Facilitating the review of new medicines through risk-based evaluations:
How can a stratification process be utilised to achieve an effective use of resources?

Good Registration Management (GRP and GSP) as critical components to enabling agencies to undertake a risk based review process

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Outline

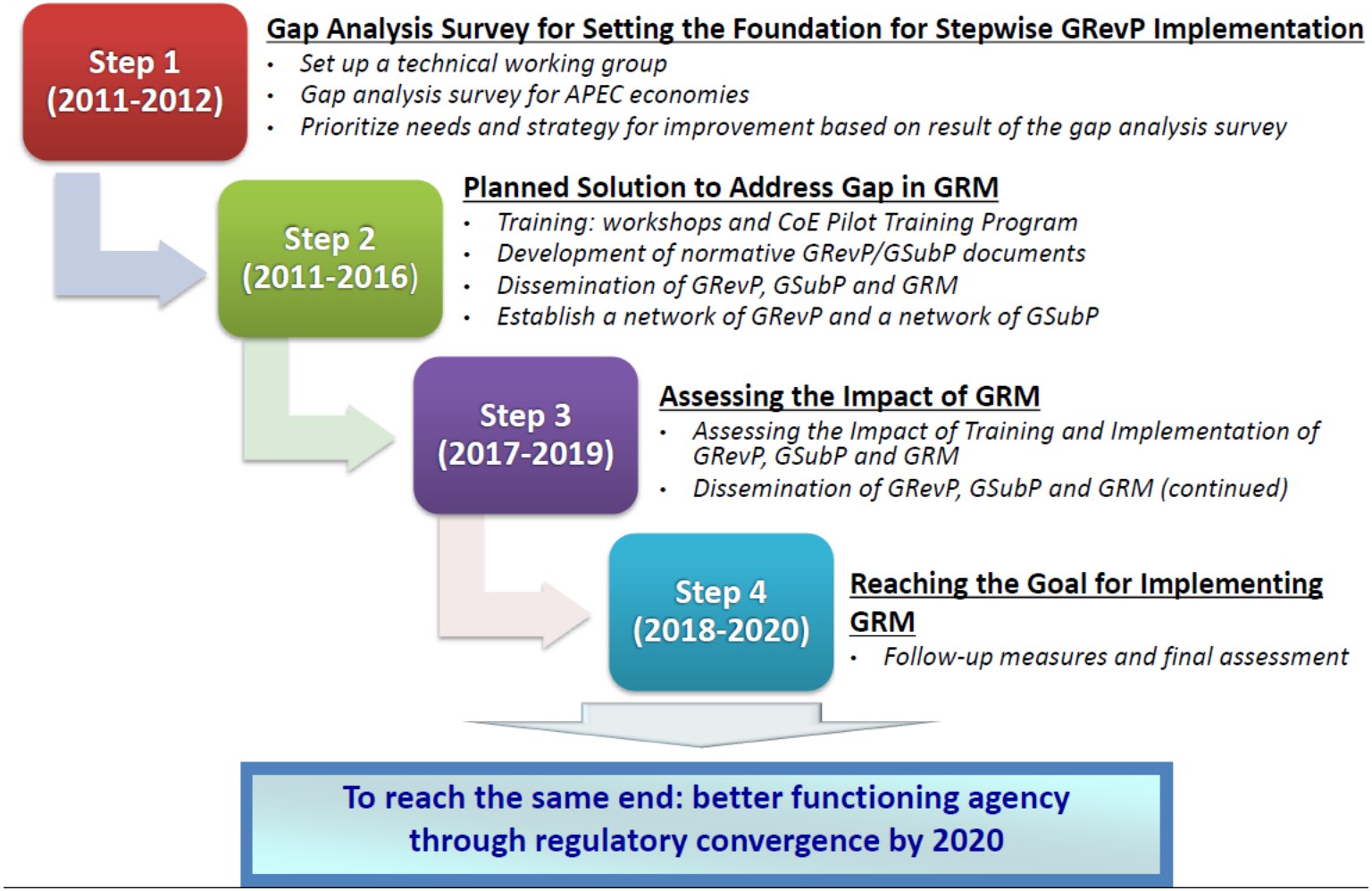
- Promotion of Good Registration Management (GRP and GSP) in APEC
- GRP and GSP are critical components to enabling agencies to undertake a risk based review process
- Future Direction

Goals of the APEC GRM roadmap and each key element

- GRM:
  - A concept to promote efficient registration process for medical products by promoting GRevP and GSubP cooperatively
- Goals of Roadmap:
  - To promote the concept of GRM
  - To enhance mutual trust for regulatory convergence among the APEC member economies by 2020

Good Review Practices (GRevP)	Good Submission Practice (GSubP)
To strengthen the **performance**, **predictability**, and **transparency** of regulatory agencies through the implementation or enhancement of GRevP and quality measures stepwise in each interested APEC economy.	To enhance the **quality** and **efficiency** of the medical product registration process by **improving the quality of submission** as well as its management.

Specific Activities and Timeframe of the GRM Roadmap



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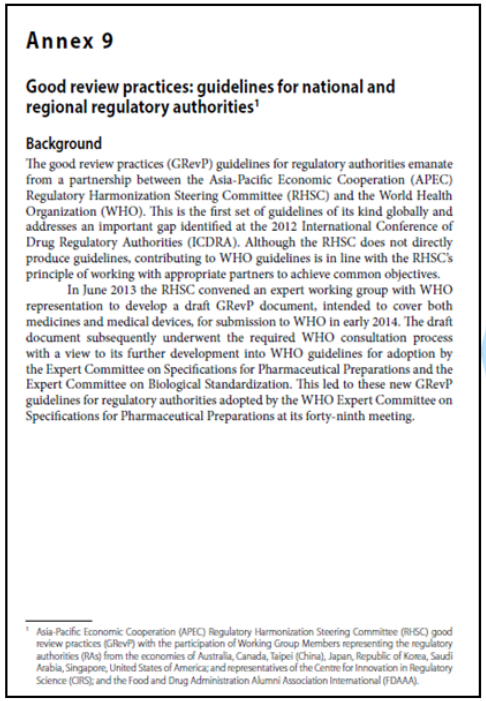
Milestones of the GRM Roadmap

Year	Milestone
2011	Good Review Practice (GRevP) was endorsed as a priority work area (PWA) by APEC LSIF-RHSC. Chinese Taipei was endorsed as the champion.
2013	APEC 2020 Roadmap for GRevP on Medical Products was endorsed by RHSC.
2014	Good Submission Practice (GSubP) was endorsed as a PWA by RHSC.
2014-2015	**Good review practices: guidelines for national and regional regulatory authorities was adopted and published by WHO.**
2016	**Good Submission Practice Guideline for Applicants was endorsed by RHSC.** **GRevP and GSubP were merged as a PWA entitled Good Registration Management (GRM).** A combined roadmap was endorsed by RHSC. Chinese Taipei and Japan were endorsed as the co-champions. **RAPS Taiwan Chapter was endorsed as a Center of Excellence (CoE) for GRM pilot program by RHSC. A CoE Pilot Workshop was held in Taipei in Nov 2016.** Mexico Cofepris was endorsed as a CoE for GRM pilot program by RHSC.
2017	**TFDA in partnership with RAPS Taiwan Chapter was endorsed as a formal APEC GRM CoE by RHSC.**

Good review practices: guidelines for national or regional regulatory authorities (WHO)



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).

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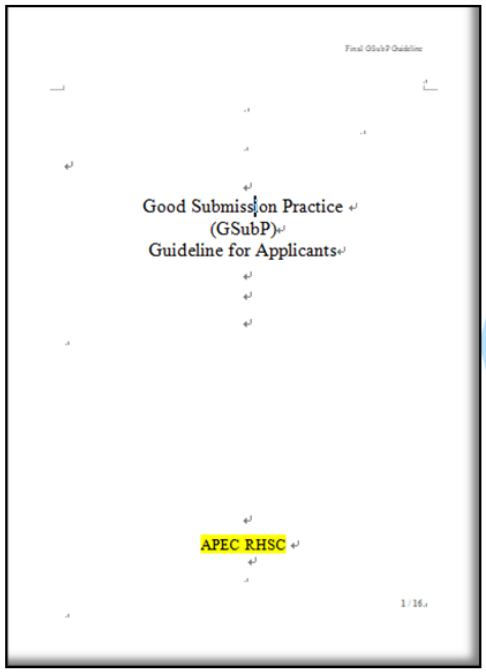
GSubP Guideline for Applicants (APEC RHSC)


Good Submission Practice
(GSubP)
Guideline for Applicants

APEC RHSC

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APEC Center of Excellence

The Vision

- A sustainable platform for promoting regulatory convergence, capacity and cooperation in areas of medical products
- Science and best practice focus

The Approach

- Partnership of academia, regulators and industry to deliver and maintain educational programs
- Benefit must be realized by all 3 partners
- Oversee & certify performance via APEC RHSC and AHC

Benefits of CoE Model

- Sustainable
- Offloads execution to training experts

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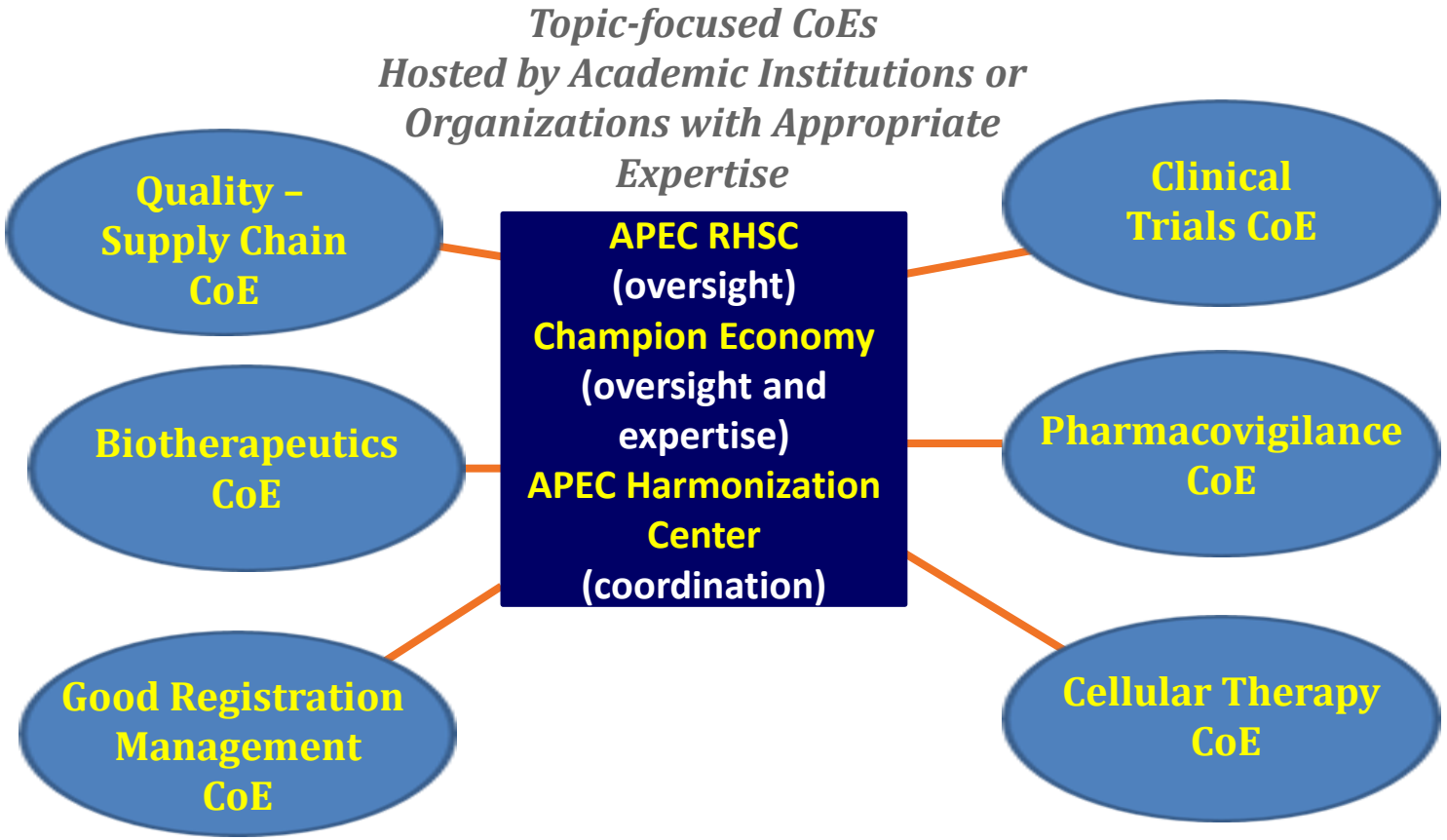
Concept Model for APEC Training Center of Excellence for Regulatory Science (CoE)



- **Champion economies:** Chinese Taipei & Japan
- **CoE:** (1) TFDA & RAPS Taiwan Chapter, (2) COFEPRIS

Networks of CoEs for a topic area are possible

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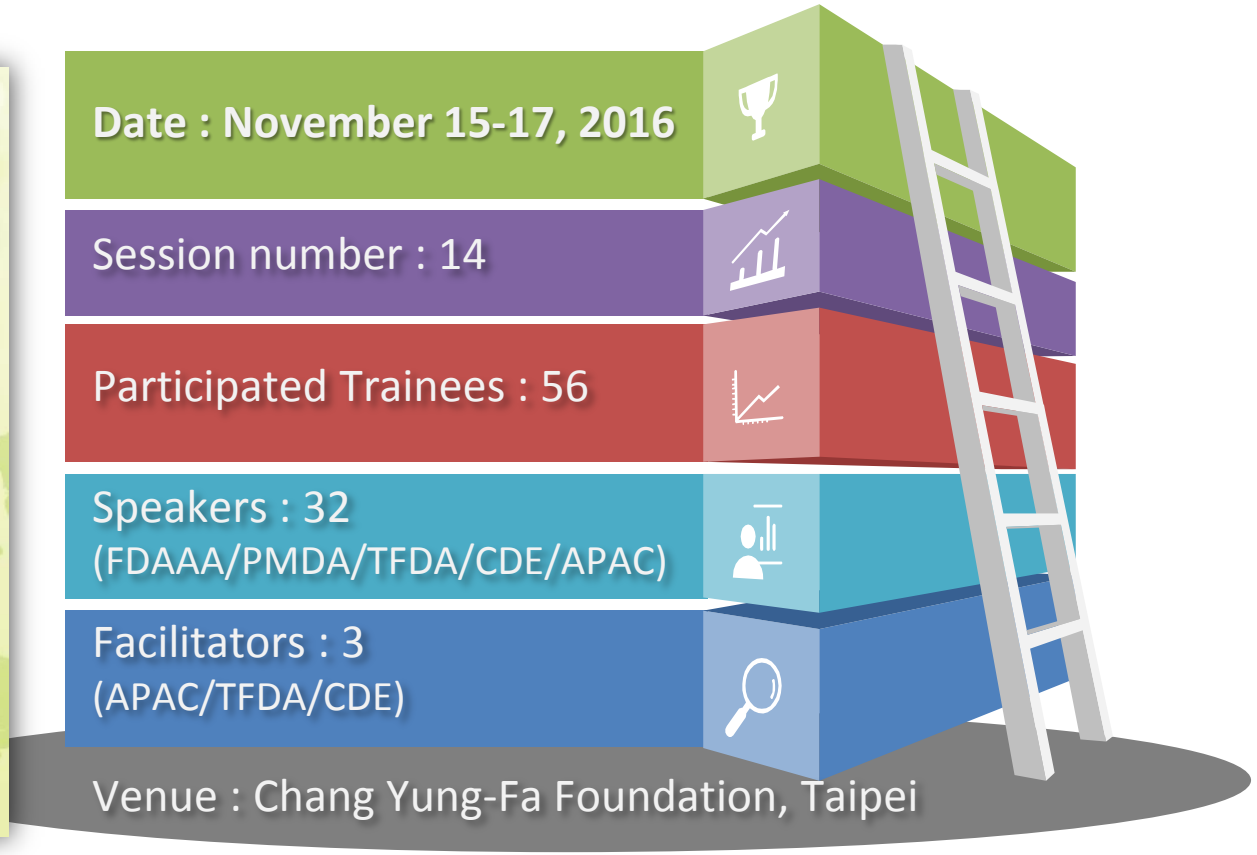
2016 APEC GRM Regulatory Science Center of Excellence Pilot Workshop



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Learning Objectives

Principles

- The principles of Good Review Practices (GRevP) and Good Submission Practices (GSubP)

Good Review

- What is needed for regulators to accomplish good review
  - **Conducting and managing the review**
  - **Good communication with applicants**
  - **Competency for regulators**

Good Submission

- What is needed for applicants to accomplish good application
  - **Planning and preparation of application dossier**
  - **Good communication with regulators**
  - **Competency for applicants**

Core Curriculum

Curriculum developed based on GRevP guidelines and GSubP guidelines

GRM
Good Registration Management

Common Sessions

- Basic concept of GRM
- An Overview of Good Review
- An Overview of Good Submission
- Case Study: Effective Communication for GRM

GRevP
Good Review Practices

Reviewers-Specific Sessions

- Managing the review
- Communication : Fundamentals and Case Studies
- Review personnel - Critical thinking
- Conducting the review
- Rolling out the GRM training program in each economy
- Panel Discussion (competencies)

GSubP
Good Submission Practices

Applicants-Specific Sessions

- Planning of Application
- Preparation of application dossier / Practice : How to prepare application dossier
- Effective communications Focusing follow-up actions during review period
- Rolling out the GRM training program in each economy
- Panel Discussion (competencies)

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Group photo for all workshop participants

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Workshop photos

Case studies

Lectures

Group discussion

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Participant Analysis (1)

Total GRM Trainees
Chile (1)
China (3)
Hong Kong (2)
Indonesia (3)
Japan (2)
Korea (2)
Malaysia (3)
Mexico (2)
Papua New Guinea (2)
Peru (1)
Philippines (3)
Singapore (3)
Thailand (5)
Taiwan (23)
Vietnam (1)
56 APEC delegates
15 APEC member economies

Applicant-specific sessions

Applicants
China (3)
Hong Kong (2)
Japan (2)
Korea (2)
Malaysia (2)
Philippines (3)
Singapore (3)
Thailand (3)
Taiwan (9)
29 APEC delegates
9 APEC member economies

Reviewer-specific sessions

Reviewers
Chile (1)
Indonesia (3)
Malaysia (1)
Mexico (2)
Papua New Guinea (2)
Peru (1)
Thailand (2)
Taiwan (14)
Vietnam (1)
27 APEC delegates
9 APEC member economies

Participant Analysis (2)

Question: How many years have you worked on the management of regulatory review or regulatory submission?

Reviewers	Responders (total 27)
about 3 years or less	11 (41%)
3 to 5 years	8 (30%)
5 to 10 years	3 (11%)
more than 10 years	5 (18%)

- 26 were from regulatory authorities and 1 was from academia.

Applicants	Responders (total 29)
about 3 years or less	3 (10%)
3 to 5 years	1 (4%)
5 to 10 years	5 (17%)
more than 10 years	20 (69%)

- 28 were from industry and 1 was from academia

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Effectiveness Analysis

General Satisfaction with the Workshop

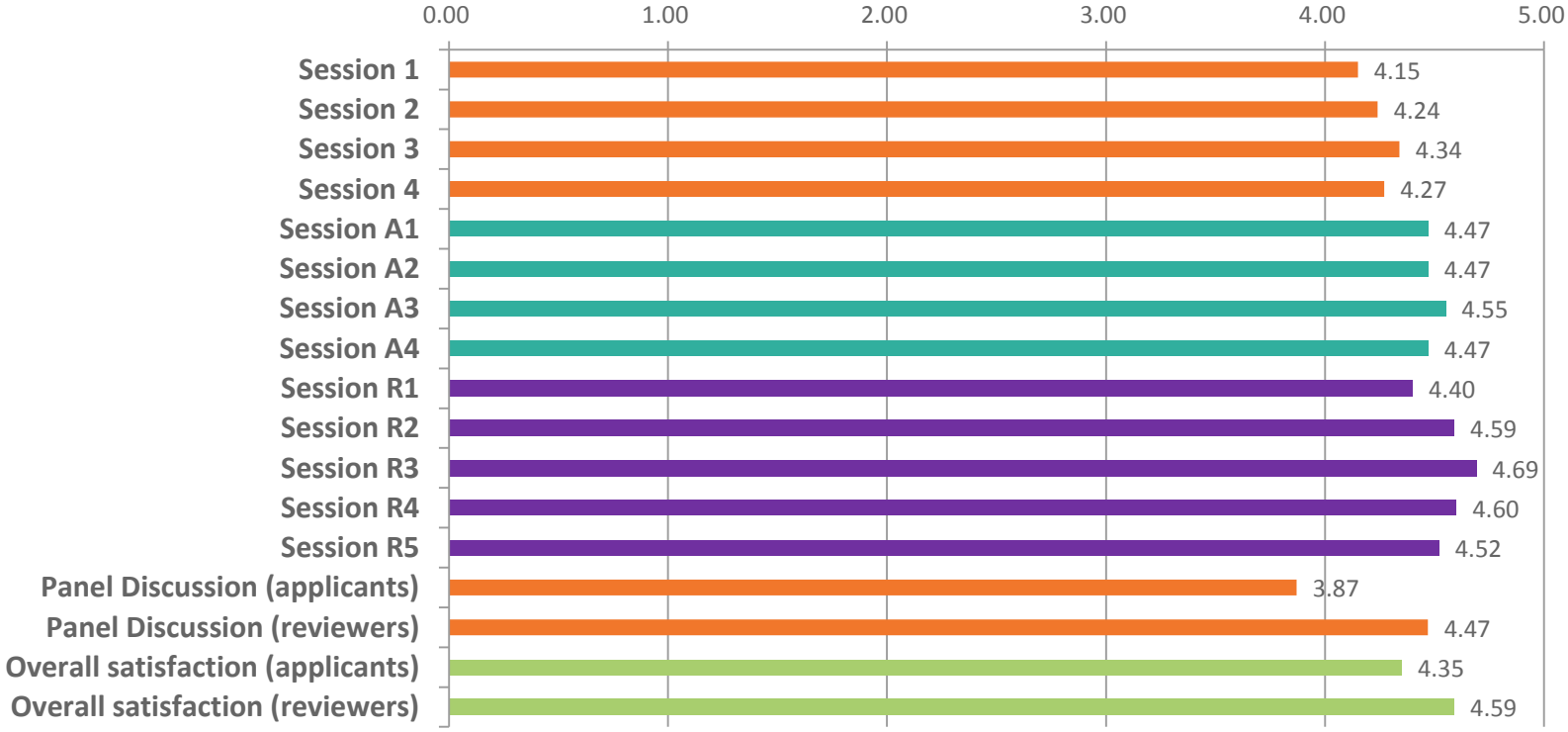
General Satisfaction	Response Average	Responders (response rate)
Were level and amount of pre-training materials adequate?	4.33	42 (75%)
Did the workshop enhanced your understanding of GRM concept?	4.49	42 (75%)
Were your expectations for this workshop met?	4.33	42 (75%)
Overall satisfaction	4.48	42 (75%)

Scale 1 = Poor and 5 = Excellent

Average rating score is above 4. The pilot is considered with good satisfaction.

Curriculum Analysis

- Onsite survey was conducted to rate each session in terms of
  - The adequacy of training materials
  - The adequacy of the time allocation for this session
  - Facilitation and presentation of the content
  - Overall evaluation



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Curriculum Analysis (1)

Rating for Common Sessions

Common Sessions	Session 1 Basic concept of GRM		Session 2 An Overview of Good Review		Session 3 An Overview of Good Submission		Session 4 Case Study: Effective Communication for GRM	
	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)
The adequacy of training materials	3.96	33 (59%)	4.03	33 (59%)	4.18	33 (59%)	4.21	33(59%)
The adequacy of the time allocation for this session	4.27	33 (59%)	4.30	33 (59%)	4.24	33 (59%)	4.27	33(59%)
Facilitation and presentation of the content	4.12	33 (59%)	4.21	33 (59%)	4.27	33 (59%)	4.24	33(59%)
Total evaluation	4.15	33 (59%)	4.24	28 (50%)	4.34	32 (57%)	4.27	33(59%)

Curriculum Analysis (2)

Rating for Reviewer-Specific Sessions

Reviewers-Specific Sessions	Session R1 Managing the review - an Overview		Session R2 Communication : Fundamentals and Case Studies		Session R3 Review personnel - Critical thinking		Session R4 Conducting the review		Session R5 Rolling out the GRM training program in each economy	
	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)
The adequacy of training materials	4.36	22 (76%)	4.45	22 (76%)	4.60	23 (79%)	4.47	23 (79%)	4.47	23 (79%)
The adequacy of the time allocation for this session	4.40	22 (76%)	4.54	22 (76%)	4.60	23 (79%)	4.52	23 (79%)	4.52	23 (79%)
Facilitation and presentation of the content	4.40	22 (76%)	4.59	22 (76%)	4.69	23 (79%)	4.52	23 (79%)	4.52	23 (79%)
Total evaluation	4.40	22 (76%)	4.59	22 (76%)	4.69	23 (79%)	4.60	23 (79%)	4.52	23 (79%)

Curriculum Analysis (3)

Rating for Applicant-Specific Sessions

Applicants-Specific Sessions	Session A1 Planning of Application		Session A2 Preparation of application dossier / Practice : How to prepare application dossier		Session A3 Effective communications Focusing follow-up actions during review period		Session A4 Rolling out the GRM training program in each economy	
	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)	Response Average	Responder (response rate)
The adequacy of training materials	4.36	22 (76%)	4.36	22 (76%)	4.7	20 (69%)	4.44	18 (62%)
The adequacy of the time allocation for this session	4.40	22 (76%)	4.36	22 (76%)	4.45	20 (69%)	4.42	19 (65%)
Facilitation and presentation of the content	4.5	22 (76%)	4.27	22 (76%)	4.5	20 (69%)	4.47	19 (65%)
Total evaluation	4.47	21 (72%)	4.47	22 (76%)	4.55	20 (69%)	4.47	19 (65%)

Curriculum Analysis (3)

Rating for Panel Discussion on Regulatory Professionals' Competencies

Session A5/R6 Panel discussion	Response Average	Responder (response rate)
The adequacy of training materials	4.26	37 (66%)
The adequacy of the time allocation for this session	4.17	39 (69%)
Facilitation and presentation of the content	4.25	39 (69%)
Total evaluation	4.22	39 (69%)

Feedback from Trainees (Applicants)

Topics/presentations of the 2016 pilot workshop most useful to trainees

Applicants
Communication
Planning for submission
QC & Dossier Preparation
Case study & group discussion are very good.
All topics
The tools, the exercises.
Section A3. Effective communications - Focusing follow-up actions during review period / Practice: Case study of how to handle inquires

Topics/areas trainees would like to see in the future GRM workshop

Applicants
Effective communication
More case studies: implementation of GRM, submission to regulatory authorities among Asia/US/EU
Interactive sessions between reviewers and applicants
Others: tools for improving quality of submissions, project management, risk management, critical thinking

Feedback from Trainees (Reviewers)

Topics/presentations of the 2016 pilot workshop most useful to trainees

Reviewers
Critical thinking, Communication
Rolling out the GRM training program in each economy
Case studies
Group discussion
All topics
Conducting the review
Managing the Review

Topics/areas trainees would like to see in the future GRM workshop

Reviewers
Critical thinking in risk/benefit considerations, different product areas, review disciplines and post-approval modifications
Communication
Interactive sessions between reviewers and applicants
Others: effective tools and approaches used for GRevPs, key aspects to perform a review

Challenges from Organizers' Perspectives

- Provide a curriculum which meets the need of all individual trainees with variability in background.
  - For Applicant-Specific Sessions, case studies were provided based on the experiences of **well-resourced companies** which focus on registration of new drugs.
  - For Reviewer-Specific Sessions, participants are from different APEC member economies with **different levels of regulatory sophistication** and with **focus in different review disciplines**.
- Provide more opportunities for regulators and applicants to efficiently interact with each other.

Conclusion from the Pilot Workshop

- It was a successful CoE pilot with
  - good partnership and collaboration,
  - significant interactive elements, such as interactive discussions, group discussions, case studies, and practices, and
  - good rating and overall satisfaction.

- For the future training program, we plan to
  - create more collaborative sessions to allow trainees from industry to talk to regulators,
  - provide more case studies and interactive discussions, and
  - put more emphasis on the topics of “communication” and “critical thinking”.

Expected impacts of GRM to enabling agencies to undertake a risk based review process

- **Good submission practices enable applicants to**
  - understand the principles of a good submission,
  - strengthen their core competency in understanding of risk-benefit analysis, and
  - clarify the nature of benefits and risks of the products when preparing for submission.
- **Good review practices enable regulators to**
  - understand the principles of a good review,
  - strengthen their knowledge and skills of risk-based analysis for reviewing a medical product application,
  - strengthen their competency in critical thinking when granting authorization,
  - determine if the application permits a conclusion about benefits and risks, and
  - apply the review strategy to understand the benefit–risk profile of the medical product.
- **Good Registration Management (GRP and GSP) could serve as critical components to enabling agencies to undertake a risk based review process.**

Future Direction

APEC CoE

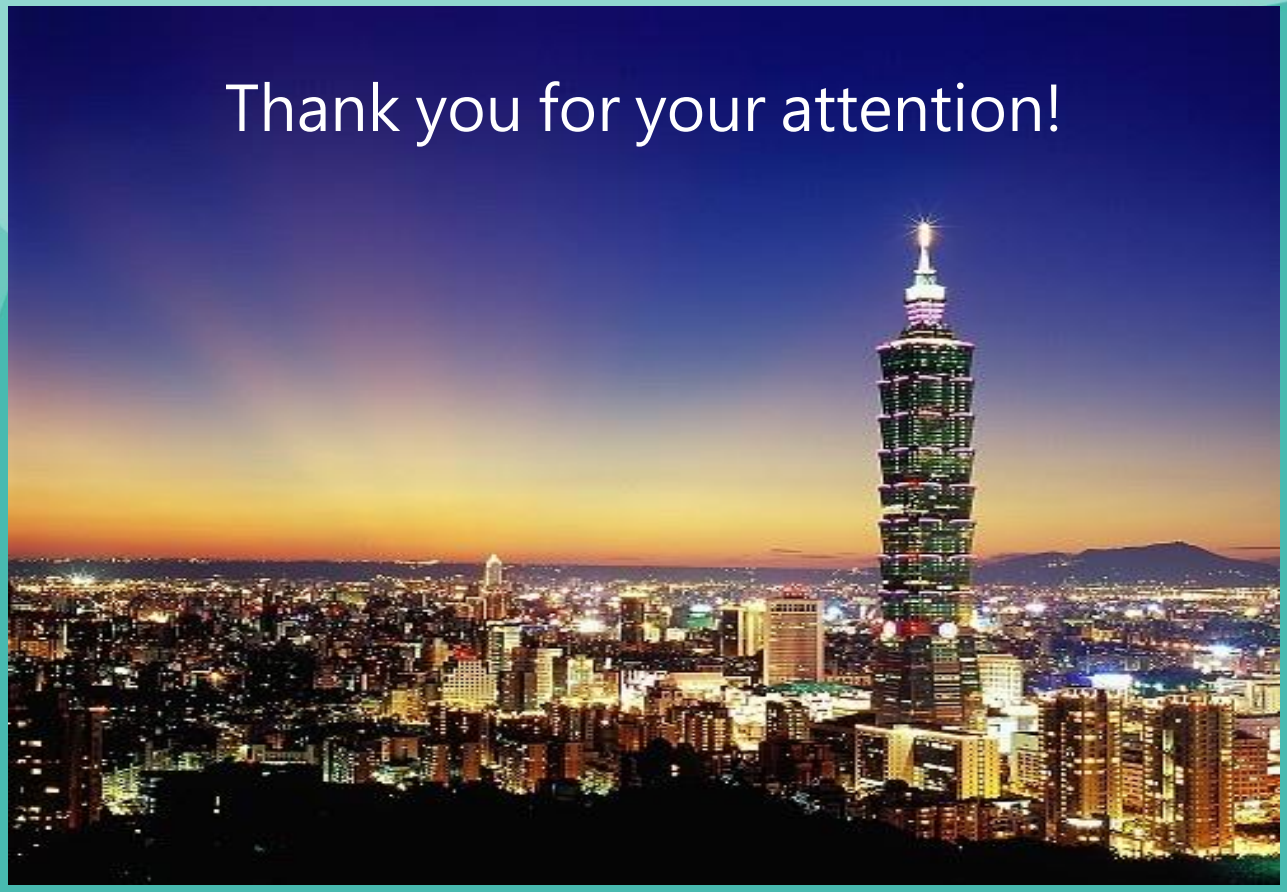
- Become a formal APEC GRM Center of Excellence (endorsed by RHSC in Feb 2017)
- To host annual training events for APEC member economies

Train-the-trainer

- Trainees are expected to develop and deliver local training in their respective APEC member economies

Objective and Goal

- Dissemination of GRM to promote efficient registration process for medical products and regulatory convergence in APEC



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