Overview of Managing and Conducting the Review Based on WHO Good Review Practice Guideline

Suchart Chongprasert, Ph.D.

Director, Bureau of Drug Control

Food and Drug Administration, Thailand

สำนักงานคณะกรรมการอาหารและยา
กระทรวงสาธารณสุข

Not only the end justifies the means, but also the means justifies the end.

Outline

- **Managing the Review**
  - Project Management
  - Quality Management
  - SOPs
  - Review Process Stages
- **Conducting the Review**
  - Defining a review strategy
  - Applying the review strategy

Managing the Review

Why Manage the Review ?

- Manage process of reviewing to maximize both the potential for a positive public health impact and Effective and efficient use of review resources

What should we do?

- We should clearly define separate steps in the process, each with specific activities and targets

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.

Managing the Review

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

[1] Project Management

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

- Techniques to monitor the progress of applications
  - individual to each RA ; a simple table or spreadsheet or computer software to monitor many applications at a time.

Project Management

- The technique most suitable will be one that enables:
  - Interpretation of the data to **show the progress of one application** as well as many applications under review at 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.**

[2] Quality Management

Quality Management is defined as

"the coordinated activities that direct and control an organization with regard to quality".

A QM system refers to

- the **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.

Quality Management

- QM includes standardized procedures to ensure that good review practices are **in place**, **regularly monitored** and subject to **continuous improvement.**

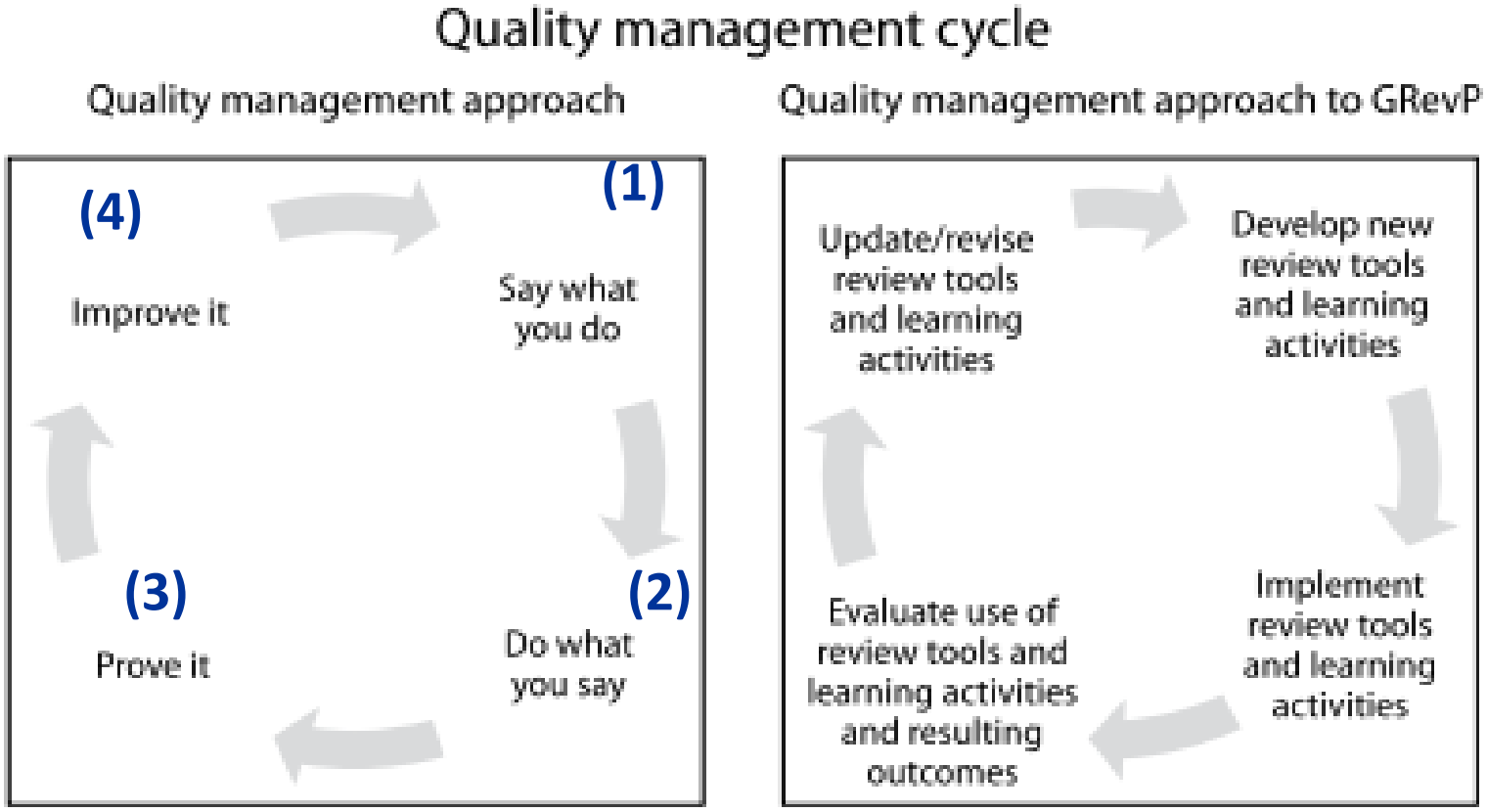
"QM has the ultimate goal of supporting a **robust** regulatory decision and action."

Successful QM implementation requires **senior management** commitment, but is ultimately the **responsibility of everyone** in the organization.

Quality Management

The quality cycle is made up of four key components:

Quality management cycle



Say What You Do

- Provide key documents, such as ***SOPs*** and ***assessment templates.***
  - indicating transparency
- Define processes for decision-making, such as decision frameworks[1], time frames for completion[2] and communication of reviews[3], use of external experts[4], public meetings and peer-review[5].

Do What You Say

- Implement processes defined in **key documents** and adhere to **specified time frames**.
- Offer professional development, mentoring and regular on-the-job training.
- Record and collect key documents, such as minutes from meetings and teleconferences, memoranda, letters and reports, i.e., documented practices

Prove It

- Ensure that review procedures and templates are being **consistently interpreted and applied**, through the assessment of various inputs, such as internal and external feedback and periodic evaluation of practices by internal and external experts.
- Assess public health impacts of regulatory decisions, such as through a lessons learned session that could include assessing the impact on disease, the health-care system and unintended consequences.

Improve It

- Review documentation and decision-making processes regularly.
- Consider introducing improvements to the review and decision-making process, such as: internal assessment of a review, peer review, internal quality audits, self-assessments, analyses of feedback from stakeholders, post-approval analysis of the decision with other authorities, the public and applicants and impact analysis on public health.
- Implement new and improved work practices, latest evaluation techniques, and scientific and technological advancements.

[3] Standard Operating Procedures (SOPs)

- SOPs enable us
  - Outline the workflow processes which 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

Standard Operating Procedures (SOPs)

- SOPs should be
  - **written clearly** to provide both instruction and consistency related to the work being performed
  - structured to contain **additional tools** that will assist in performing the procedure.
  - **companion documents (guidelines, templates, checklists, etc.)** can be created to give more detailed instruction and structure in support of an SOP.

[4] Review Process Stages

Two key stages in the process of reviewing:

1. **Validation (preliminary screening an application)**

   - ensuring completeness of the application, in order to subsequently facilitate the scientific review.

   - ensure that application is well-organized and all required forms and relevant documents have been submitted.

   - Identifying missing information in the application prior to scientific review

2. **Scientific review**

Review Process Stages [2]

- It is essential that applicants are aware of the RA's expectations at both stages, including target time frames, guidelines, requirements and templates/checklists.
- This results in a more ***predictable*** and ***clear*** process for applicants.
  - clear and predictable regulatory environment for applicants
- In turn, the RA benefits when applicants submit complete applications at the outset, i.e., high-quality submissions.

Conducting the Review

- **Defining and Apply review strategy ensures**

  - soundness of the review process

  - the quality of the report

  - the efficient use of resources

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

Conducting the Review

Key elements in defining a review strategy includes:

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

Applying the Review Strategy

Consider the followings

- Who to review this application (team or individual based)
- Need of input from external experts
- Information necessary to approve the product application
- Questions to the applications during the review
- Internal review process (meetings or senior management)
- Understanding the benefit-risk profile
- Evidence-based and public health-focused decision making
- Well documented review report
- Convey the final decision to applicants
- Post-action communication

Applying the Review Strategy

- The way a review is conducted will depend on the **resources** available.
- While a multidisciplinary team will provide broader expertise, in some cases an application may be assigned to a **single reviewer**.
  - same aspects several reviewers
- In the latter case, use of external experts and/or the information and decisions of other RAs may be necessary to ensure that scientific and evidentiary standards for safety, efficacy and quality are adequately met.

Applying the Review Strategy

- The review should be evidence-based, 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**.

Applying the Review Strategy

- 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 form a conclusion.
- In other models, the review is completed on the information submitted and a list of questions returned to the applicant, with a specified time for response and one further round of assessment of the responses prior to a decision being made
  - normally practiced Thai FDA

Applying the Review Strategy

- 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 views from 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.

Applying the Review Strategy

- The review strategy should ultimately enable the reviewer or review team to understand the benefit-risk profile of the medical product given the indication and context of use.
- The nature of the benefits and types of risks should be described as part of the review.
- Benefits and risks can be quantified or qualitatively characterized, including the levels of certainty surrounding the benefits and risks. The review should address generalizability of the data, the clinical significance of findings and what (if any) additional information may be needed to clarify benefits and risks.

Applying the Review Strategy

- Various methodologies exist that quantify benefits and risks. These could be used depending on circumstances such as complexity of issues and utility to the RA.
- 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 (such as conducting responder analyses to identify a population more likely to experience benefits).

Applying the Review Strategy

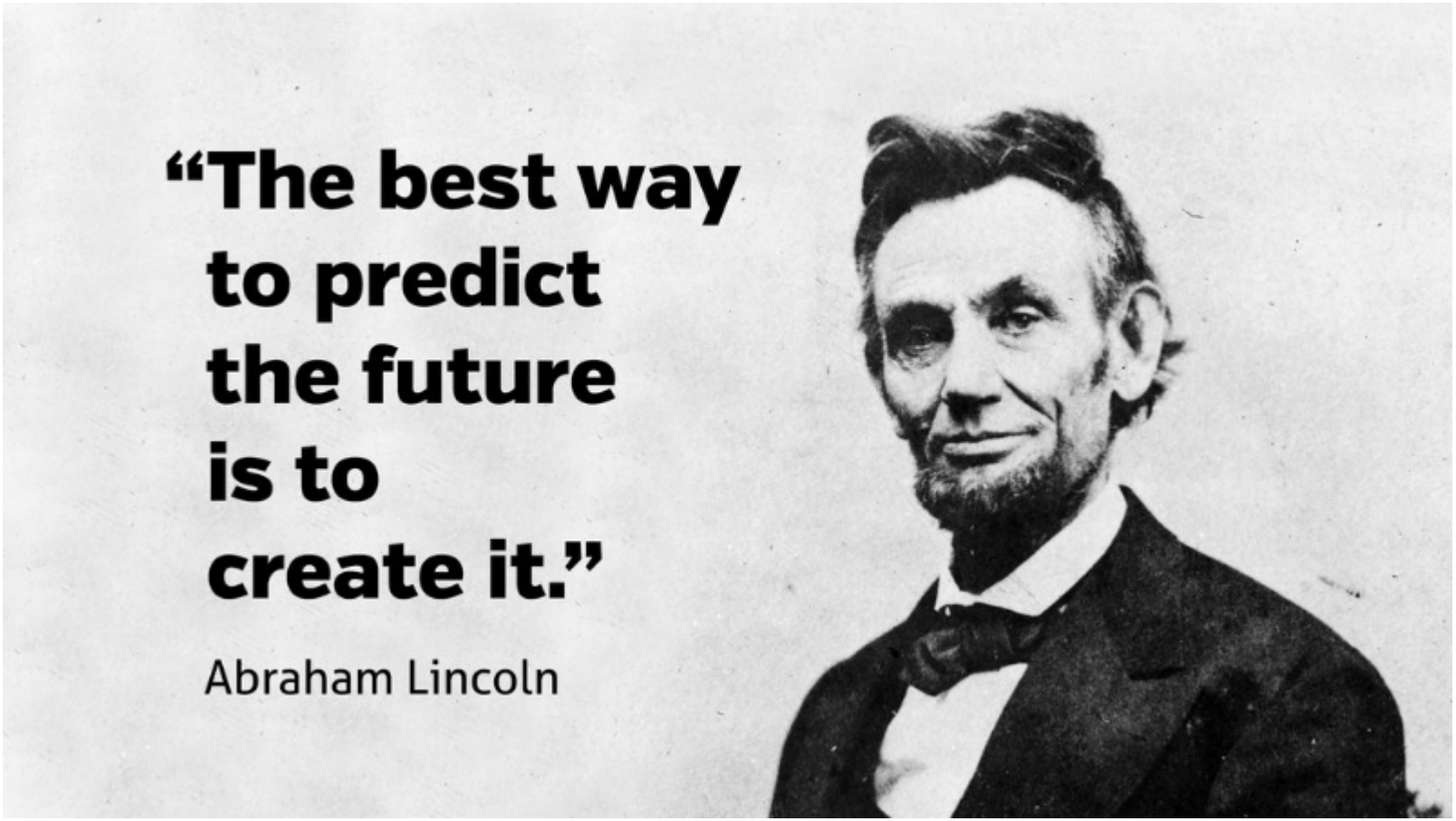
- It is important to note that the **benefit-risk profile may vary depending on intrinsic and extrinsic factors** that may differ among countries and regions.
- Moreover, judgment may vary from within and among RAs.
- Evidence-based and public health-focused decision-making principles may serve to mitigate some variation.
  - In any situation, avoid politics-based decision making

Applying the Review Strategy

- 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.
- An appeal mechanism should be provided to ensure that applicants have an opportunity to present their case to an independent arbiter.

Applying the Review Strategy

- Some RAs may offer post-action discussion with the applicant to help mitigate future application deficiencies.
  - in case of incompleteness of the application
  - review serves as a springboard for future improvement
- The RA may also have mechanisms for communication with the public on the approval of the product and/or action taken in relation to the application.
  - e.g., EMA Public Assessment Report (PAR)
- Publication of information on the approval of products increases transparency of regulatory actions.


“The best way to predict the future is to create it.”
Abraham Lincoln