An Overview of WHO Good Review Practice (GRevP) Guideline

Suchart Chongprasert, Ph.D.

Director, Bureau of Drug Control

Food and Drug Administration, Thailand

สำนักงานคณะกรรมการอาหารและยา
กระทรวงสาธารณสุข

You can’t go back to the beginning and change, but you can start where you are and change the ending.

Outline

- What is a Review?
- What is Good Review Practice (GRevP)?
- WHO GRevP Guideline
- Objectives of GRevP
- Key Elements of WHO GRevP Guideline

What is a Review?

A highly complex, multidisciplinary assessment of medical product applications in meeting scientific and evidentiary standards for **safety, efficacy, and quality.** It forms the scientific foundation for **regulatory decisions.**

What is a Review?

The first stage of the review process, **validation**[1] (sometimes referred to as screening/preliminary checking for completeness), occurs before the **scientific review**[2] with the aim of ensuring completeness of the application in order to subsequently facilitate the scientific review.

Good Review Practice Guidelines

Good Review Practice Guideline

- U.S. FDA
  - GRP (MAPP 6025.1, 2017)
- **WHO**
  - GRevP (WHO Technical Report Series No. 992, 2015)

Annex 9

Good review practices: guidelines for national and regional regulatory authorities[1]

Background

The good review practices (GRevP) guidelines for regulatory authorities emanate from a partnership between the Asia-Pacific Economic Cooperation (APEC) Regulatory Harmonization Steering Committee (RHSC) and the World Health Organization (WHO). This is the first set of guidelines of its kind globally and addresses an important gap identified at the 2012 International Conference of Drug Regulatory Authorities (ICDRA). Although the RHSC does not directly produce guidelines, contributing to WHO guidelines is in line with the RHSC's principle of working with appropriate partners to achieve common objectives.

In June 2013 the RHSC convened an expert working group with WHO representation to develop a draft GRevP document, intended to cover both medicines and medical devices, for submission to WHO in early 2014. The draft document subsequently underwent the required WHO consultation process with a view to its further development into WHO guidelines for adoption by the Expert Committee on Specifications for Pharmaceutical Preparations and the Expert Committee on Biological Standardization. This led to these new GRevP guidelines for regulatory authorities adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations at its forty-ninth meeting.

[1] Asia-Pacific Economic Cooperation (APEC) Regulatory Harmonization Steering Committee (RHSC) good review practices (GRevP) with the participation of Working Group Members representing the regulatory authorities (RAs) from the economies of Australia, Canada, Taipei (China), Japan, Republic of Korea, Saudi Arabia, Singapore, United States of America; and representatives of the Centre for Innovation in Regulatory Science (CIRS); and the Food and Drug Administration Alumni Association International (FDAAA).

191

http://edu.tcfst.org.tw/edm/2017_APEC/images/Annex9-TRS992%20(final%20GRevP%20Guideline).pdf

WHO Good Review Practice (GRevP)

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

WHO Good Review Practice (GRevP)

Good Review Practices (GRevPs) are an integral part of overall Good Regulatory Practices (GRPs) and focus on the medical product review aspect of regulatory work.

GRevPs ensures that the review process have **the critical thinking skills** and tools needed to **optimize scientifically sound and evidence-based decision**

Objectives of GRevP

To provide **high-level guidance** on the principles and processes of good review practice (GRevP) for use across a range of regulatory authority (RA) **maturities**.

To achieve

- Timeliness
- Predictability
- Consistency
- Transparency
- Clarity
- Efficiency
- High quality

in both the content and management of **reviews of medical products.**

Key Elements of WHO GRevP

[1] Fundamental Values and Principles of a Good Review;

[2] Managing review;

[3] Communication of a review;

[4] Review personnel;

[5] How to conduct a review

[1] Fundamental Values for Review Process

- Quality;
  - always comes first
- Efficiency (and timeliness);
- Clarity;
  - clarity is power
- Transparency; and
- Consistency (and Predictability)

The principles of good review are intended to help achieve a successful review outcome that can satisfies all involved parties regarding quality, transparency, consistency, in a well- managed , well-documented and timely manner.

10 Principles of GRevP

- Balanced
- Considers context
- Evidenced-based
- Identifies signals
- Investigates and solve problems
- Make linkages
- Thorough
- Utilizes critical analysis
- Well documented
- Well managed

10 Principles of GRevP

- **Balanced**
  - objective and unbiased
- **Consider Context**
  - 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**
  - evidence-based and reflects both scientific and regulatory state-of-the-art.
  - integrating legislative, regulatory, and policy frameworks with emerging science

10 Principles of GRevP

- **Identifies signals:**
  - comprehensively highlights potential **areas of concern** identified by the applicant and the reviewers.
- **Investigates and solve problems:**
  - 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.

10 Principles of GRevP

- **Makes linkages:**
  - provides integrated analysis across all aspects of the application: pre-(non-)clinical, clinical, chemistry/biocompatibility, manufacturing and risk management plan.
  - It includes **timely communication and consultation** with applicants, internal stakeholders, and as needed, external stakeholders with expertise relevant to the various aspects of the application.

10 Principles of GRevP

- **Utilizes critical analyses:**
  - assesses the scientific integrity, relevance and completeness of the data and proposed labeling, as well as the interpretation thereof, presented in the application.
- **Thorough**
  - reflects adequate follow-through of all the issues by the reviewers.

10 Principles of GRevP

- **Well documented**
  - 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 involved parties and could be leveraged by others**.**
- **Well managed**
  - applies project and quality management processes, including clearly defined steps with specific activities and targets.

[2] Managing the Review

The practices to maximize the efficiency and effectiveness of the review;

- planning and monitoring review activities
- timely, informative communications within the RA
- clearly-defined **work instructions** for the reviewers

The principles of project management and quality management are critical to well-functioning RAs.

[2] Managing the Review

- **Managing the review consists of 4 main areas;**
  - Project Management;
  - Quality Management;
  - Standard Operating Procedures; and
  - Review Process Stages

[3] Communications

- improve the efficiency of the development and review process
- improve the quality of the review by providing access to **additional expertise**

[3] Communications

- Intra-agency

  different organizational units within the RA, such as pre- and post-marketing scientific disciplines, pharmacovigilance, inspection and others.

- Interagency

  RA to RA communications

- With applicants

  Public availability of **RA guidelines, notices, questions and answers** as well as finalized RA review reports and decision summaries, provide insight into the RA's current thinking and expectations.

[3] Communications

- With external experts

  Expertise, academic institutions, industry associations, patient organizations, and medical and scientific organizations

- With the public

  foster greater public awareness, understanding of, and confidence

[4] Review Personnel

- The core competencies for personnel involved in the various aspects of managing and conducting reviews.
- **Adequate** review capacity (number and competence)
  - Sufficient number of reviewers
  - Core competencies

Reviewer expertise, competencies and training

Critical thinking skills

Review Personnel

- The quality, timeliness, and success of medical product application reviews are dependent much on **adequate authority review capacity.**
- In addition to having a sufficient amount of reviewers, capacity relates to many personnel factors.
- Among the important considerations are the **knowledge, skills, abilities, and attitudes of** reviewers.
- Together, these considerations define the core competencies for personnel involved in the various aspects of managing and conducting reviews.

Reviewer's Critical Thinking

- Critical thinking requires an **objective and systematic approach** to analyzing information and 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.
- The decision should be reproducible and clearly understood by others.
  - different reviewers should not provide stark/marked difference in the review and evaluation results

Reviewer's Critical Thinking [2]

- Nevertheless, every regulatory decision involves judgment.
- Therefore, core competence in public health, bioethics, and the ability to integrate up-to-date scientific knowledge with an understanding of the evidentiary standards for regulatory action (including the flexibility inherent in those standards and regulations), can guide decisions.

[5] Conducting the Review

Define the review strategy → Apply the review strategy

Review Strategy

- Public health priority of the medical product application
- Understanding other regulatory authority's action on the application
- Understanding specific intrinsic and extrinsic factors
- Identification of major scientific questions and their possible resolution

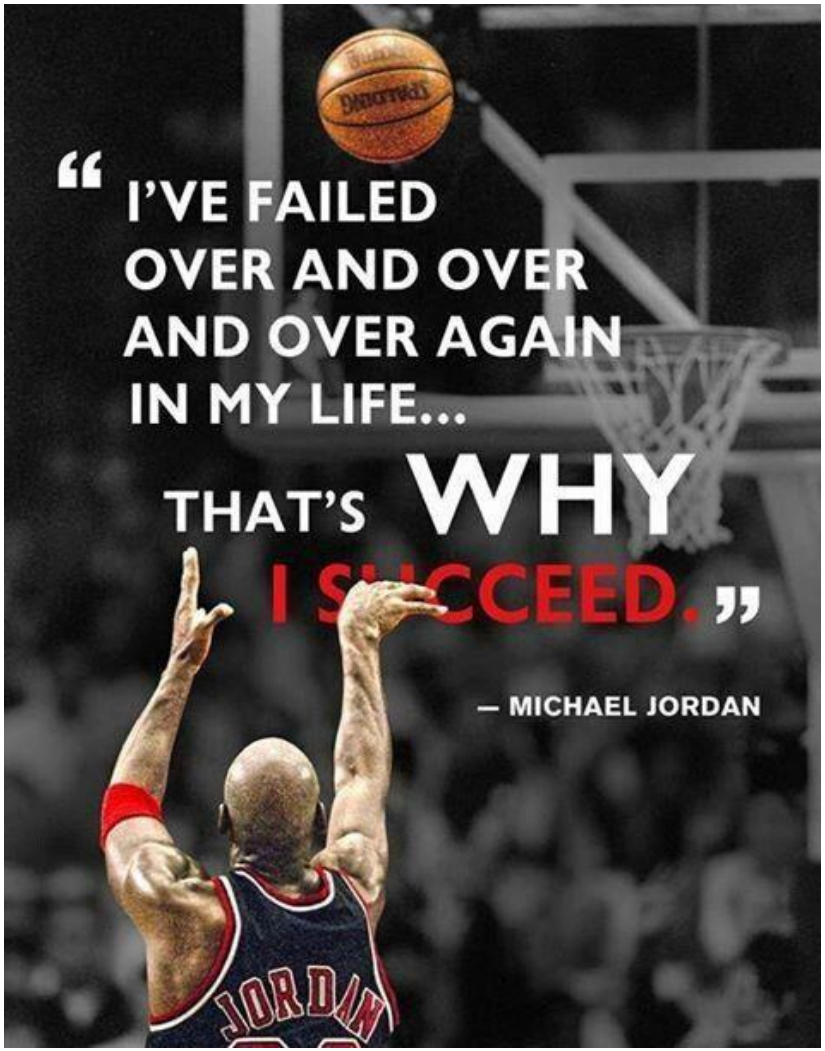
Review Strategy

- Defining and then following an application-specific **review strategy,** amending 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.
  - **review strategy:** the approach or plan of action that a reviewer or review team uses to review a medical product application.
  - standardized review process

Conclusions

- Regulatory authorities can introduce ways of monitoring and improving the review process by moving towards **stepwise implementation** of GRevP.

- The GRevP principles and elements can be adapted to meet continuous needs for the improvement of a review process.



“Thank You for your attention”