WHO GUIDELINE ON THE IMPLEMENTATION OF QUALITY MANAGEMENT SYSTEMS FOR NATIONAL REGULATORY AUTHORITIES

(July 2019)

DRAFT FOR COMMENTS

Medicines Quality Assurance working documents will be sent out electronically only.
They will also be placed on the Medicines website for comment under "Current projects".
http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en

If you have not already received our draft working documents, please send your email address (**jonessi@who.int**) and we will add you to our electronic mailing list.

Note from WHO Secretariat: *this working document was prepared by the Regulatory Systems Strengthening (RSS) Group with the support of the Medicines Quality Assurance (MQA) Group.*

WHO GUIDELINE ON THE IMPLEMENTATION OF QUALITY MANAGEMENT SYSTEMS FOR NATIONAL REGULATORY AUTHORITIES

1 BACKGROUND

Implementation of the Thirteenth World Health Organization (WHO) General Programme of Work (2019-2023), as adopted by the Seventy-First World Health Assembly (2018) and the WHO Leadership Priorities, has attracted much international public health attention to the theme of Universal Health Coverage and to increased access to safe and effective medical products.

Several World Health Assembly (WHA) resolutions, including WHA67.20 (2014), mandate WHO to provide support to its Member States (MS) in strengthening national regulatory systems for medical products. It recognizes that "effective regulatory systems are an essential component of health system strengthening and contribute to better public health outcomes; that regulators are an essential part of the health workforce, and that inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products" [1]. Accordingly, to facilitate access to these products, WHO's vision is for all MS to have a regulatory system that ensures medical products and other health technologies in the market meet internationally recognized standards of quality, safety and efficacy.

National Regulatory Authorities (NRAs) are responsible for ensuring safety, quality and efficacy of medical products within the respective MS, demonstrating that the services they provide consistently meet legal and regulatory requirements, delivering effective and efficient services, evaluating performance and making improvements. A quality management system (QMS) can ensure that the products or services an NRA provides consistently meet statutory and regulatory standards and meet customers' expectations. A QMS provides opportunities to enhance customer satisfaction, address context-associated risks and opportunities for continuing improvement, demonstrate conformity to specific QMS requirements, and assure the quality, safety and efficacy of medical products.

In 2015, WHO developed and launched the WHO Global Benchmarking Tool (GBT). This tool assists regulators worldwide in evaluating the developmental status of their regulatory system and its related functions. The GBT includes one indicator that assesses the NRA's level of development with respect to QMS.[1] Benchmarking results of low and middle-income countries indicate that most NRAs need to establish and implement a QMS or, if already established, enhance and maintain the QMS.

QMS implementation is challenging for NRAs due to the diversity of NRA legal mandates and organizational structures, to the different levels of NRA development and to the number of regulatory functions that need to be addressed. WHO has developed this guideline to respond to requests by MS to have an international guideline on implementation of QMS by NRAs.

2 OBJECTIVE

The aim of this guideline is to assist NRAs to develop, implement and improve QMSs based on principles from International Standardisation Organization (ISO) document ISO 9001 Standard requirements [2]. It provides recommendations on what NRAs should implement and maintain under the QMS to effectively and efficiently support the execution of NRA functions as mandated by national laws and regulations. The guideline is expected to promote consistency in regulatory practices within and across NRAs to facilitate harmonisation, mutual reliance and recognition mechanisms among MS.

Therefore, the guideline has the following objectives:

a) Describe principles for implementing a QMS to support planning, execution, monitoring and evaluation of performance of all applicable functions and activities for NRAs.

b) Provide requirements for the QMS to support and facilitate systematic linkages and integration of different processes and systems of the regulatory functions and activities within NRAs.

c) Provide requirements that NRAs should consider for evaluating the performance of the QMS and measures that the NRA should implement for continually improving the QMS.

[1] References to the GBT VI.

3 SCOPE OF THE GUIDELINE

This is an overarching guideline that should be applied across all regulatory functions and activities, including registration and marketing authorization, vigilance, market surveillance and control, licensing establishments, regulatory inspections, laboratory access and testing, clinical trials oversight, national lot release and others as applicable to the implementing NRA. The guideline should be implemented to cover all types and categories of medical products and technologies under the responsibility of an implementing NRA.

The guideline can be used for other regulatory activities which are mandated by the national laws and regulations to ensure public health safety by assuring quality, safety and effectiveness of medical products. This extends to areas of medical products pricing, professional training and regulation and procurement of medical products, as well as to other areas within the legislative mandates and functions of the NRA.

This guideline provides recommendations for QMS implementation for all models of NRAs. NRAs can be legally, organisationally and operationally structured as follows:

a) **Discrete** – two or more institutions involved in partial or full enforcement of national laws and regulations for medical products in a country (e.g. one institution with legal mandates to enforce marketing authorizations (MAs) and another one within the same country for licensing establishments (LI) regulatory function).

b) **Decentralised** – one NRA with full legal mandates to enforce national laws and regulation of medical products within the country. Legally defined amount of enforcement, authority and operations are executed in localised zones or geopolitical zones of the country while the rest is enforced at country level. This model exists in MS having a federal governance system where laws and regulations are enforced at state/province and national levels.

c) **Centralised** – one NRA with full legal mandates to enforce national laws and regulation of medical products within the country. The enforcement, authority and operations are executed, managed and controlled centrally for all applicable regulatory functions and activities.

The provided recommendations are applicable to all sizes as the principles and intended results remain the same regardless of the complexity of NRA. Therefore, this guideline describes the requirements which should be implemented; the MS and respective NRAs reserve the right to decide on how to address these requirements within the existing contexts and provisions of the laws. This guideline can be utilized by institutions which are responsible for single or multiple specific regulatory functions related to medical products.

Use of this guideline is voluntary. NRAs are free to use this guideline or to choose other methods for implementing QMS. The implemented QMS should be demonstrated by documented evidence to have systematic processes which are controlled, maintained and evaluated for continuous improvement. NRAs are free to use any appropriate national or international standard or guideline as a basis for the implementation of the QMS.

Where different units within the NRA have already implemented QMS for specific regulatory functions (such as laboratory testing and/or regulatory inspection), this guideline could be used by the NRA to determine the functions and processes that have not been addressed by the already implemented management systems. This is to avoid duplications and overlaps of management systems and to ensure gradual integration of all existing management systems with the overall QMS of the NRA. The implementing NRA should determine the extent to which this guideline should be implemented without leaving out any of its processes and activities that are mandated by national laws and regulations.

Effective implementation of this guideline will not lead to any WHO certifications and WHO will not conduct any audits for verification of implementation of QMS for already certified NRAs. However, as part of the regulatory systems strengthening program, WHO will conduct the benchmarking of the MS regulatory functions including QMS related processes using the GBT to determine the strengths and gaps, if any, for capacity building and continuous improvements. This guideline should be implemented to cover regulatory functions which are part of the GBT and other functions and activities of the NRA that are addressed by national laws and regulations but which are not part of the GBT. References to GBT VI [6] provides a linkage of GBT indicators with the relevant chapters of this guideline.

The guideline should be implemented on the foundation of the principles and recommendations as provided in the current version of WHO guideline on Good Regulatory Practices (GRP) [3]. The implementation of the QMS should ensure that the GRPs are integrated to the extent possible without affecting the effectiveness and efficiency of the NRA to execute its functions.

4 GLOSSARY

The definitions given below apply to the terms used in this guideline which are not defined in existing WHO terms and definitions databases. They may have different meanings in other contexts.

Competence
Knowledge, skills and attitude required for successful work performance.

Correction
Any action that is taken to eliminate a nonconformity. However, corrections do not address causes.

Corrective actions
Steps that are taken to eliminate the causes of existing nonconformities in order to prevent recurrence. The corrective action process tries to make sure that existing nonconformities and potentially undesirable situations do not happen again.

Customer
A person or organization that could or does receive a product or a service that is intended for or required by this person or organization. Customers of NRA include individuals or parties who receive or could receive and use products and services which are provided and offered by NRA. These parties include the general public, patients, manufacturers, distributors, health practitioners, researchers, Ministry of Health (MOH) and other individuals and intuitions that rely on the NRA products and services to make public health decisions.

Customer satisfaction
A customer's perception of the degree to which the customer's expectations have been fulfilled. This relates to the expectations that different parties have from the NRA. The expectations include assurance that safe, efficacious and high-quality medical products will be available under the NRA mandate to regulate and that the NRA will provide other products such as guidelines, public reports and related regulatory services that meet the expectations of different types of customers.

Internal audit
An examination and assessment of all or part of a quality system with the specific purpose of improving it. An internal audit is usually conducted by an independent (i.e., of the function to be audited) and qualified team of experts designated by the management for this purpose.

Process
A set of interrelated or interacting activities that use inputs to deliver an intended result.

Product
Output of an organization that can be produced without any transaction taking place between the organization and the customer. They are also called regulatory products in this guideline. Products of NRAs relate to the tangible items which the NRA produces for its customers. These items include regulatory guidelines, public health notices, guidance notes, alerts, databases, mobile phone applications, reports and other materials which are intended to provide regulatory information and communications to customers. Before their production, some of these products may require lengthy consultations for designing them.

Quality
The total set of characteristics of an entity that affect its ability to satisfy stated and implied needs and to ensure the consistent and reliable performance of services or products in conformity with specified requirements.

Quality Management System (QMS)
An appropriate infrastructure, encompassing the organizational structure, procedures, processes, resources and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

Quality policy
A brief statement that describes the organization's purpose, overall intentions and strategic direction, provides a framework for quality objectives and includes a commitment to meet applicable requirements.

Senior (Top) management
Person(s) who direct and control a company or site at the highest levels and who have the authority and responsibility to mobilize resources within the company or site. In NRAs, senior management or top management (TM) can be used interchangeably.

Services
Output of an organization with at least one activity necessarily performed between the organization and the customer. They are also called regulatory services in this guideline. This includes, for example, activities such as evaluation of applications for market authorisations, inspections of facilities and testing of health product samples.

5 QUALITY MANAGEMENT SYSTEM REQUIREMENTS FOR NRAS

NRAs should implement a QMS that is supported by the process approach concept, Plan-Do-Check-Act (PDCA) cycle and risk-based thinking. NRAs should ensure that the implemented QMS meets its needs without making it unnecessarily complex to avoid it negatively affecting its effectiveness and efficiency. The QMS should be simple, fit-for-purpose and understandable.

An effective QMS should be implemented based on internal processes as identified and documented by the NRA from the input requirements, through the intermediate activities, and up to the output results shown in Figure 1.

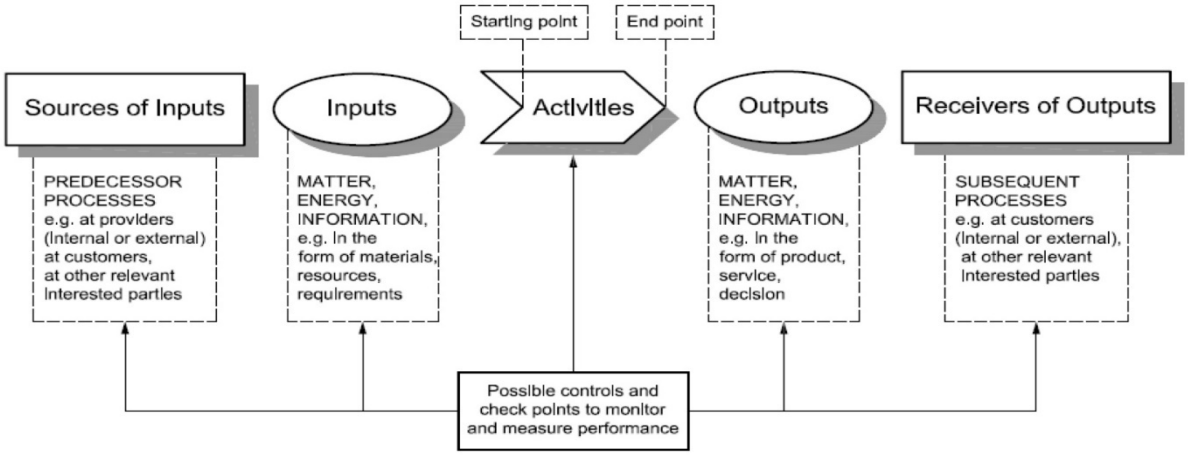

Figure 1: Process approach (ISO 9001:2015[2])

The PDCA cycle requires NRAs to carry out planning, performing (implementing), checking (evaluating) and acting (to improve) processes in the QMS. The applied PDCA cycle covering the chapters in this guideline is provided in Figure 2. ISO 9001 standard [2] provides the following brief description of the PDCA process:

- **Plan:** establish the objectives of the system and its processes, obtain the resources needed to deliver results in accordance with customers' requirements and the NRA's policies, and