Session 3:

An Overview of Good Submission Practice - APEC GSubP Guidelines

26 June, 2018

Osamu Inagaki, Ph.D.

APAC RA-EWG / JPMA

1st Thailand GRM Conference
Bangkok, Thailand, June 26-28, 2018

Objectives of this session

1. ***To have good understanding on the key principles of good submission***
2. ***To learn the outline of GSubP guideline***

For regulators:

- ✓ *To understand general process & activities of application submissions by applicants as the basis of the Reviewers Session*

For applicants:

- ✓ *Introduction of the GSubP and GSubP guideline*

Agenda

1. Introduction
    - ***GRevP & GSubP: Two sides of the same coin***
    - Why applicants need GSubP?
2. Outline of GSubP Guideline for Applicants
    - Introduction
    - Principles of Good Submission
    - Management of submission
    - Communications
    - Competency and training
3. Summary

GRevP: Good Review Practice,
GSubP: Good Submission Practice

Historical background of GRM

2011
- APEC RHSC started implementing GRevP topic
  - Champion authority: TFDA

2014
- APAC advocated GRM concept and started GSubP activities
- GSubP was proposed as new topic in APEC RHSC

2015
- WHO adopted GRevP Guidelines as Annex 9 of the Technical Report Series No. 992, 2015
  http://apps.who.int/iris/bitstream/10665/176954/1/9789240693968_eng.pdf?ua=1
- GRM was adopted by APEC RHSC as combined topic of GRevP & GSubP
  - Champion authorities: TFDA & PMDA

2016
- GSubP Guideline prepared by APAC got the endorsement of APEC RHSC
  http://apac-asia.com/images/achievements/pdf/5th/2_APEC_RHSC%20Endorsed%20GSubP%20Guideline.pdf
- GRM CoE Pilot training program started

APEC

Asia-Pacific Economic Cooperation

- **APEC RHSC**: The Regulatory Harmonization Steering Committee of the Life Sciences Innovation Forum (LSIF) in APEC

http://www.apec.org/Groups/Committee-on-Trade-and-Investment/Life-Sciences-Innovation-Forum.aspx

APAC

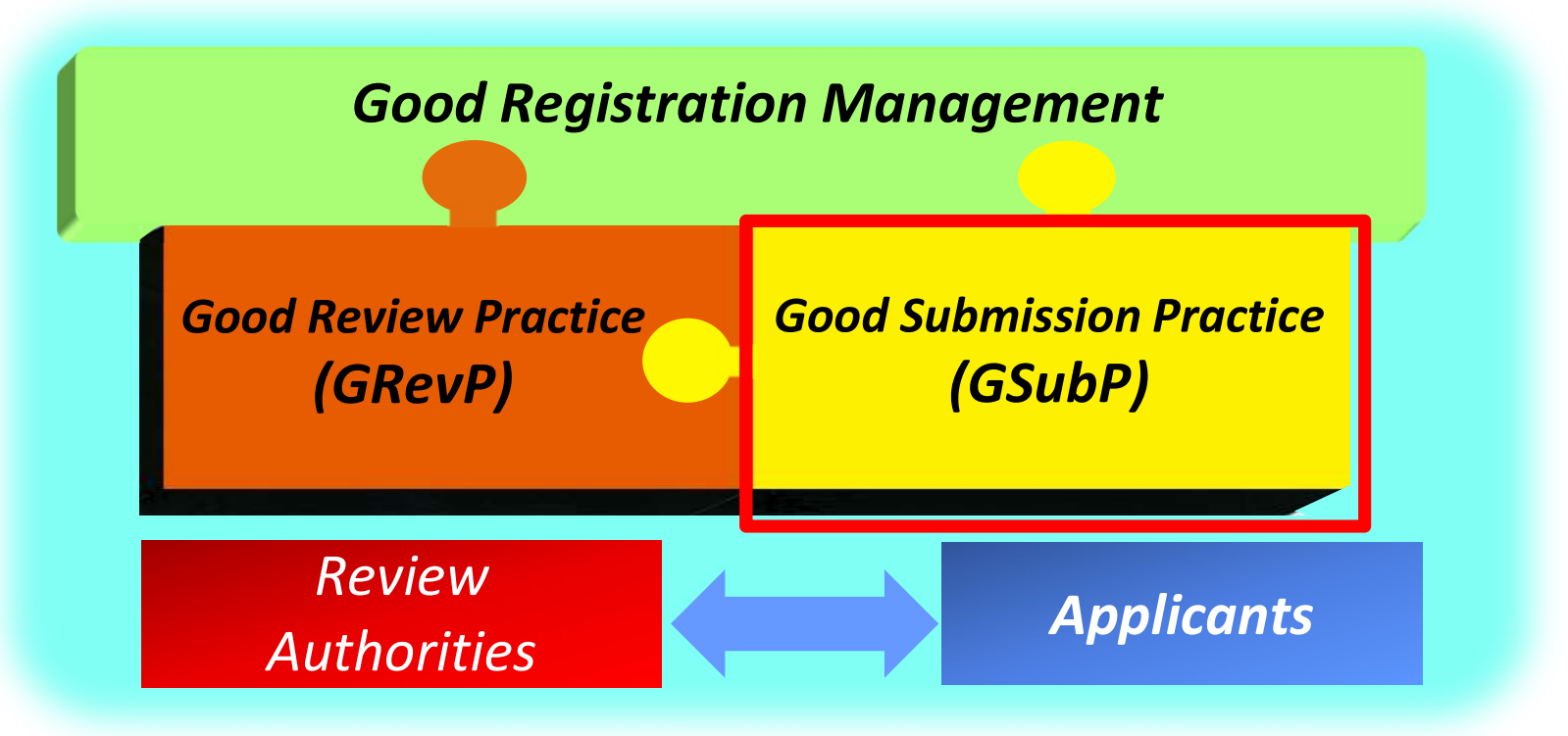
Asia PArtnership Conference of Pharmaceutical Associations

- Started in 2012 by 12 R&D based pharmaceutical associations in Asia
- Industry driven initiative
- **MISSION**: "To expedite the launch of innovative medicines for the peoples in Asia"

http://apac-asia.com/

7th APAC
10-11 April 2018

Concept of GRM



GRM is the concept to promote GRevP and GSubP cooperatively

GRevP & GSubP: Two sides of the same coin

- GSubP and GRevP are complementary each other
- It is necessary to promote GSubP and GRevP concomitantly in order to enhance overall quality and efficiency of medical product registration process

GRevP & GSubP Guidelines: Table of Contents

Good review practices: guidelines for national and regional regulatory authorities
WHO Technical Report Series, No. 992, 2015, Annex 9

1. Introduction
2. Glossary
3. Principles of a good review
4. Managing the review
5. Communications
6. Review personnel
7. Conducting the review

Bibliography

http://www.who.int/medicines/areas/quality_safety/quality_assurance/Annex9-TRS992.pdf?ua=1

Good Submission Practice (GSubP) Guideline for Applicants
Endorsed by APEC LISF-RHSC

1. INTRODUCTION
2. PRINCIPLES OF GOOD SUBMISSION
3. MANAGEMENT OF SUBMISSION
4. COMMUNICATIONS
5. COMPETENCY AND TRAINING
6. GLOSSARY
7. REFERENCES

http://apac-asia.com/images/achievements/pdf/5th/2_APEC_RHSC%20Endorsed%20GSubP%20Guideline.pdf

Principles of good review/submission

PRINCIPLES OF A GOOD REVIEW
(from GRevP Guidelines)

10 key principles of a good review

1. *Balanced*
2. *Considers context*
3. *Evidence-based*
4. *Identifies signals*
5. *Investigates and solves problems*
6. *Makes linkages*
7. *Thorough*
8. *Utilizes critical analyses*
9. *Well-documented*
10. *Well-managed*

PRINCIPLES OF GOOD SUBMISSION
(from GSubP Guideline)

Key Principles of Good Submission

1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*
2. *Compliance to Up-to-date Regulatory Requirements*
3. *Well-Structured Submission Dossier with Appropriate Cross-references*
4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*
5. *Effective and Efficient Communications*

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Communications

Critical element in both Good Review & Good Submission

1. Between the review authorities and applicants

Access to up-to-date regulations

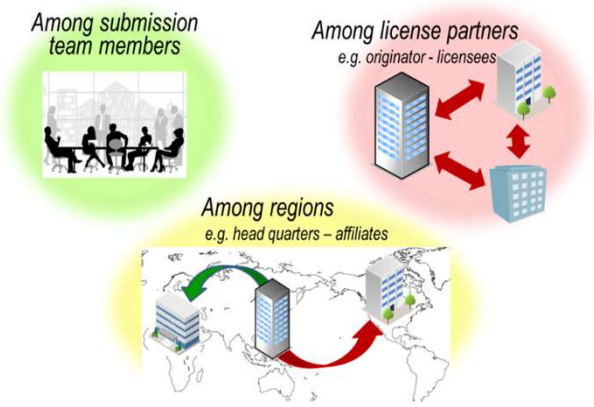
Consultation /Meeting

2. With other stakeholders …

GRevP Guideline

- *Intra-agency*
- *Interagency*
- *With external experts*
- *With the public*

GSubP Guideline



Review personnel/Competency & training

Good review practices: guidelines for national and regional regulatory authorities
WHO Technical Report Series, No. 992, 2015, Annex 9

6. Review personnel
   6.1 Reviewer expertise, competencies and training
   6.2 Critical thinking

Good Submission Practice (GSubP) Guideline for Applicants
APEC LISF-RHSC

5. COMPETENCY AND TRAINING
   5.1 Core Competency of Applicants
   5.2 Training and Capacity Building

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1. Introduction
    - GRevP & GSubP: Two sides of the same coin
    - ***Why applicants need GSubP?***
2. Outline of GSubP Guideline for Applicants
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GRevP: Good Review Practice,
GSubP: Good Submission Practice

Introduction - Why applicants need GSubP?

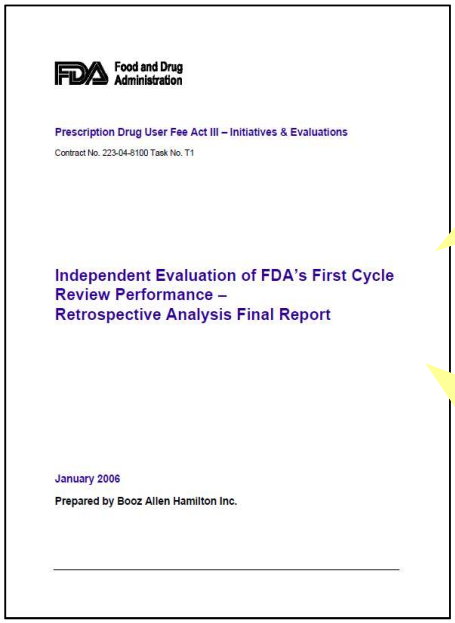
- ***Quality of regulatory submission has been recognized as an issue by review authorities ……..***

Quality of submission

Independent Evaluation of FDA's First Cycle Review Performance – Retrospective Analysis Final Report

January 2006 Prepared by Booz Allen Hamilton Inc.

http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm109759.pdf



FDA Food and Drug Administration

Prescription Drug User Fee Act III – Initiatives & Evaluations

Contract No. 223-04-8100 Task No. T1

Independent Evaluation of FDA's First Cycle Review Performance – Retrospective Analysis Final Report

January 2006

Prepared by Booz Allen Hamilton Inc.

…… *application quality* and communication emerged as having significant influence on the FDA first cycle review performance …….

……. unfamiliarity with FDA regulations and the drug application process is a key problem for inexperienced sponsors and results in *poor quality submissions* …..

Quality of submission

Characterizing Good Review Practices: A Survey Report Among Agencies of APEC Member Economies

2013 Therapeutic Innovation & Regulatory Science http://dij.sagepub.com/content/47/6/678

Article

DIA

Characterizing Good Review Practices: A Survey Report Among Agencies of APEC Member Economies

Li-Ling Liu, MS, RPh[1], Neil McAuslane, PhD[2], Meir-Chyun Tzou, PhD[3], Hemg-Der Chern, MD, PhD[4], Lawrence Liberti, MS, RPh, RAC[5], Mike Ward, BSc[5], and Jaw-Jou Kang, PhD[6]

Abstract

As a first step in the implementation of the Asia-Pacific Economic Cooperation (APEC) Best Regulatory Practice Project, the Centre for Innovation in Regulatory Science conducted a gap analysis survey among regulatory agencies of 14 APEC member economies to assess the current use of good review practices (GRevP) to support transparent, consistent, predictable, and good-quality regulatory decision making. Although the majority of responding agencies have established some form of GRevP, most practices are currently evolving and are applied on an informal basis. Most agencies have developed standard operating procedures and guidelines and use a variety of training methods. The use of a common approach to regulatory review across jurisdictions would help build trust and confidence in each agency's processes, setting the stage for the possibility of work sharing across resource-constrained agencies and bringing consistency and transparency to the review process.

Keywords

APEC, regulatory review, good review practices, CIRS, Taiwan FDA

Introduction

National regulatory agencies, especially those within the rapidly emerging Asia-Pacific Economic Cooperation (APEC) member economies, are seeking ways to expedite the scientific review of market authorization applications for new medical products while ensuring a high level of certainty regarding the product's quality, efficacy, safety, and effectiveness, especially as these relate to their specific constituents.[1]

Accordingly, the APEC Best Regulatory Practice Project[2] led by the Taiwan Food and Drug Administration and initiated at the APEC Good Review Practice Workshop on Medical Products in 2010, strives to implement and improve good review practices (GRevP) as the basis for improved regulatory quality decision making.[3] The overall objectives of this program are to promote the adoption of best regulatory review practices in order to improve the quality, consistency, timeliness, and transparency of scientific assessments of medical products and the efficiency of regulatory systems to

- recognize the importance of GRevP to a well-functioning regulatory system, and
- establish mutual confidence in the regulatory practices of APEC member economies.

Workshop participants recognized that the function and activities of review processes across all regulatory agencies are similar in regard to their overall mission, procedures, and steps employed to assess a medicine for quality, efficacy, safety, and

[1] Division of Medical Devices and Cosmetics, Food and Drug Administration, Taipei, Taiwan
[2] Centre for Innovation in Regulatory Science, London, UK
[3] Division of Drugs and New Biotechnology Products, Food and Drug Administration, Taipei, Taiwan
[4] Center for Drug Evaluation, Taipei, Taiwan
[5] International Programs Division, Therapeutic Products Directorate, Health Canada, Ottawa, ON, Canada
[6] Food and Drug Administration, Taipei, Taiwan

Submitted 30-Mar-2013; accepted 17-May-2013

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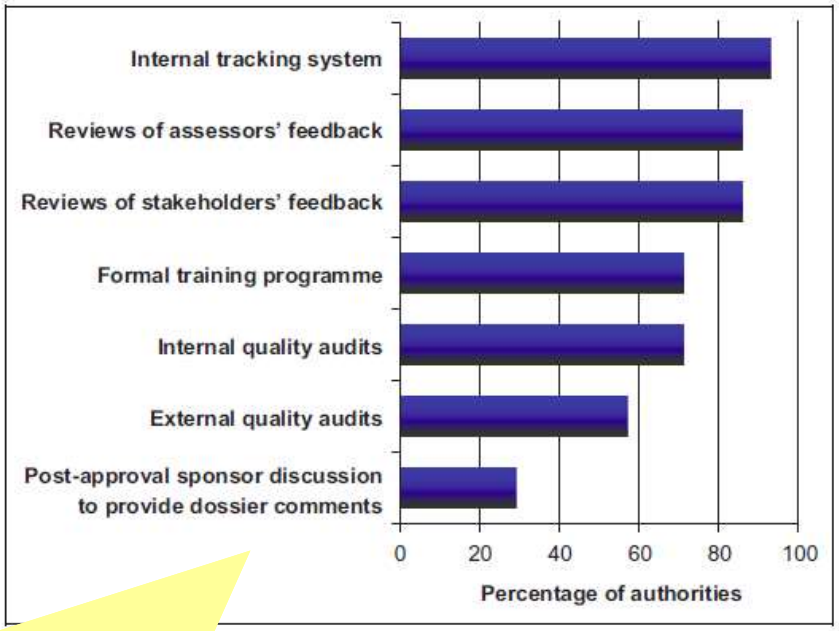

..... comparatively fewer agencies have discussions with sponsors with the goal of improving the *quality of submissions* .....

What is GSubP?

Good Submission Practice (GSubP)

- *Industry initiative in response to GRevP*
- *To enhance the quality and efficiency of the product registration process by improving the **quality of submission** as well as its management*

What dose "Quality of Submission" actually means?

Let's enjoy practice

Start with the question

What is "quality of submission"?

Let's enjoy practice

Practice #1 :

- *What are the necessary elements or conditions to achieve "good quality submission" ?*
- *Please list up 5 items based on your own opinion*

Time given: 5 min

Let's enjoy practice

Practice #2 :

- *Compare the list with your neighbor's*
- *Discuss if there is any difference, and select 5 agreed items of higher priority*

Time given: 5 min

Time is up now !

Let's move to the summary of this practice in next page

What is "good quality submission", and how to achieve it?

1. *There should be many conditions and approaches for achieving good quality submission*
2. *It is important that applicants always seek for the way to improve quality of submission*
3. *The GSubP Guideline has defined **5 key principles of good submission** which applicants are encouraged to follow*

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GRevP: Good Review Practice,
GSubP: Good Submission Practice

Table of Contents of GSubP Guideline

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GRevP: Good Review Practice,
GSubP: Good Submission Practice

1. INTRODUCTION: Objective and scope

1. *Provides general and high level guidance on GSubP*
2. *Sufficiently expandable to accommodate additional annexes or ancillary documents in the future*
3. *Applies to any aspects related to the regulatory submission of medical products and associated activities in planning, submission and review stages up to approval*
4. *Applicable to submissions in entire product lifecycle from investigational testing to new product applications, variations and maintenance of the existing products.*

Possible documentation structure of GSubP

GSubP Guideline

- ✓ Provides general & high level guidance for applicants in all regions

Country specific GSubP guideline or annex

- ✓ Based on regulatory system/process and requirements in the country

SOPs/manuals for submission

- ✓ To be prepared in each applicant's organization

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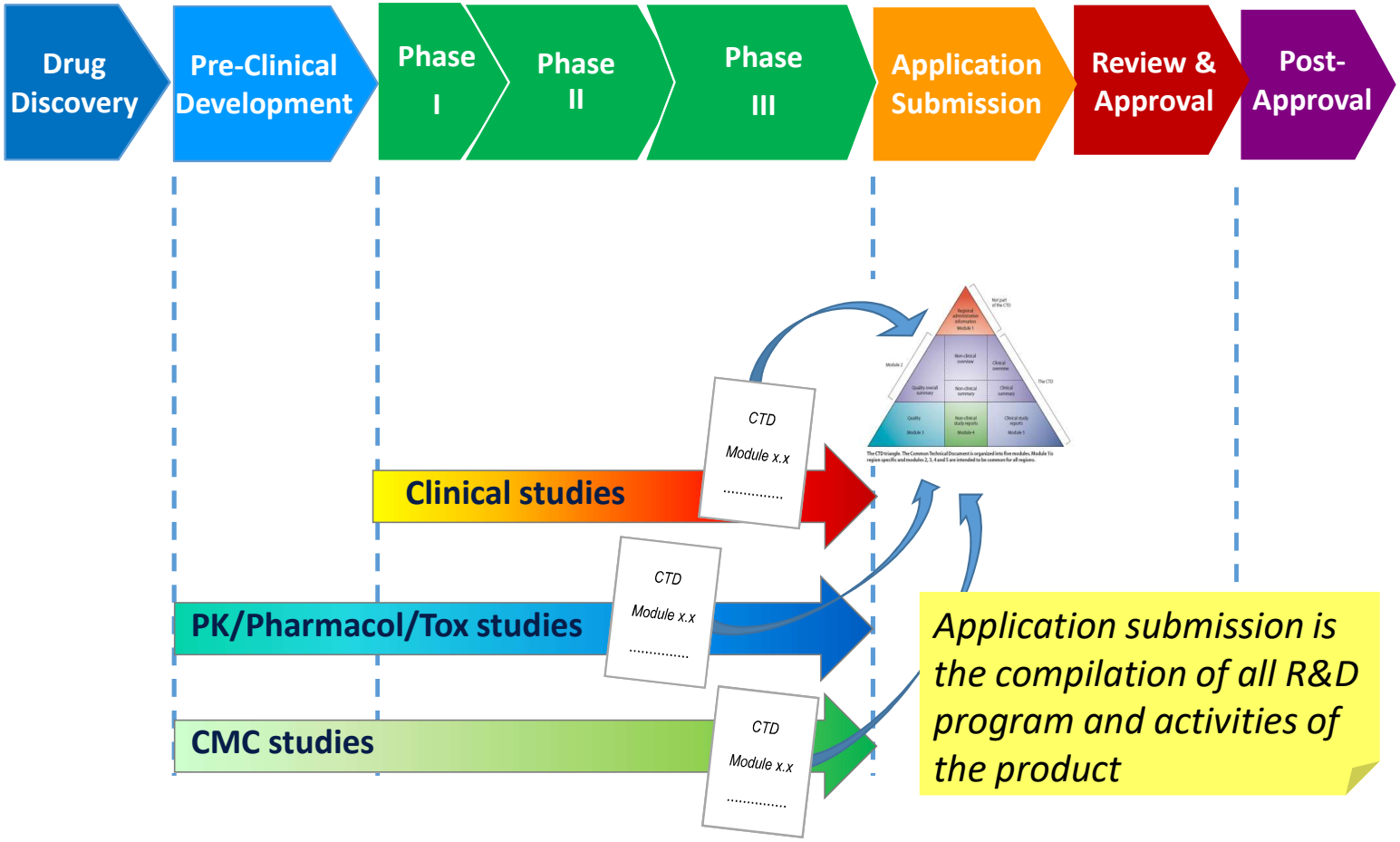
1. INTRODUCTION: Background



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GRevP: Good Review Practice,
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2. PRINCIPLES OF GOOD SUBMISSION

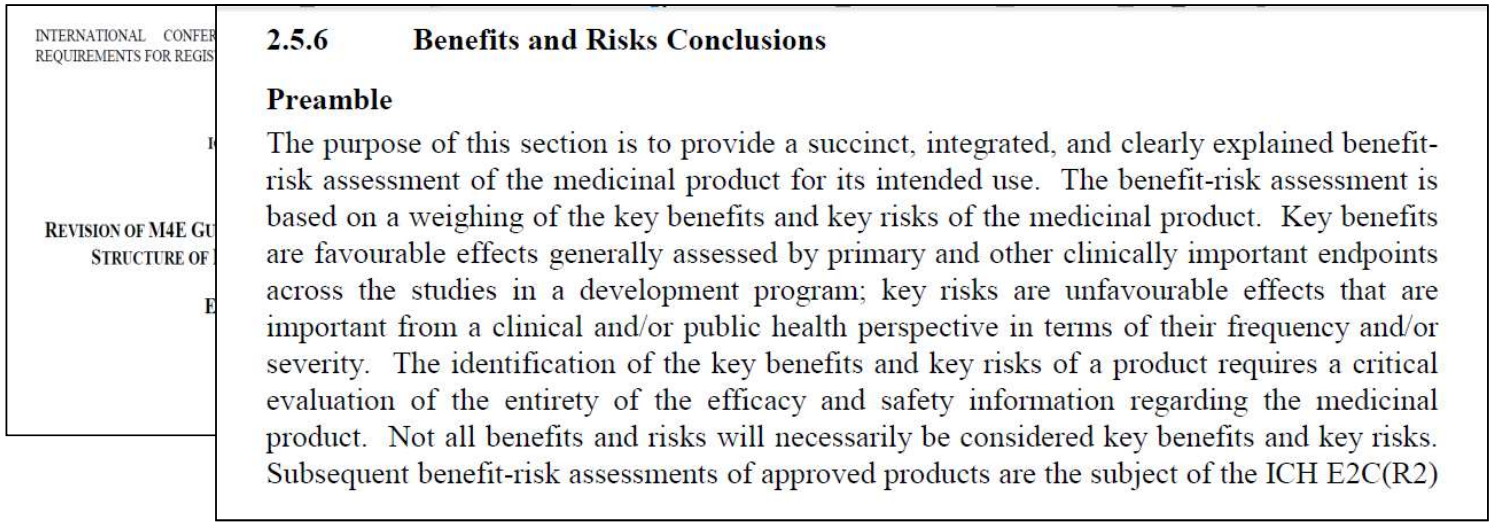
1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*
2. *Compliance to Up-to-date Regulatory Requirements*
3. *Well-Structured Submission Dossier with Appropriate Cross-references*
4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*
5. *Effective and Efficient Communications*

2. PRINCIPLES OF GOOD SUBMISSION

1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*

- **ICH EFFICACY - M4E(R2) REVISION OF M4E GUIDELINE ON ENHANCING THE FORMAT AND STRUCTURE OF BENEFIT-RISK INFORMATION IN ICH**

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4E_R2_Efficacy/M4E_R2__Step_4.pdf



INTERNATIONAL CONFER
REQUIREMENTS FOR REGIS

REVISION OF M4E GU
STRUCTURE OF

2.5.6 Benefits and Risks Conclusions

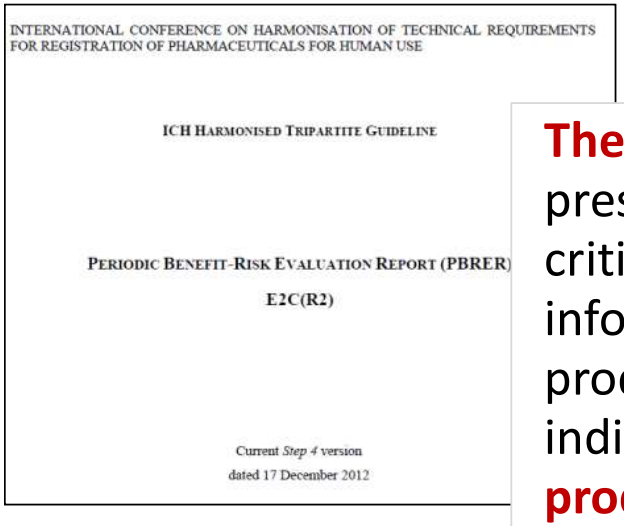
Preamble

The purpose of this section is to provide a succinct, integrated, and clearly explained benefit-risk assessment of the medicinal product for its intended use. The benefit-risk assessment is based on a weighing of the key benefits and key risks of the medicinal product. Key benefits are favourable effects generally assessed by primary and other clinically important endpoints across the studies in a development program; key risks are unfavourable effects that are important from a clinical and/or public health perspective in terms of their frequency and/or severity. The identification of the key benefits and key risks of a product requires a critical evaluation of the entirety of the efficacy and safety information regarding the medicinal product. Not all benefits and risks will necessarily be considered key benefits and key risks. Subsequent benefit-risk assessments of approved products are the subject of the ICH E2C(R2)

2. PRINCIPLES OF GOOD SUBMISSION

1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*

- **ICH E2C(R2) PERIODIC BENEFIT-RISK EVALUATION REPORT (PBRER)**
  http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2C/E2C_R2_Step4.pdf


INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

PERIODIC BENEFIT-RISK EVALUATION REPORT (PBRER)

E2C(R2)

Current *Step 4* version

dated 17 December 2012

The main objective of a PBRER is to present a comprehensive, concise, and critical analysis of new or emerging information on the risks of the medicinal product, and on its benefit in approved indications, **to enable an appraisal of the product's overall benefit-risk profile.**

2. PRINCIPLES OF GOOD SUBMISSION

2. *Compliance to Up-to-date Regulatory Requirements*

- **Section 5.1 of GSubP Guideline**

5.1 Core Competency of Applicants

Good understanding of up-to-date regulations

Applicants should always keep abreast with the latest regulatory environment. This can be done by ***following the regulatory authorities' website and check updated news, notices or highlights***.

... Applicants should carefully study published regulations, technical guidelines, notices, Q&A documents etc. Applicants can also ***attend training programs*** provided by the regulatory authorities, industry associations or other third parties to help understand the contents and background of these regulations. .

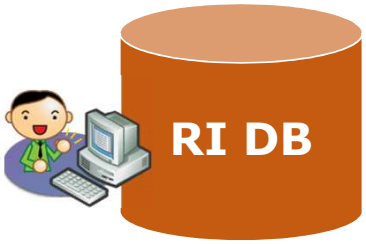
2. PRINCIPLES OF GOOD SUBMISSION

2. *Compliance to Up-to-date Regulatory Requirements*

- ***How applicants can get access to the up-to-date regulatory environment ?***

Regulatory authorities' Website

Regulatory information Database



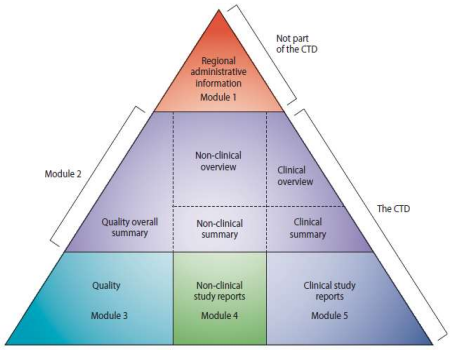
Training workshop/ seminar/symposium

Via industry association network

2. PRINCIPLES OF GOOD SUBMISSION

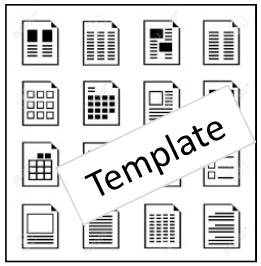
3. *Well-Structured Submission Dossier with Appropriate Cross-references*

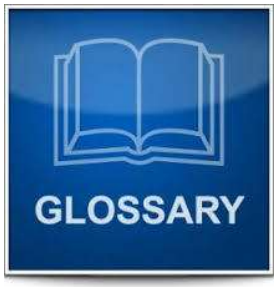
- ***Follow the dossier structure accepted by review authorities***



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

- ***Use template & glossary to keep consistency in format & terminology throughout a dossier***

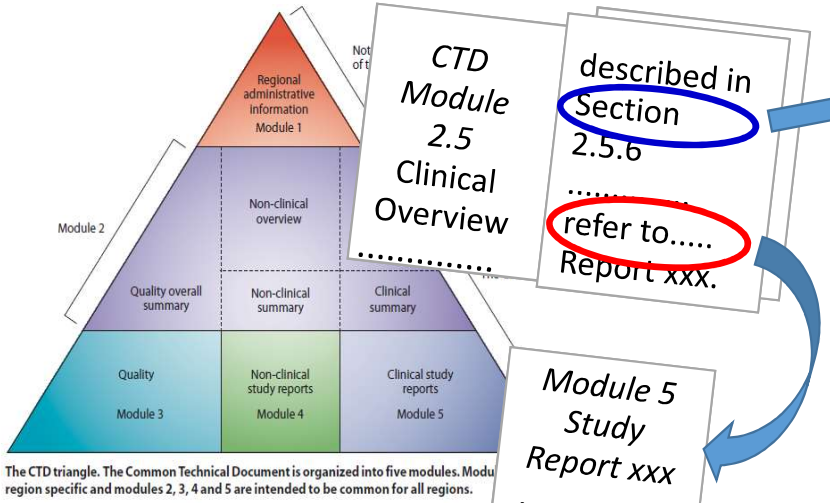




2. PRINCIPLES OF GOOD SUBMISSION

3. *Well-Structured Submission Dossier with Appropriate Cross-references*

- ***Use appropriate cross-references to ensure readability of dossier***



Cross-references in
- eCTD
- NeeS (Non-eCTD electronic Submissions)
- Paper dossier

2. PRINCIPLES OF GOOD SUBMISSION

4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*

◆ *Subjects of evaluation by review authorities*

Medical review report by US-FDA

3.1 Submission Quality and Integrity

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203415Orig1s000

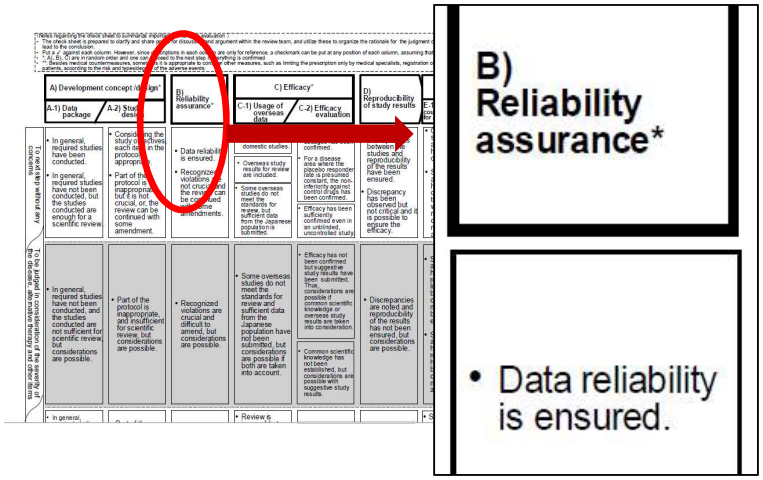
MEDICAL REVIEW(S)

3 Ethics and Good Clinical Practic

3.1 Submission Quality and Integrity

The overall quality and integrity of the submitted data in this NDA were found adequate and acceptable. The applicant submitted safety and efficacy datasets in raw and analysis forms for both the CRPC2 trial and the integrated safety population, allowing the reviewers to examine and verify efficacy and safety findings. Information contained in datasets was found to be consistent information collected in the submitted CRFs. Across the datasets, information is also consistent. However, some clinical or statistical issues were identified during the review and conveyed to the applicant for clarification. As of today, all issues have been addressed and resolved satisfactorily.

Points to Be Considered by the Review Staff Involved in the Evaluation Process of New Drug (PMDA)



2. PRINCIPLES OF GOOD SUBMISSION

5. *Effective and Efficient Communications*

◆ ***Described two types of critical communications for applicants***

1. Communications with review authorities

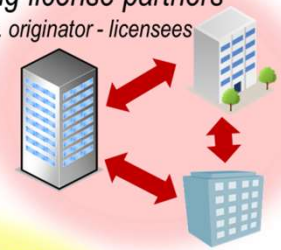
Access to up-to-date regulations

Consultation /Meeting

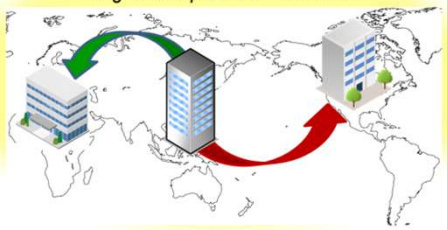
2. Communications amongst applicants

Among submission team members

Among license partners
e.g. originator - licensees



Among regions
e.g. head quarters – affiliates



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4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*
5. *Effective and Efficient Communications*

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1. Introduction
    - GRevP & GSubP: Two sides of the same coin
    - Why applicants need GSubP?
2. **Outline of GSubP Guideline for Applicants**
    1. Introduction
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    3. ***Management of submission***
    4. Communication
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GRevP: Good Review Practice,
GSubP: Good Submission Practice

3. MANAGEMENT OF SUBMISSION

3.1 Planning for submission

- *Start discussion on submission strategy from **early stage of product development***
- *Make use of **support tools** effectively e.g. check-list, template, glossary, timeline table*

Support tools

Check-list:

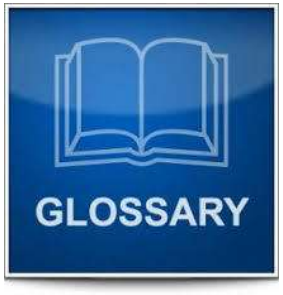
……. may include name of each document with information such as responsible person/party, target date and status. …. useful not only ***to check if there is any missing component*** *but also* ***to manage the whole process of submission preparation efficiently***

The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

Support tools

Glossary:

It is important to ***keep consistency of terminology used throughout a submission dossier****. …. recommended to create a list of general glossary before initiating preparation of study reports and summaries.*

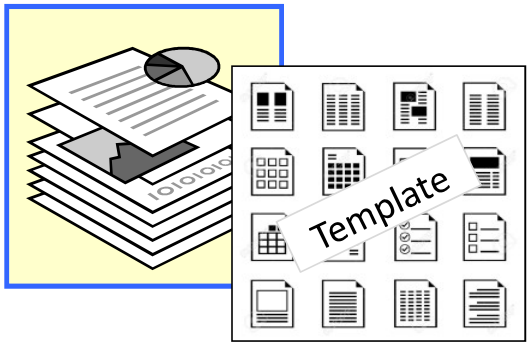


- Use standard terminology e.g. MedDRA (ICH M1)
- Prepare a glossary to define
  - abbreviations
    e.g. SE: Standard Error ? or Side Effect?
  - the word to be used in the dossier
    e.g. Drug Substance? or Active Ingredient?

Support tools

Template:

*..... help authors to **prepare each component document in structured and consistent manner** complying with the required format and contents.... It will also **enhance efficiency of preparation**. Submission with a unified format of study reports and summaries also **enables reviewers to perform review smoothly.***

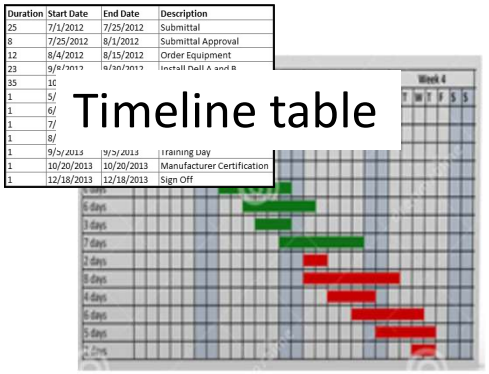


Support tools

Timeline table:

Development and management of timeline is one of the most important tasks in submission planning phase

especially when the submission is performed by collaborations among multiple parties of applicants ….



Duration	Start Date	End Date	Description
25	7/1/2012	7/25/2012	Submittal
8	7/25/2012	8/1/2012	Submittal Approval
12	8/4/2012	8/15/2012	Order Equipment
23	9/8/2012	9/30/2012	Install Dell A and B
35	10		
1	5/		
1	6/		
1	7/		
1	8/		
1	9/3/2013	9/3/2013	Training Day
1	10/20/2013	10/20/2013	Manufacturer Certification
1	12/18/2013	12/18/2013	Sign Off

Timeline table

- Make timeline of each event required for submission
  e.g. Study data, sample, dossier, meeting with RA
- Identify rate-limiting event and decide target submission date
- Manage and maintain overall submission schedule

3. MANAGEMENT OF SUBMISSION

3.1 Planning for submission

- *Start discussion on submission strategy from **early stage of product development***
- *Make use of **support tools** effectively e.g. check-list, template, glossary, timeline table*

3.2 Preparation and Submission of Application Dossier

- *Provide general instructions on **report/summary writing, compiling and submission***
- *Encourage creating **SOPs** for submission preparation & management*

Points to consider in report/summary writing

- Comply with up-to-date standards and regulations
- Consider alignment with current international standards and guidelines

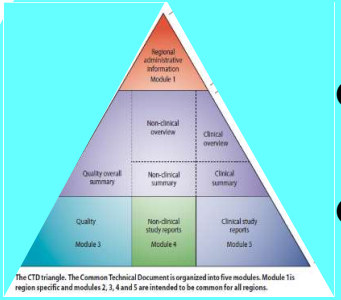
Study Report
CTD
Mx.x

- Based on strong rationale and robust data with scientific evidence
- Ensure reliability, integrity and traceability of data
- Refer to the relevant guidelines on the format and contents of study reports which can be accepted by the review authorities, e.g. ICH M4 & E3

Summary/Overview
CTD
M2.x

- Provide clear rationale with justification
- Clarify the nature of benefits and risks of the product based on sound scientific evidence
- To be concise and easy to read document

Points to consider in compiling the dossier



The CTD triangle. The Common Technical Document is organized into five modules. Module 1is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

- Review the structure and format of dossier accepted by the national regulatory authorities, e.g. ICH-CTD
- To be performed in reference to defined table of contents and checklist
- Ensure that every document has been prepared consistently and placed in the correct location of the dossier
- Follow the relevant instructions when submitting application electronically

SOPs for submission preparation & management

Application submission is

- Complicated and time-consuming process
- Often requires collaborations among applicants' parties or group of organizations locally and globally

..... It is therefore beneficial for applicants to generate SOPs and share them within the parties or organizations ***for proper management of the whole process of submission preparation.***

- SOP is not a regulatory requirement
- SOP in GSubP Guideline means procedure/operation manual for submission and not subject of strict compliance like SOPs in GCP, GMP

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3.2 Preparation and Submission of Application Dossier

- *Provide general instructions on **report/summary writing, compiling and submission***
- *Encourage creating **SOPs** for submission preparation & management*

3.3 Quality Check

- *Provide instructions on QC required in the process of submission preparation*

Quality Check (QC)

Purpose:

- *To ensure accuracy, integrity and traceability of scientific data/information*
- *To check compliance to pre-defined format, template and structure*
- *To ensure accuracy of translation*

Types :

- *QC of study reports and summary documents*
- *QC of submission dossier*
- *QC of electronic dossier*

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4. COMMUNICATIONS

4.1 Communications with review authorities

- *Make effective use of **pre-/post- submission meetings***
- *Manage **inquiry and response** appropriately*
  e.g. clarifications, timeline management

Effective use of pre-/post- submission meetings

- Points to consider for holding effective and productive meeting with the review authorities

1. Study and follow the defined rules and procedure for the meeting
2. Clarify the purpose and discussion points
3. Prepare good quality meeting materials
4. Discuss based on reasonable scientific rationale
5. Prepare and circulate meeting minutes/memo on discussion points and agreements
6. Take appropriate follow-up measures on comments and advice received from the authorities

Manage inquiry and response appropriately

Inquiry and response
....., it is important for applicants to clarify and understand the background as well as intention of the reviewer with that inquiry. To make it possible, the review authorities often allow applicants to ask for clarification. Applicants should make the best use of such opportunity.

Example of clear inquiry

Regarding the treatment for <proposed indication>, efficacy & safety data provided in the dossier are not sufficient to support the use in pediatric patients. Please provide additional clinical and PK data to justify the dosage and administration for use in pediatric patients as claimed in the proposed package insert.

Please put special effort to elucidate the reasons and basis for the differences in doses between pediatric patients over and under <xx> Kg body weight.

4. COMMUNICATIONS

4.1 Communications with review authorities

- *Make effective use of **pre-/post- submission meetings***
- *Manage **inquiry and response** appropriately*
  e.g. clarifications, timeline management

4.2 Communications amongst applicants

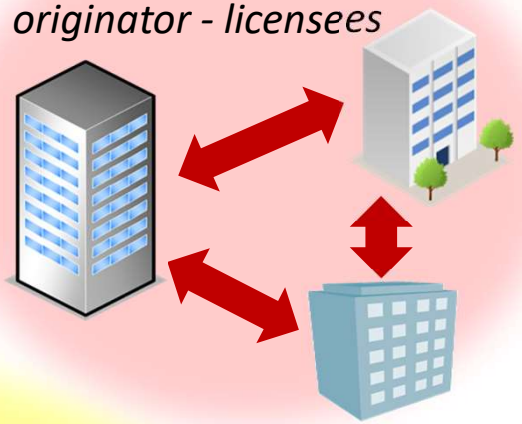
- *Confirm **operation model, role and responsibility** of the submission team & members*
- *Establish **standard working procedure and communication platform** in submission team*

Communications amongst applicants

Among submission team members

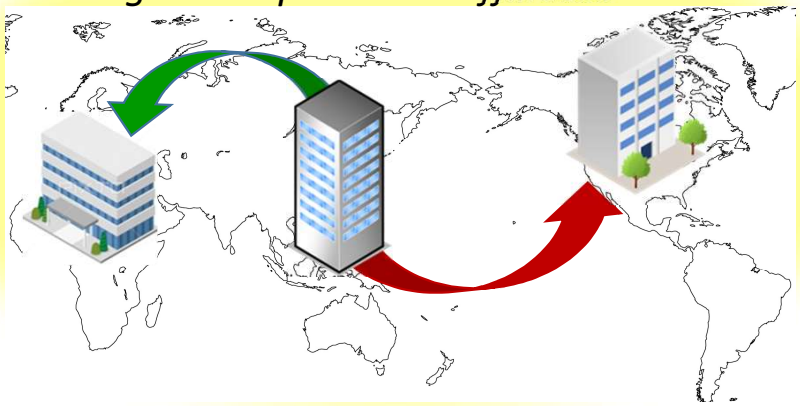
Among license partners

e.g. originator - licensees



Among regions

e.g. head quarters – affiliates



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5. COMPETENCY AND TRAINING

5.1 Core Competency of Applicants

- ***Scientific knowledge and expertise***
- ***Good understanding of up-to-date regulations***
- *Other hard and soft skills,*
  e.g. ***Planning & PJ management, medical writing, IT skills for e-submission, problem solving, communication***
- ***Integrity, reliability and ethical standards***

5.2 Training and Capacity Building

- *Participate in* ***external training programs***
- *Gain experiences through* ***day-to-day operations,***
  e.g. in-house training, self-training, OJT
- *Create and use* ***archive of experiences and knowhow***

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Summary

The GSubP Guideline provides

- Five key principles of good submission
  1. *Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile*
  2. *Compliance to Up-to-date Regulatory Requirements*
  3. *Well-Structured Submission Dossier with Appropriate Cross-references*
  4. *Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data*
  5. *Effective and Efficient Communications*
- High level guidance on planning, preparation and post-submission management to realize good quality submission


Thank
you !