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Good Review Practice Guideline

Contents

I. Introduction:

Good review practices (GRevPs) are considered an important way for improving the authority performance and ensuring the quality of the regulatory system. It is a good tool also for insuring consistency, transparency, timeliness, and predictability of the review process.

The objective of this document is to provide high-level guidance on the principles and processes of good review practice (GRevP) for use within the Agency, and to help achieve timeliness, predictability, consistency, transparency, clarity, efficiency and high quality in both the content and management of reviews. This is done through the development of review tools (for example, standard operating procedures (SOPs) and templates) and reviewer learning activities (for example, training courses, mentoring, orientation packages and discussion sessions). To promote continuous improvement, all aspects of GRevPs should be continuously evaluated and updated.

This document is not intended to provide detailed instruction on how to conduct a scientific review. It is an Contextualise of the WHO Good review practices: guidelines for national and regional regulatory authorities (Technical Report Series 992, Annex 9) (1) and is envisioned as one building block in a set of tools and is sufficiently expandable to accommodate additional annexes or ancillary documents in the future.

II. Scope:

GRevPs are documented best practices for any aspect related to the process, format, content and management of products review.

This document applies to the review of safety, efficacy and quality data in biological product applications for marketing authorization.

III. Definitions:

Applicant: The person or company who submits an application for marketing authorization of a new medical product, an update to an existing marketing authorization or a variation to an existing marketing authorization.

Application: The information provided by the applicant for evidence-based review and marketing authorization decision.

Good Review Practice: Documented best practices for any aspect related to the process, format, content and management of a medical product review.

Marketing Authorization: Also referred to as product license or registration certificate. A legal document issued by the Agency that authorizes the marketing or free distribution of a medical product in the country after evaluation of safety, efficacy and quality.

Principles (of a good review): The important GRevP elements to implement in order to achieve successful review outcomes.

Project management (for the review process): The planning, organization and resources to achieve a complete and high quality review of an application within a specified time frame.

Quality Management (QM): The coordinated activities that direct and control an organization with regard to quality.

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

Regulatory Authority (RA): The agency responsible for the registration of and other regulatory activities concerning medical products.

Regulatory Convergence: The process whereby regulatory requirements, approaches and systems become more similar or aligned over time as a result of the adoption of internationally recognized technical guidance, standards and best practices.

Review: A highly complex, multidisciplinary assessment of marketing authorization applications to assess whether they meet scientific and evidentiary standards for safety, efficacy and quality. It forms the scientific foundation for regulatory decisions. The first stage of the review process, validation (sometimes referred to as screening), occurs before the scientific review with the aim of ensuring completeness of the application in order to subsequently facilitate the scientific review.

Review strategy: The approach or plan of action that a reviewer or review team uses to review the product's application.

Standard Operating Procedure (SOP): An authorized written procedure giving instructions for performing operations (both general and specific).

Stringent Regulatory Authority (SRA): The national drug regulatory authorities which are members or observers or associates of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) (as before 23 October 2015).

Transparency: Defining policies and procedures in writing and publishing the written documentation and giving reasons for decisions to the public.

IV. Body of Data:

1. Principles of good review.

EDA will follow the ten WHO listed principles during applying GRevP in order to achieve the desired objectives

Balanced	A good review is objective and unbiased.
Considers context	A good review considers the data and the conclusions of the applicant in the context of the proposed conditions of use and storage, and may include perspectives from patients, health-care professionals and other RAs' analyses and decisions.
Evidence-based	A good review is evidence-based and reflects both the scientific and regulatory state of the art. It integrates legislative, regulatory and policy frameworks with emerging science.
Identifies signals	A good review comprehensively highlights potential areas of concern identified by the applicant and the reviewers.
Investigates and solves problems	A good review provides both the applicant's and the reviewers' in-depth analyses and findings of key scientific data and uses problem-solving, regulatory flexibility, risk-based analyses and synthesis skills to devise and recommend solutions and alternatives where needed.
Makes linkages	A good review provides integrated analysis across all aspects of the application: preclinical; nonclinical; clinical;

	chemistry/biocompatibility; manufacturing; and risk management plan. It includes timely communication and consultation with applicants, internal stakeholders and, as needed, with external stakeholders who have expertise relevant to the various aspects of the application.
Thorough	A good review reflects adequate follow-through of all the issues by the reviewers.
Utilizes critical analyses	A good review assesses the scientific integrity, relevance and completeness of the data and proposed labelling, as well as the interpretation thereof, presented in the application.
Well-documented	A good review provides a well-written and thorough report of the evidence-based findings and conclusions provided by the applicant in the dossier, and the reviewers' assessment of the conclusions and rationale for reaching a decision. It contains clear, succinct recommendations that can stand up to scrutiny by all the parties involved and could be leveraged by others.
Well-managed	A good review applies project and quality management processes, including clearly defined steps with specific activities and targets.

2. Managing the review

The review process should be handled through project management principles. The practices of planning and monitoring review activities coupled with timely, informative communications and clearly-defined work instructions for the reviewers, can maximize the efficiency and effectiveness of the review.

2.1 Project management principles:

Project management for the review process refers to the planning, organizing and resourcing necessary to achieve a complete and high-quality review of an application within a specified time frame.

Progress monitoring should be done through written procedures that is appropriately documented. Data should be collected and interpreted periodically to assess the

effectiveness of the review strategy for completing reviews within the specified time frame.

The technique most suitable should be the one that enables: ■ Interpretation of the data to show the progress of one application as well as that of many applications under review at any one time; ■ Interpretation of the data to help in decision-making with respect to balancing workload against resources; ■ Monitoring that can be performed and/or interpreted by the relevant people.

Planning, monitoring and management of review/assessment shall be coordinated by team leader, director of the registration department and higher officials of the authority as appropriate. In addition, there shall be quality assurance manager or expert responsible for the organization, monitoring and quality assurance of the assessment processes.

As the conditions, resources and workload evolve, the techniques and complexity of project management should also be adapted.

2.2 Quality Management principles:

The review process should follow the principles of QMS in an iterative process that incorporates lessons learned regarding improved processes and decision-making.

Documented SOPs and assessment templates should be available to define the processes for decision-making. These also outlines decision frameworks, time frames for completion and communication of reviews, use of external experts, public meetings and peer-review.

Processes are implemented and monitored in a productive way to ensure continuous improvement within the frame of the quality cycle four key components: ■ say what you do ■ do what you say ■ prove it ■ improve it.

2.3 Standard operating procedures:

SOPs are authorized written procedures giving instructions for performing operations (both general and specific). They describe procedures (or processes) in a step-by-step manner. They should be brief, but should describe the overall procedure from start to

finish. SOPs should be written clearly to provide both instruction and consistency related to the work being performed.

A set of SOPs should be maintained to enable the following aspects:

■ outline the workflow processes that facilitate project management when multiple reviewers assess different parts of the same application and when there are multiple applications to review;

■ handle and review product applications in a consistent manner;

■ facilitate staff training.

SOPs, guidelines, templates and checklists should be continuously updated to accommodate scientific progress, international harmonization of guidelines, changes in review strategy, available resources, increased volume of applications and national laws and regulations, among others.

2.4 Review Process Stages:

Two key stages in the process of reviewing medical product applications are validation and scientific review. The validation stage occurs first, with the aim of ensuring completeness of the application in order to facilitate the subsequent scientific review.

EDA sets key stages in the process of reviewing medical products. Those includes application submission, screening, verifying and scientific review. Applicants should be aware on the expectations at all stages including the target time frames, guidelines, requirements, templates and checklists. All applications undergo validation first for ensuring that it is well-organized and that all the required forms and relevant documents have been in a more predictable and clear process. All the review process stages shall be done according to agreed laws, guidelines, checklists and templates provided for each category of applications.

3. Communication:

Ensuring good communication among RA, applicant and the public is a main aim for improving the efficiency of the development and review process, allowing patients faster

access to important medical products. It can also improve the quality of the review by providing access to additional expertise.
Providing information on our websites is among the active form of communication that help engaging with the international community on EDA projects.

3.1 Intra-agency

Product reviews are conducted in a collaborative environment. Therefore, expertise from different organization units within EDA collaborate and coordinate together during the reviewing process.
Intra-agent communication include meeting establishment, forms for exchanging ideas among the reviewers, checklist of personnel or departments involved on specific issue or action that may be helpful.
In this manner, good communication help in achieving the objective of GRevP. Open, clear, constructive and timely communications regarding the progress of the review, review findings, differing data interpretations and discussion of possible solutions and actions within the RA are desirable. In addition to establishing

3.2 Interagency

The Authority may communicate, collaborate and jointly work in medical products review with other RA s
As a means of peer collaboration and cooperation, interagency communications can facilitate greater regulatory convergence. This, in turn, can increase the efficiency and quality of medical product development and review processes and improve patient access.
Interagency communication may include the following forms;

- Accessing information from other RAs' public websites, such as guidelines, application decisions and product recalls;
- Using information from other RAs, such as review reports and certificates of pharmaceutical product;
- Actively sharing information between RAs
- Actively working with other RAs

3.3 With applicants

EDA communicate with the applicant through Public availability of EDA guidelines, notices, questions and answers and presentations, as well as checklists used for screening the submitted application which help in providing insight into the our current thinking and expectations. These communications allow applicants to provide better quality applications.

Communication between the RA and individual applicants on specific applications before, during and after the review process is also implemented.

3.4 With external experts

Expertise in the scientific assessment of the safety, efficacy and quality of medical products is not limited to applicants and RAs. Academic institutions, industry associations, patient organizations and medical and scientific organizations all have extensive expertise that may be useful to the review.

Asking for the input of external experts into RA decision-making improves public confidence, provides additional perspectives for the RA to consider and provides expertise that otherwise may be lacking.

3.5 With public

Communication with the public about the mission and accomplishments of the EDA can foster greater public awareness, understanding of and confidence in the RA.

Transparency initiatives involve web-based information about how it is organized and operates, its decision-making processes and criteria and its actions, such as application approvals and product.

4. Review personnel:

4.1 Reviewer expertise, competency, and training

Reviewers should have professional qualifications, training and expertise in scientific or medical fields that relate to the assessment of medical product safety, efficacy and/or

quality. Both practical and theoretical knowledge is desirable in order to achieve a good understanding of the issues likely to be associated with the product under review. Reviewer competencies depend on the duties and scope of review work. Scientific writing, presentation of data, data analysis, inferential and deductive reasoning, risk-based analyses and problem-solving are important skills for reviewing a medical product application. EDA shall conduct review of actual or perceived conflicts of interests when the Authority use external experts for dossier review and shall require the external experts to declare and sign the conflict of interest form prior to their participation in the dossier assessment.

Review staff should also follow sound ethical practices. General competencies required to conduct review work include:

■ Knowledge of statutes, regulations, guidelines and precedents, including international guidelines and precedents, and their applicability;

■ Knowledge of the process of medical product development from early development phases to post marketing surveillance and risk management;

■ Scientific communication skills for written evaluations, public presentations and negotiation and consensus building with applicants and stakeholders.

4.2 Critical thinking

Critical thinking requires an objective and systematic approach to analyzing information and to problem-solving. It relies on the collection of data and evidence-based decision-making instead of generalizing from one's own experience, intuition or trial and error. Decisions should be reproducible and clearly understood by others.

Beyond their professional qualifications, reviewers should have the ability to critically appraise the information presented in an application and not just accept it as presented. This skill may often be developed or strengthened during the training process, for instance, by evaluating the responses to questions raised by a senior reviewer so that the questioning process becomes a learning tool.

5. Conducting the review:

Defining and then following an application-specific review strategy that is amended only as needed when new information comes to light, ensures soundness of the review process, the quality of the report and the efficient use of resources.

5.1 Key elements in defining a review strategy

A review strategy is the approach or plan of action that a reviewer or review team uses to review a medical product application. The strategy employed may be shaped by the following.

a. Public health priority of the medical product application
b. Understanding other RAs' action on the application, especially SRAs
c. Understanding specific intrinsic and extrinsic factors
d. Identification of major scientific questions and their possible resolution

5.2 Applying the review strategy

EDA shall follow risk-based review approach including categorization based on risk level and reliance approaches, taking into account national laws and regulations, regional and international guidelines, and, where applicable, monographs and standards. The reviewer should determine the information necessary to approve the product application and consider whether further information can be obtained in post-approval studies without compromising safety.

The model adopted for review may allow for questions to be asked during the review to supplement or clarify information supplied, until the reviewer is satisfied that enough information has been provided to allow a conclusion to be reached.

The Authority shall develop well defined strategy to facilitate marketing authorization processes including Stringent Regulatory Authority (SRA) procedure, mutual recognition approach, WHO collaborative registration, and regional collaborations

There are a number of internal processes that may be implemented to help ensure an efficient, consistent and effective review process. These include:

- periodic meetings to allow consideration of the views of different reviewers
- peer review, in the context of a co-rapporteur, or a team meeting

- an internal panel review
- an external panel review
- The involvement of senior management.

Various methodologies can be used to quantify benefits and risks. The choice depends on circumstances such as complexity of issues and utility to the EDA. The acceptability of benefits and risks will depend on public health priorities, presence of available alternative therapies, size and certainty of the treatment effect versus that of the adverse reactions and possible risk mitigation or benefit enhancement that can be implemented.

The findings and conclusions of the review must be described in a well-documented review report. Once the final decision is made it should be conveyed to the applicant. If an RA decides not to grant authorization, a statement of reasons should be provided, which details the documents, information and applicable regulatory requirements taken into account in reaching the decision.

IV. Glossary:

EDA:	**Egyptian Drug Authority**
GRevP:	**Good Review Practice**
ICH:	**International council for harmonization**
QM:	**Quality Management**
QMS:	**Quality Management System**
RA:	**Regulatory Authority**
SOP:	**Standard Operating Procedure**
SRA:	**Stringent Regulatory Authority**
WHO:	**World Health Organization**
WHO:	**World Health Organization**

VI. References:

- WHO TRS 992-Annex 9