Croatia
- Badan Pengawas Obat dan Makanan (Indonesian Food and Drug Authority [PADAN POM]), Indonesia
- Bill & Melinda Gates Foundation (BMGF)
- Centro Para el Control Estatal de la Calidad de los Medicamentos (Cuba Center for State Control of Drugs [CECMED]), Cuba
- Comisión Federal para la Protección contra Riesgos Sanitarios (Federal Commission for the Protection against Sanitary Risk [COFEPRIS]), Mexico
- Drugs for Neglected Diseases Initiative (DNDi)
- European Medicines Agency (EMA)
- GAVI, the Vaccine Alliance
- Health Sciences Authority (HSA), Singapore
- Indian Pharmacopoeia Commission, India
- Instituto de Salud Pública de Chile (Public Health Institute of Chile [ISP]), Chile
- Instituto Nacional de Vigilancia de Medicamentos y Alimentos (National Institute of Food and Drug Monitoring [INVIMA]), Colombia
- International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
- Management Sciences for Health (MSH)
- Médecins Sans Frontières (Doctors Without Borders [MSF])
- Ministry of Food and Drug Safety (MFDS), Republic of Korea
- National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria
- Pharmaceuticals and Medical Devices Agency (PMDA), Japan
- Saudi Food and Drug Authority (SFDA), Saudi Arabia
- SWISSMEDIC, Switzerland
- Therapeutic Goods Administration (TGA), Australia
- U.S. Food and Drug Administration (FDA), United States of America
- United States Pharmacopeia (USP), United States of America

This document and the accompanying performance evaluation manual were written by Alireza Khadem

Broojerdi, Anna Laura Salvati, Hiiti Sillo, Mike Ward, Mohamed Refaat and Razieh Ostad Ali Dehaghi of the Regulatory Systems Strengthening Team, Regulation and Safety Unit, in the Department of Regulation and Prequalification at WHO headquarters. The following WHO staff also contributed to the two documents: WHO headquarters – Mohammed Alali, Claudia Alfonso, Samvel Azatyan, Madhav Ram Balakrishnann, Andrew Chemwolo, Laura Di Trapani, Petra Doerr, Rolando Domingo Morales, Alan Fauconnier, Ayako Fukushima, Johanna Gouws, Luther Gwaza, Andrea Keyter, Akida Khea, Elham Kosary, Rutendo Kuwana, Olivier Christian Lapujade, Dianliang Lei, Leticia Josefina Megias Lastra, Alexandrine Maes, Yvonne Melounou, Ryoko Miyazaki-Krause, Deusdedit Mubangizi, Mario Musonda, Lawrence Musyoka

Nzumbu, Rogerio Paulo Pinto De Sà Gaspar, Mariana Roldão Santos, Ute Rosskopf, Vimal Sachdeva, Gaby Henriette Vercauteren, Marie Valentin & Maria Bernadette Yap; WHO Regional Office for Africa – Bartholomew Dicky Akanmori & Stanislav Kniazkov; WHO Regional Office for the Americas – Mauricio Beltran, Jose Luis Castro, Jose Vicente Coto, Murilo Freitas Dias, Alexandre Lemgruber, Fernanda Lessa, Alexandra Mata-Espinoza, Maria Luz Pombo-Castro, Analia Porras & Edgar Robin Rojas; WHO Regional Office for South-East Asia – Anil Kumar Chawla & Adrien Inoubli; WHO Regional Office for Europe – Dorina Pirgari; WHO Regional Office for the Eastern Mediterranean – Al-Nuiserat Adi & Houda Langar; WHO Regional Office for the Western Pacific – Socorro Escalante, Hitomi Kubota & Jinho Shin.

Abbreviations

CT	clinical trial (oversight)
EOI	expression of interest
GBT	Global Benchmarking Tool
LI	licensing establishments
LR	(RA) lot Release
LT	laboratory testing
MA	(registration and) marketing authorization
MC	market (surveillance and) control
ML	maturity level
NRA	national regulatory authority
PE	performance evaluation
RA	regulatory authority
RI	regulatory inspection
RS	regulatory system
RRS	regional regulatory system
tWLA	transitional WHO-listed authority
VL	vigilance
TAG-WLA	technical advisory group on WHO-listed authorities
WHO	World Health Organization
WLA	WHO-listed authority

1. Introduction

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

Although ultimate responsibility for the decision to use a WLA 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.

The WLA framework (referred to as “the framework”), comprises the following documents:

- this operational guidance
- *Evaluating and publicly designating regulatory authorities as WHO-listed authorities: policy document (1)*
- *Manual for performance evaluation of regulatory authorities seeking designation as WHO-listed authorities* (hereinafter referred to as “the PE manual”) (2)
- *WHO Global Benchmarking Tool (GBT) (3)* and manual (4).

The framework is underpinned by World Health Assembly *resolution 67.20 – Regulatory system strengthening for medical products (5)* and the WHO *Roadmap for access to medicines, vaccines and health products 2019–2023: comprehensive support for access to medicines, vaccines and other health products (6)*.

In order to gain a thorough understanding of the regulatory attributes WLAs are expected to exhibit, this document should also be read in conjunction with other relevant WHO guidance documents, which include: *Good regulatory practices in the regulation of medical products (7)*, *Good reliance practices in the regulation of medical products: high-level principles and considerations (8)*, and the *WHO guideline on the implementation of quality management systems for national regulatory authorities (9)*.

This document 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 document was developed following international consultative meetings with Member States and interested stakeholders, broad public consultations, technical working group discussions on performance evaluation, a review of comments received on the draft operational guidance published in July 2021, subsequent consultations with Member States on transitional arrangements, and experience gained from piloting the WLA framework.

2. Purpose

This document 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 *Evaluating and publicly designating regulatory authorities as WHO-listed authorities: policy document (1)*.

Details are provided of the steps, timelines and processes involved in evaluating and designating a WLA. This document also describes the process and criteria for renewal, re-evaluation and possible delisting, the role and responsibilities of the technical advisory group on WHO-listed authorities

(TAG-WLA), and the undertakings of WHO and eligible regulatory authorities.

For the purposes 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). A glossary giving definitions for the terms used in this document is provided in Annex 1.

For details of the performance evaluation process for each function, see the PE manual.

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 purposes of this document, 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 (see Fig. 1).

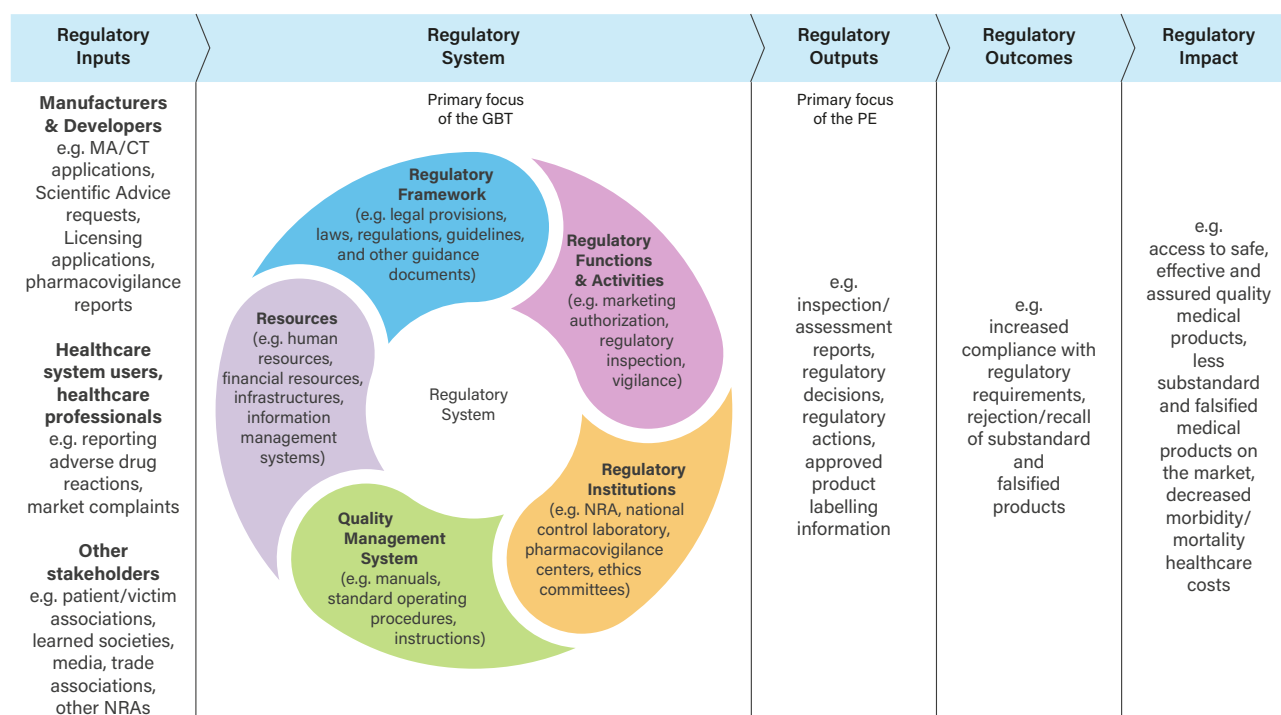
Performance evaluation (PE), in the WLA context, refers to the process of evaluating the performance of a RA in terms of specific regulatory functions and/or product categories, with a focus on regulatory outputs rather than outcomes and impact, as these often involve factors beyond the control of the regulatory authority.

The WHO benchmarking tool and methodology represent the foundation for assessing and classifying regulatory systems according to maturity level

(ML). To determine how well a regulatory authority *is configured* to provide effective regulatory oversight of medical products, the GBT provides a robust and structured approach to analysing the required inputs, regulatory processes and intended outputs.

To provide a more comprehensive assessment of how well the regulatory system *operates*, the results obtained from the benchmarking exercise are complemented by the collection and review of output data related to key regulatory parameters and activities. This is done through the PE activity conducted for the WLA listing process. This includes 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).

Fig. 1. Elements to be considered for evaluating performance of a regulatory system



4. Performance evaluation framework

The performance evaluation (PE) framework is designed to promote trust and reliance in regulatory systems in the context of the international supply of medicines and vaccines. To avoid the duplication of effort, the PE framework has also been designed to ensure that all available information, internal and external to WHO, is taken into account before additional information is requested or further activities undertaken 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.

PE distinguishes between technical performance (for example, scientifically sound decision-making, quality of regulatory outputs and their consistent implementation) and operational performance (for example, the time it takes to render a decision on

a marketing authorization application). In addition, PE builds on the GBT and on the well-established mechanisms already used by WHO for capacity-building purposes (specifically the Observed Audit for Good Manufacturing Practices inspections and the Vigilance Field Visit), by expanding their objectives to include performance evaluation of related functions. The standard PE process comprises:

- an audit against mandatory GBT ML4 sub-indicators
- an audit against PE indicators
- an 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 PE tools.

The components of a standard PE process are presented in *Table 1*.

Table 1. Components of the Standard PE process

I - Audit against indicators*			II - Evaluation of selected regulatory functions using PE tools
Regulatory system and functions	Mandatory ML4 sub-indicators**	PE indicators	
Regulatory system	14	4	not applicable
Registration and marketing authorization	3	3	Expert review of MA application assessment reports Off-site evaluation
Vigilance	4	7	Vigilance field visit On-site evaluation
Market surveillance and control	2	2	not applicable
Licensing establishments	2	-	not applicable
Regulatory inspection	5	-	Good manufacturing practices/ good clinical practices observed audit On-site evaluation
Laboratory testing	3	1	Expert review of laboratory activities On-site evaluation
Clinical trials oversight	2	3	Expert review of clinical trial application assessment reports Off-site evaluation
RA lot release (vaccines)	1	-	not applicable
TOTAL	36	20	

* 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 (see also .7.1.2 below).

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 section 7.1 below. See section 7.4.1 for an overview of PE pathways, and the PE manual for details on the performance evaluation process, indicators, and tools.

Responsibility for conducting all activities required for the designation of a regulatory authority as a WLA lies with WHO headquarters, regional offices and country offices, working together under a unified plan.

5. Considerations for regulatory authorities seeking WLA designation

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

While all good regulatory practice principles and enablers are important to “smart regulation”, two warrant special mention within the context of the WLA framework: i) transparency and ii) regulatory cooperation as an enabler of efficiency and effectiveness (7). Transparency is a critical prerequisite to building trust and confidence in the regulatory system.

“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 to build trust and maximize opportunities for cooperation and reliance as part of a shared regulatory community responsibility” (7).

Regulatory authorities are both the audience and the 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 the*

regulation of medical products: high-level principles and considerations (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 WLA 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. Regulatory 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, information exchange and other forms of collaboration, thereby contributing to improved regulatory practices.

6. Transitional arrangements

The *Interim list of national regulatory authorities* published in 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.

Regulatory authorities on the Interim list have a history of investment in regulatory system strengthening and cooperation and 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.

In recognition of the above, WHO developed transitional arrangements that provide all regulatory authorities on the Interim list the opportunity to be placed on a time-limited, public list of transitional WLAs or tWLAs (10) signalling the commitment of both listed authorities and 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 WLA.

With the introduction of transitional arrangements, WHO has replaced the Interim list with the tWLA list. A regulatory authority will be moved from the tWLA list to the WLA list upon successful completion of the WLA evaluation process. At the same time, WHO will maintain a 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.

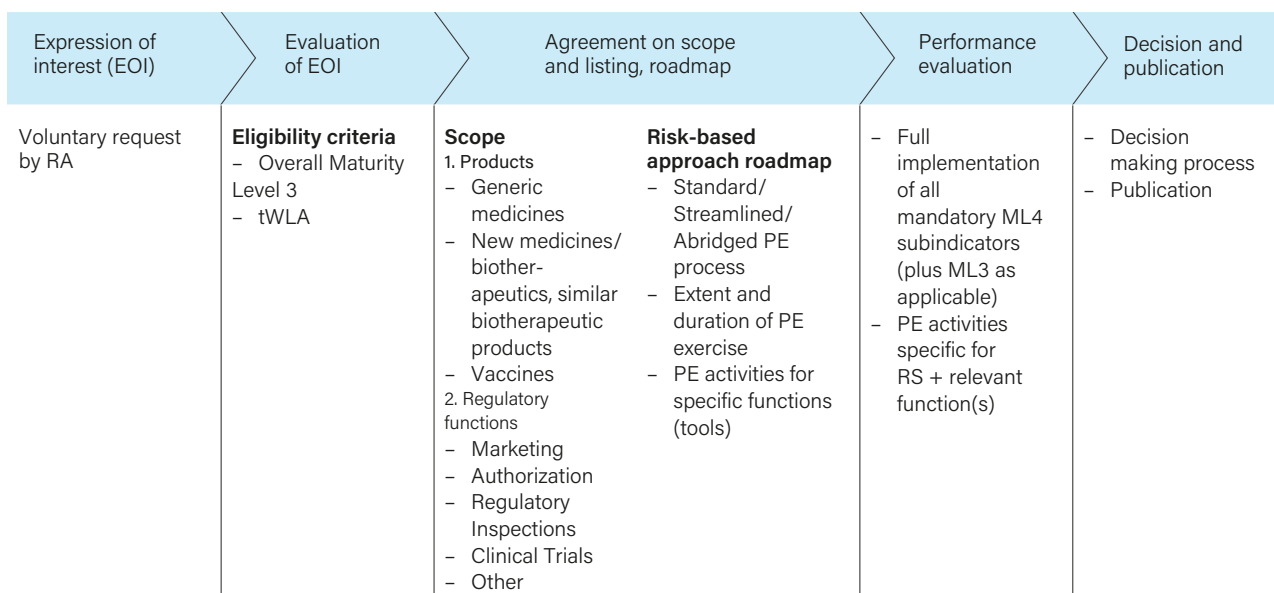
1. Regulatory authorities previously on the Interim list have been placed on the tWLA list.
2. A transition period of five (5) years is established from the date of publication of *the interim Operational guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities* (31 march 2022).
3. The tWLA list will exist only for the duration of the transition period. During the transition 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 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.
9. If an authority decides 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 Fig. 2, is divided into the following steps.

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

Fig. 2. Overview of the application, evaluation and listing steps



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 7.1.2 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 for being designated as a WHO-listed authority* (Annex 3).
- 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.
- While WHO promotes the practice of reliance whenever possible to optimize the use of resources, a WLA is expected to possess the capacity to perform the regulatory functions relevant to the scope of listing, thereby serving as an international reference for other RAs.
- Outsourcing (i.e. through 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 PE 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.

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 2. A RA interested in seeking listing 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 the Regulation and Safety Unit, WHO headquarters, through the appropriate WHO regional office.

The request must include a completed EOI (see Annex 2) 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 or categories being sought, provide evidence that eligibility criteria are met, and confirm acceptance with the general provisions described in the *Agreement on the conditions to be designated as a WHO-listed authority* (see Annex 3).

A national regulatory authority (NRA) or a regional regulatory system (RRS) (including individual member authorities) which meets the eligibility criteria in section 7.1.2 can be listed for one or more regulatory functions (see Table 3) and/or one or more product categories (see Table 4).

The WLA framework does not cover export-only products. 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 regulatory oversight, including through the WHO certification scheme on the quality of pharmaceutical products moving in international commerce as documented by the issuance of a Certificate of Pharmaceutical Product (CPP).

Table 2. WLA process steps and estimated timelines

Calendar days		Responsibilities	
		WHO	RA
1. Evaluation of Expression of Interest	30	✓	Not applicable
2. Agreement on scope of listing and evaluation plan	60	✓	✓
3. Performance evaluation and report	60 – 180*	✓	✓
4. Opinion of Technical Advisory Group on WLA	60	✓	Not applicable
5. Notice of Listing Decision and publication on WHO website	60	✓	Not applicable

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

Table 3. Elements assessed for the listing of eligible regulatory functions

Eligible Regulatory Functions	Function(s) to be assessed for listing									
	RS ⁱ	MA	VL	MC ⁱⁱ	LI ⁱⁱⁱ	RI ^{iii, iv}	CT	LT	LR ^v	
Registration and marketing authorization (MA)	✓	✓								
Vigilance (VL)	✓		✓							
Market surveillance and control (MC)	✓	✓	✓	✓		✓		✓		
Licensing establishments (LI)	✓				✓	✓				
Regulatory inspection (RI)	✓				✓	✓				
Clinical trial oversight (CT)	✓						✓			
Laboratory access and testing (LT)	✓							✓		
RA lot release (LR)	✓							✓	✓	

- ⁱ RS is not eligible for listing. Evaluation of the regulatory system is always performed in conjunction with the function(s) for which listing is sought.
- ⁱⁱ A regulatory authority seeking listing for MC must also meet the requirements for MA, VL, RI (GMP/GSDP), LT.
- ⁱⁱⁱ A regulatory authority seeking listing for LI must also meet the requirements for RI. Conversely, a regulatory authority seeking listing for RI must, where applicable, meet requirements for LI.
- ^{iv} RI listing can be achieved separately for GMP/GSDP and GCP components.
- ^v A regulatory authority seeking listing for LR must also meet the requirements for LT.

Table 4. Elements assessed for the listing of eligible product categories

Eligible Regulatory Functions	Function(s) to be assessed for listing									
	RS	MA	VL	MC	LI	RI	CT	LT	LR	
Multisource (generics)	✓	✓	✓	✓	✓	✓	ⁱ	✓		
New medicines (new chemical entities) and/or biotherapeutics and/or similar biotherapeutic products	✓	✓	✓	✓	✓	✓	✓	✓		
Vaccines	✓	✓	✓	✓	✓	✓	✓	✓	✓	

- ⁱ Bioequivalence studies are covered under both MA and RI functions and assessed under criterion 2.3.1.1 of the MA PE tool.

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.

An overall maturity level rating of 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 PE process (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 (4)*.

The RA must agree also with the general provisions and obligations described in the *Agreement on the conditions to be designated as a WHO-listed authority* (Annex 3). The Agreement covers the resources needed to complete the PE, 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 to RRSs.

- The EOI should be submitted by the regional body (where it exists) or by another institution representing the RRS.
- 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 PE.
- 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 PE is communicated. The start date is proposed based on a prioritization and planning schedule (see section 7.3).

- 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

The RA and WHO will sign the *Agreement on the conditions to be designated as 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 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 the sharing of further information with other WLAs (see section 7.5.3)¹.

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 WHO and the 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.

¹ WHO holds in confidence all information pertaining to the submission of an EOI and subsequent steps preceding a positive listing decision, and thereafter discloses only i) information described in Annex 5 for the purpose of public listing and ii) access by other WLAs on a secure WHO regulatory platform. If not already in place and requested by the RA, WHO will sign a confidentiality agreement with the RA. A confidentiality undertaking and declaration of interest are required for all WHO RA assessors (see Manual for benchmarking of the national regulatory system of medical products and formulation of institutional development plans).

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 Prequalification 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 minimize 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, 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. 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

Evaluation pathway		Eligibility	Evaluation methodology
Transitional arrangements (tWLAs)	Abridged	Stringent regulatory authorities (SRAs) for medicines and highly performing NRAs for vaccines	<ol style="list-style-type: none"> 1. RA self-assessment against pre-selected GBT and PE indicators that primarily target good regulatory practices and quality management systems. 2. WHO desktop review of self-assessment report
	Streamlined	ML3 and ML4 RAs (medicines and/or vaccines)	<ol style="list-style-type: none"> 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 PE**
		Regional reference RAs of the Americas (medicines and/or vaccines) Functional RAs (vaccines)	<ol style="list-style-type: none"> 1. RA self-assessment against pre-populated GBT as well as PE indicators* 2. WHO desktop review of self-assessment; may involve an audit against selected GBT indicators to verify findings 3. WHO assessment against PE**
Routine arrangements (All other authorities)	Standard	Overall ML3 or ML4 RAs (medicines and/or vaccines) through GBT benchmarking	<ol style="list-style-type: none"> 1. RA self-assessment against PE indicators (GBT ML4 + PE) 2. WHO desktop review of self-assessment report 3. WHO assessment against PE**

* The need for self-assessment against pre-populated GBT is dependent on the outcome and validity of the earlier benchmarking.

** PE 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 (PE Manual), 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 WLA 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 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 when 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 stringent regulatory authorities/ highly performing regulatory authorities, the self-assessment involves a set of pre-selected GBT sub-indicators and PE indicators (see PE Manual).

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 above).

PE-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 technical advisory group on WHO-listed authorities (TAG-

WLA) will provide an opinion to WHO on the listing of a RA following a review of the PE report. The TAG-WLA review process provides an additional level of assurance that due process was followed and that listing recommendations are supported by findings.

The TAG-WLA 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 TAG-WLA is described in Annex 4.

WHO will convene meetings of the TAG-WLA and serve as secretariat. The TAG will render an opinion on whether the listing recommendation documented in the PE report is supported.

The TAG-WLA opinion should be issued no later than 60 calendar days after the meeting has been held.

7.5.2 Decision on listing and Notice of Listing Decision

The “Notice of Listing Decision” serves as the official decision on listing. The decision on listing resides with the Assistant Director-General responsible for access to medicines and health products.

The Notice of Listing Decision includes the following information:

- decision on listing
- rationale for the decision
- scope of listing.

In addition, the PE report and the TAG-WLA opinion will accompany the Notice of Listing Decision.

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 website² within a target of 60

² See <https://www.who.int/initiatives/who-listed-authority-reg-authorities>.

calendar days from the issuance of the TAG-WLA opinion. A sample listing is provided in Annex 5. The listing comprises:

- scope of the designation, for example vaccines or multisource (generic) 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.

For the format and content of the public WLA listing, see Annex 5.

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 Notice of Listing Decision and addressed to the Assistant Director-General 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 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 (Annex 6). 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 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 Notice of listing decision – Renewal 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 *Notice of listing decision – Renewal* 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)
- information requested pertinent to a renewal of listing decision has not been provided, or
- ongoing reporting requirements are not met.

See section 9.2 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 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.

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).

9. Re-evaluation and delisting

9.1 Re-evaluation

WHO reserves the right to request information on events that potentially impact the WLA listing and 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* signed by the Assistant Director-General responsible for access to medicines and health products. The Notice of Concern describes the nature of the concern and the proposed re-evaluation plan. An abbreviated version of the Notice of Concern 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* 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 *Notice of listing decision – Re-evaluation* together with the re-evaluation report. WHO would meet with the WLA to discuss and agree 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 TAG-WLA to make a recommendation on delisting.

c. *grounds for delisting the WLA exist*

The conclusion is communicated to the WLA through a *Notice of Listing Decision – Re-evaluation* together with the re-evaluation report and a description of the delisting process, which provides for the convening of the TAG-WLA and

the right of appeal. The *Notice of Listing Decision – Re-evaluation* 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 WHO Assistant Director-General responsible for access to medicines and health products may convene a special meeting of the TAG-WLA to render an independent opinion on delisting based on the Re-evaluation report. In exceptional circumstances, the WHO Assistant Director-General may choose to proceed with delisting the WLA without convening the TAG-WLA if concerns are of an urgent public health nature.

The decision to delist a WLA resides with the WHO Assistant Director-General. The decision is communicated to the WLA as a *Notice of Delisting*.

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

The *Notice of Delisting* 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 7.5.4. 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 *Notice of Delisting*. 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 PE is 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.

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Annex 1. Glossary

Common regulatory framework	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 that 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 a regulatory body from the public WLA list due to evidence of changes, serious and persistent lapses in regulatory oversight or other events that have an impact on the function(s) and/or product category or categories 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 (such as ISO or pharmacopeial standards) and guidelines (such as International Council for Harmonization 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 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 (PE)	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 based on the function(s) and/or the product category(ies) included in the Expression of Interest. Evaluation of the regulatory system is always performed in conjunction with the function(s) for which listing is sought.
Product category(ies)	For the purpose of this document, refers to medical products and 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, the term Regulatory Authority includes both National Regulatory Authorities and Regional Regulatory Systems.
Re-evaluation	Assessment of a WLA to determine 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 seven common regulatory functions and one non-common regulatory function. Common regulatory functions that apply to all medical products are registration and marketing authorization (MA), vigilance (VL), market surveillance and control (MC), licensing establishments (LI), regulatory inspection (RI), laboratory testing (LT), clinical trials oversight (CT) as well as the overarching regulatory system (RS). RA 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 so they may make informed decisions. Regulatory systems are expected to be transparent. Regulatory requirements and decisions should be made known, and input should be sought on regulatory proposals.

WHO-listed authority
(WLA)

A regulatory authority or a regional regulatory system that 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.

Annex 2. Expression of Interest (EOI) of a regulatory authority to be listed as a WHO-listed authority (WLA)

Information contained in the completed form is confidential

1. National regulatory authority (NRA) or regional regulatory system (RRS): general information	
Name of the regulatory authority applying for listing:	
Country or Region: ¹	
Address of the organization:	
Name of contact person:	
Title/position in the organization:	
E-mail address:	Tel. no:

2. Eligibility criteria		
NRA or RRS		
a) Included in transitional WLA list: <input type="checkbox"/> Yes <input type="checkbox"/> No		
If yes,	please indicate for which product category(ies):	
b) benchmarked by WHO: <input type="checkbox"/> Yes <input type="checkbox"/> No		
If yes,	please indicate for which product category:	
	Date of last benchmarking:	Overall maturity level attained:
Additional information related to RRS only		
Member NRAs have been benchmarked by WHO: <input type="checkbox"/> Yes <input type="checkbox"/> No		
If yes, please list all NRAs benchmarked by WHO (add rows as necessary):		
	NRA:	Country:
	Date of last benchmarking:	Overall maturity level attained:

¹ For regional regulatory systems, indicate the region represented by the regulatory body, including the list of member national regulatory authorities.

3. Listing application ²	
NRA or RRS	
Please indicate the regulatory function(s) sought for listing (RS mandatory):	
<input type="checkbox"/> RS <input type="checkbox"/> MA <input type="checkbox"/> VL <input type="checkbox"/> MC <input type="checkbox"/> LI <input type="checkbox"/> RI <input type="checkbox"/> LT <input type="checkbox"/> CT <input type="checkbox"/> LR	
Please indicate the product category(ies) sought for listing:	
<input type="checkbox"/> Multisource (generics) <input type="checkbox"/> New medicines (new chemical entities) and/or biotherapeutics and/or similar biotherapeutic products <input type="checkbox"/> Vaccines	
Additional information related to regional regulatory systems only	
Common legal framework exists: <input type="checkbox"/> Yes <input type="checkbox"/> No	
Regional regulatory system applying as single entity: ³ <input type="checkbox"/> Yes <input type="checkbox"/> No	

4. Additional information	
National regulatory authority or regional regulatory system	
Any further information you would like to provide related to the EOI (Optional)	

Further information

For further information on the WHO listing process, please visit WLA website at: <https://www.who.int/initiatives/who-listed-authority-reg-authorities>

For further information on the WHO benchmarking process, please visit WHO website at: <https://www.who.int/tools/global-benchmarking-tools>

For queries about the procedure for applying for designation as a WLA , please contact the WHO Regulatory System Strengthening Team at: <https://www.who.int/teams/regulation-prequalification/regulation-and-safety/rss>.

2 See Table 3 and 4 in the *Operational guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities*.

3 Regional regulatory systems 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 3. Agreement on the conditions for being designated a WHO-listed authority (WLA)

Background

The WLA framework was established to provide a transparent and evidence-based pathway for regulatory authorities operating at an advance level of performance to be recognized globally.

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 surveillance and control / licensing establishments / regulatory inspections / clinical trial oversight / laboratory testing / RA 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 for being 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 reduce 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. Provide translations, as applicable, of key documents relevant for the performance evaluation, upon agreement of both parties.
- v. 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.
- vi. The public disclosure of the listing information described in Annex 5 of the *Operational Guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities* following a positive WLA listing decision.
- viii. The disclosure of additional information related to the WLA evaluation on a secure WHO regulatory platform accessible by other WLAs.
- ix. Comply with post-listing reporting requirements as outlined in section 8 of the *Operational Guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities*.

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 i) described in Annex 5. of the *Operational Guidance for evaluating and publicly designating regulatory authorities as WHO-listed authorities* for the purpose of public listing and ii) access by other WLAs on a secure WHO regulatory platform.

Focal points

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

WHO			[Name of regulatory authority] _____		
Contact person	Role	Contact details	Contact person	Role	Contact details

Annex 4: Technical Advisory Group on WHO-listed authorities (TAG-WLA): terms of reference

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 and transparency of the WLA decision-making process, WHO will call upon the technical advisory group on WHO-listed authority (TAG-WLA) to provide advice to WHO on the listing or possible delisting of a regulatory authority, thereby providing an additional level of assurance that due process was followed and that WHO decisions are supported by findings.

The TAG-WLA will act as an advisory body to WHO in this field.

I. Functions

In its capacity as an advisory body to WHO, the TAG-WLA shall have the following function:

- Provide advice on whether the listing/delisting recommendation of WHO is supported by the findings from the evaluation process.

II. Composition

The TAG-WLA shall have 15 members¹, who shall serve in their personal capacities to represent the broad range of expertise relevant to evaluating the performance of candidate WLAs. Members should have a wide knowledge of and senior level experience in regulatory systems for medicines and vaccines, or related fields. In the selection of the TAG-WLA members, consideration shall be given to attaining

an adequate distribution of technical expertise, geographical representation and gender balance.

Members of the TAG-WLA, including the Chairperson, shall be selected and appointed by WHO following an open call for experts. The Chairperson's functions include the following:

- to chair the meeting of the TAG-WLA;
- to liaise with the WHO Secretariat between meetings.

In appointing a Chairperson, consideration shall be given to gender and geographical representation.

Members of the TAG-WLA shall be appointed to serve for a period of 3 years, shall be eligible for reappointment but may not serve for more than two consecutive terms. A Chairperson is eligible for reappointment as a member of the TAG-WLA, but is only permitted to serve as Chairperson for one term. Their appointment and/or designation as Chairperson may be terminated at any time by WHO if WHO's interest so requires or, as otherwise specified in these terms of reference or letters of appointment. Where a member's appointment is terminated, WHO may decide to appoint a replacement member.

TAG-WLA members must respect the impartiality and independence required of 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 of their appointment, shall be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.

Following a determination that a proposed member's participation in the TAG-WLA would not give rise to a real, potential or apparent conflict of interest, the proposed member will be sent a letter inviting them to be a member of the TAG-WLA. Their appointment to the TAG-WLA is subject to WHO receiving the countersigned invitation letter and letter of agreement.

¹ Members serve as full participants and partake in the decision-making process of the meeting in which they are involved.

Notwithstanding the requirement to complete the WHO declaration of interest form, TAG-WLA members have an ongoing obligation to inform the WHO of any interests real or perceived that may give rise to a real, potential or apparent conflict of interest.

As contemplated in paragraph II.4 above, WHO may, from time to time, request TAG-WLA members to complete a new declaration of interest form. This may be before a TAG-WLA meeting or any other TAG-WLA -related activity or engagement, as decided by WHO. Where WHO has made such a request, the TAG-WLA member's participation in the TAG-WLA activity or engagement is subject to a determination that their participation would not give rise to a real, potential or apparent conflict of interest.

Where a TAG-WLA member is invited by WHO to travel to an in-person TAG-WLA meeting, WHO shall, subject to any conflict of interest determination as set out in paragraph II.6 above, issue a letter of appointment as a temporary adviser and accompanying memorandum of agreement (together 'Temporary Adviser Letter'). WHO shall not authorize travel by a TAG-WLA member, until it receives a countersigned Temporary Adviser Letter.

TAG-WLA members do not receive any remuneration from the Organization for any work related to the TAG-WLA. 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.

III. Operation

The TAG-WLA shall normally meet at the request of WHO to review the WLA recommendations of one or more countries. TAG-WLA meetings will be convened by WHO and will be held virtually, via video or teleconference, or in-person (at WHO headquarters in Geneva or another location, as determined by WHO).

TAG-WLA meetings may be held in open and/or closed session, as decided by the Chairperson in consultation with WHO.

- a. Open sessions: Open sessions shall be convened for the sole purpose of the exchange of non-confidential information and views, and may be attended by Observers (as defined in paragraph III.3 below).
- b. Closed sessions: The sessions dealing with the formulation of recommendations and/or advice to WHO shall be restricted to the members of the

TAG-WLA and essential WHO Secretariat staff. The quorum for TAG-WLA meetings shall be two thirds of the members.

WHO may, at its sole discretion, invite external individuals from time to time to attend the open sessions of an advisory group, or parts thereof, as "observers." Observers may be invited either in their personal capacity, or as representatives from a governmental institution / intergovernmental organization, or from a non-State actor. WHO will request observers invited in their personal capacity to complete a confidentiality undertaking and a declaration of interests form prior to attending a session of the advisory group. Invitations to observers attending as representatives from non-State actors will be subject to WHO internal due diligence and risk assessment including conflict of interest considerations in accordance with the Framework for engagement with non-State actors (FENSA). Observers invited as representatives may also be requested to complete a confidentiality undertaking. Observers shall normally attend meetings of the TAG-WLA at their own expense and be responsible for making all arrangements in that regard.

At the invitation of the Chairperson, observers may be asked to present their personal views and/or the policies of their organization. Observers will not participate in the process of adopting recommendations of the TAG-WLA.

TAG-WLA members are expected to attend meetings. If a member misses two consecutive meetings, WHO may end his/her appointment as a member of the TAG-WLA.

Reports of each meeting shall be submitted by the TAG-WLA to WHO (the Assistant Director-General of the Access to Medicines and Health Products MHP) not later than 20 working days after the TAG-WLA meeting. All recommendations from the TAG-WLA are advisory to WHO, who retains full control over any subsequent decisions or actions regarding any proposals, policy issues or other matters considered by the TAG-WLA.

The TAG-WLA shall normally make recommendations by consensus. If, in exceptional circumstances, a consensus on a particular issue cannot be reached, minority opinions will be reflected in the meeting report.

Active participation is expected from all TAG-WLA members, including in working groups, teleconferences, and interaction over email. TAG-WLA members may, in advance of TAG-WLA meetings,

be requested to review meeting documentation and to provide their views for consideration by the TAG-WLA.

WHO shall determine the modes of communication by the TAG-WLA, including between WHO and the TAG-WLA members, and the TAG-WLA members among themselves.

TAG-WLA members shall not speak on behalf of, or represent, the TAG-WLA or WHO to any third party.

IV. Secretariat

WHO shall provide the secretariat for the TAG-WLA, including necessary scientific, technical, administrative and other support. In this regard, the WHO Secretariat shall provide the members in advance of each meeting with the agenda, working documents and discussion papers. Distribution of the aforesaid documents to Observers will be determined by the WHO Secretariat. The meeting agenda shall include details such as: whether a meeting, or part thereof, is closed or open; and whether Observers are permitted to attend.

V. Information and documentation

Information and documentation to which members may gain access in performing TAG-WLA 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 referred to in section II(5) above, TAG-WLA members undertake to abide by the confidentiality obligations contained therein and also confirm that any and all rights in the work performed by them in connection with, or as a result of their TAG-WLA-related activities shall be exclusively vested in WHO.

TAG-WLA members and Observers shall not quote from, circulate or use TAG-WLA documents for any purpose other than in a manner consistent with their responsibilities under these Terms of Reference.

WHO retains full control over the publication of the reports of the TAG-WLA, including deciding whether or not to publish them.

Annex 5. Sample listing

Country	Regulatory Authority (RA)	Link to the RA and contact point	Listed product stream(s) ¹	Listed function(s) ²	Date of first listing	Date of renewal	Link to the listing summary ³
A							
B							
C							
D							

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

3 Listing summary includes: an outline of the RA's organizational structure; a summary of evidence reviewed and process undertaken to support the listing; steps and timelines associated with the PE and listing process; a link to relevant websites of the RA.

Annex 6. Renewal reporting form for WHO-listed authorities (WLA)

Information contained in the completed form is confidential.

1. National regulatory authority (NRA) or regional regulatory system general information		
Name of the regulatory body applying for listing:		
Country or Region ¹ :		
Address of the organization:		
Name of contact person:		
Title/position in the organization:		
E-mail address:	Tel. no:	

2. Major changes ²			
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:			
Description	Date of the change	Documents provided ³	Current status (ongoing, completed)

Further information

For further information on the WHO listing process please visit the WLA website at: <https://www.who.int/initiatives/who-listed-authority-reg-authorities>

For further information on the WHO benchmarking process please visit the WHO website at: <https://www.who.int/tools/global-benchmarking-tools>

For queries about the procedure for applying for designation as a WLA, please contact the WHO Regulatory System Strengthening Team (<https://www.who.int/teams/regulation-prequalification/regulation-and-safety/rss>).

- For regional regulatory systems, indicate the region represented by the regulatory body, including the list of member national regulatory authorities.
- 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 or categories) assessed as part of the WLA benchmarking-performance evaluation.
- Accompanying information in electronic format should be uploaded on the WHO NRA SharePoint and the Regulatory System Strengthening 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.

**Department of Regulation
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