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Global Benchmarking Tool (GBT) for Evaluation of National Regulatory Systems



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ABSTRACT

The GBT is designed to evaluate the overarching regulatory framework and the component regulatory functions (e.g. clinical trial oversight) through a series of sub-indicators that may also be grouped and examined according to nine cross-cutting categories or themes, for example, quality and risk management systems. Fact sheets have been developed for each sub-indicator to guide the benchmarking team and ensure consistency in the evaluation, documentation, and rating of the sub-indicator. The WHO Global Benchmarking Tool (GBT) is a means by which WHO evaluates regulatory systems through comprehensive and systematic benchmarking. The tool and benchmarking methodology.



History of Global Benchmarking Tools:

An inventory of performance of National Regulatory Functions in 55 vaccine-producing countries in the world has shown that many of these countries are not fulfilling the necessary role in the assurance of vaccine quality. In 1996, only 36 of 55 producing countries (65%) were exercising the necessary six critical control functions. Furthermore, in-depth assessment of some countries according to indicators established by the countries themselves shows that even these functions may not be performed to a depth sufficient to assure vaccine quality.

As a first step, countries must commit resources, both human and financial to the assurance of vaccine quality. Second, they must critically assess the functioning of their NRAs and develop a systematic plan that will indicate how identified gaps will be filled, including targets, goals, milestones, and the costs for each step. This plan should include a plan for staff training and accessing needed technical and financial inputs. They must implement these plans and monitor their impact.

WHO¹ can and is provide technical assistance for the development and implementation of these plans. Support to countries for assessment of their NRA functions is ongoing.

In 1997, WHO launched an initiative to strengthen National Regulatory Authorities to ensure that 100% of all vaccines used by national immunization programs meet standards of quality, safety, and efficacy. In January 2014 the WHO Executive Board discussed a draft WHA resolution regarding the strengthening of national regulatory systems which will be presented to the World Health Assembly (WHA) in May 2014. In the Americas' region, for example, a Regional Committee Resolution (CD50.R9), endorsed in 2010 urges the Member States and PAHO/WHO to strengthen national regulatory authorities for medicines and biologicals across the region.

Other WHO regions also emphasize the need to ensure access to medicines of assured quality. For example, the "Regional Strategy for Improving Access to Essential Medicines" in the western Pacific Region (2005-2010) which was endorsed by all Member States, provides a comprehensive and practical approach to prioritizing goals for the pharmaceutical sector and identifies the strategies to attain them. This includes providing guiding principles on WHO's role to continue to support medicines regulatory authorities strengthening.

The development of the current GBT Revision VI takes into consideration input received from two international consultations with the Member States in 2015, public consultation in early 2018, and a series of meetings involving experts from regulatory authorities from different parts of the world.

The WHO Global Benchmarking Tool (GBT)²⁻⁴ is a means by which WHO evaluates regulatory systems through comprehensive and systematic benchmarking. The tool and benchmarking methodology;

- identifies strengths and areas for improvement;
- facilitates the formulation of an institutional development plan (IDP) to build upon strengths and address the identified gaps;
- aids in the prioritization of IDP interventions; and
- helps to monitor progress and achievements.

The development of the WHO Global Benchmarking Tool is the result of a collaborative effort between WHO headquarters and Regional Offices with support from country regulators. The tool builds on other WHO tools including the WHO Vaccine data collection tool, WHO Data Collection Tool for the Review of Drug Regulatory Systems, and the WHO Regional Office for the Americas (PAHO/AMRO) assessment tools and includes features of proven benefit from these tools such as computerization, categorization of indicators/sub-indicators and inclusion of fact sheets.

New features include:

- incorporation of good regulatory practices (GRP) principles;
- adoption of the maturity level concept referenced in ISO 9004 standard;
- inclusion of a group of indicators to assess regulatory measures to prevent, detect, and respond to substandard and falsified (SF) medical products;
- integration of the regulatory relevant indicators from the WHO good governance for medicine (GGM) assessment; and

➤ expansion of the indicators for measurement of Quality Management Systems (QMS) of different regulatory functions.

The current version addresses the regulation of medicine and vaccine. Future revisions are expected to address blood products including whole blood, blood components plasma-derived medicinal products; and medical devices including diagnostics.

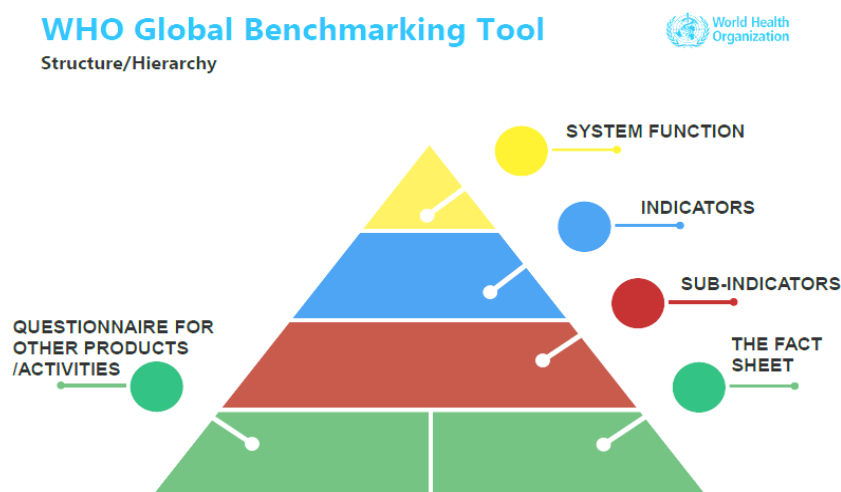


Figure No. 1: Global Benchmarking Tools Description

Functions of Global Benchmarking Tools are summarized as follows:

1. NATIONAL REGULATORY SYSTEM (RS):

The National Regulatory System (RS) provides the framework that supports the WHO-recommended regulatory functions. The National Regulatory Authority (NRA) is the institution in charge of assuring the quality, safety, and efficacy of medical products as well as ensuring the relevance and accuracy of product information. A sustainable-well functioning regulatory system will assure an independent and competent oversight of medical products.

2. REGISTRATION AND MARKETING AUTHORIZATION (MA)⁵:

The issuance of marketing authorization (also referred as product licensing or registration) is critical to any National Regulatory Authority (NRA). It is a procedure of releasing a medical product for marketing after it has undergone a process of evaluation to determine its safety, efficacy and quality and the appropriateness of the product information. The objective of this

regulatory function is to provide a system that ensures that only medical products which have been duly authorized by the NRA are allowed to be manufactured, imported, distributed or sold/supplied to end-users. The process of assessment for marketing authorization includes the review of data on quality, safety and efficacy submitted by the applicant, applying the same standards to imported and locally manufactured medical products.

3. VIGILANCE (VL):

Medical products vigilance, defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medical products related problems, is of outstanding importance to guarantee that safe and effective medical product of high quality are used within the country. Vigilance activities should be established in the countries based on a risk management approach. A reporting system should be established to monitor medical product's safety including adverse events and other related problems.

4. MARKET SURVEILLANCE⁵ AND CONTROL (MC):

Market surveillance and control function plays a crucial role in the field of the medical products consumer product safety since its objective is to ensure compliance of the products placed on the market with a pre set criteria for quality, safety and efficacy (marketing authorization and good practices). Market surveillance and control function encounters four themes (1) control of import and export activities, (2) prevention, detection and response to SF medical products, (3) market surveillance program for checking the quality of medical products throughout the supply chain, and (4) control of promotion, marketing and advertisement activities.

5. LICENSING ESTABLISHMENTS⁶ (LI):

To protect public health, licensing activities are of outstanding importance and fundamental, together with inspections activities, to guarantee the quality, safety and efficacy of medical products used within and/or exported out of the country. The NRA responsible for coordinating licensing activities should have available and published legal provisions, regulations and guidelines to ensure licensing of facilities throughout the supply chain based on compliance with Good Practices (GXP) and to empower the NRA to issue, suspend or revoke licenses for premises/establishments. Premises, facilities, establishments and/or companies throughout the

supply chain including, but not limited to, manufactures, distributors, wholesalers, importers, and/or exporters shall possess a license issued by the NRA to operate. The process of issuing licenses shall be based on the implementation of and compliance with quality standards of Good Practices (GXP). Inspection for confirmation of compliance with Good Practices (GXP) is required for granting and/or re-granting a license or substantial modification approval.

6. REGULATORY INSPECTION⁷ (RI):

Inspection of establishments across the supply chain including medical products manufacturers, distributors, importers, wholesalers and retailers is an essential regulatory function. Its purpose is to ensure that operations at the mentioned establishments are carried out following the approved standards, norms, and guidelines, as well as in compliance with the national medical products legislations and regulations, which in turn should be in line with WHO recommendations and/or other internationally recognized guidelines. So, it is worth mentioning that the scope of the function applies to different Good Practices (GxP) and not limited to Good Manufacturing Practices (GMP). Rather, Good Distribution Practices (GDP) and Good Clinical Practices (GCP) come under the scope of this function.

7. LABORATORY TESTING⁸ (LT):

This regulatory function is intended to ensure the National Regulatory Authority (NRA) can assess the quality of medical products by performing quality tests on them in certain situations. This testing can be a requirement to corroborate the manufacturer's test results during the evaluation for marketing authorization or a variation to marketing authorization.

8. CLINICAL TRIALS OVERSIGHT⁹ (CT):

National Regulatory Authorities (NRAs) should have the legal mandate to authorize and regulate clinical trials, including terminating clinical trials if necessary. They should develop the requirements, guidelines, procedures and forms in line with major international guidelines on clinical trials including the Declaration of Helsinki and WHO Good Clinical Practices guidelines. Clinical trials oversight is aimed to: protect the safety and rights of human subjects participating in clinical trials, ensure that trials are adequately designed to meet scientifically sound objectives, and prevent any potential fraud and falsification of data.

9. NRA LOT RELEASE (LR):

NRA lot release (also called official authority batch release) is a non-common regulatory function. It is a system specifically established for the regulatory release of biological products. This regulatory function is aimed to ensure the quality, safety, and efficacy of biological products through a regulatory release on a lot-by-lot basis taking into account the nature and inherent variability of these products.

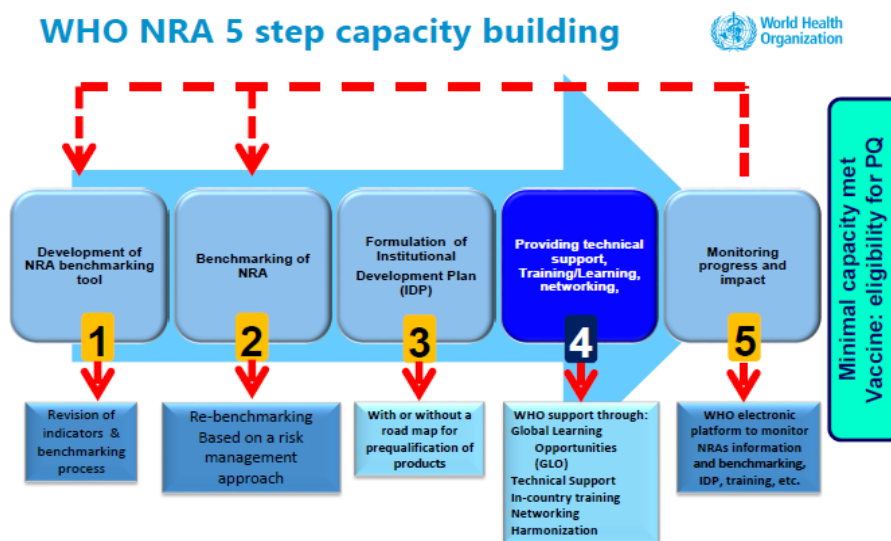


Figure No. 2: WHO Approach for Capacity Building

WHO GBT Performance Maturity Level:

1. Level 1: NRA has no formal approach but some elements of the regulatory system exist.
2. Level 2: Evolving national regulatory system that partially performs essential regulatory functions and has a reactive approach.

NRAs with maturity levels 1 and 2 may be considered functional if rely on other regulators for some specific functions

3. Level 3: Stable, well functioning, and integrated regulatory system
4. Level 4: Regulatory system operating at the advanced level of performance and continuous improvement

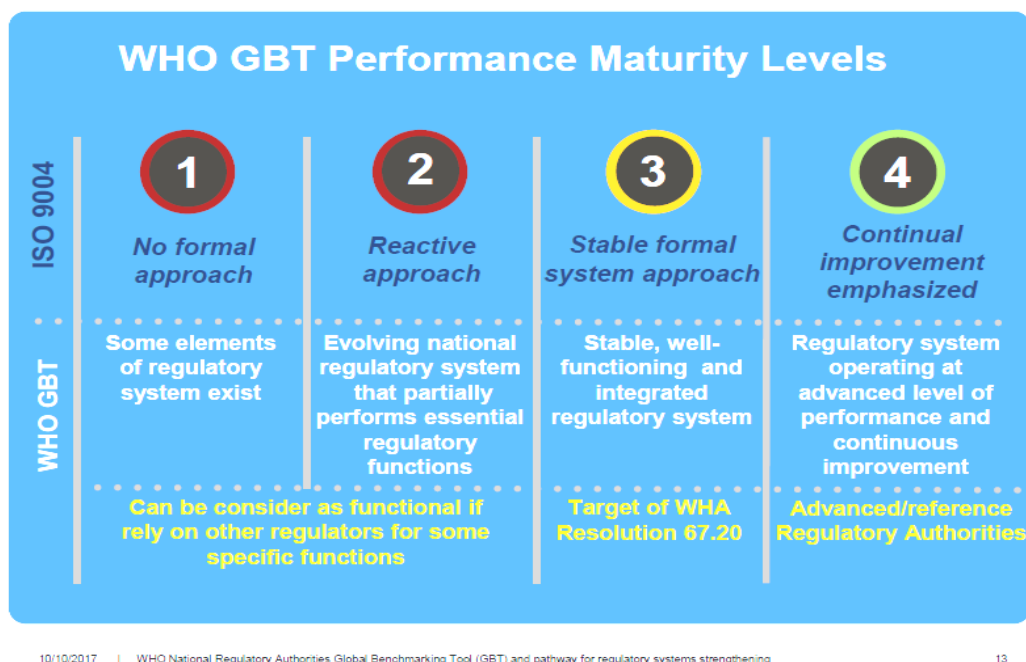


Figure No. 3: GBT Performance maturity levels

SUMMARY AND CONCLUSION:

Medicines are used to prevent illnesses and treat diseases, helping many people to lead full and productive lives. However, if produced, stored, or transported improperly, if falsified, or used incorrectly or abused, medicines can be hazardous and can lead to hospitalization and even death. For these reasons, it is important to have effective regulatory systems that also serve to promote timely access to quality medicines.

The GBT is designed to evaluate the overarching regulatory framework and the component regulatory functions (e.g. clinical trial oversight) through a series of sub-indicators that may also be grouped and examined according to nine cross-cutting categories or themes, for example, quality and risk management systems. Fact sheets have been developed for each sub-indicator to guide the benchmarking team and ensure consistency in the evaluation, documentation, and rating of the sub-indicator.

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