BEST PRACTICES FOR PREDICTABILITY & TRANSPARENCY TO FACILITATE RELIANCE

Siti Noor Haryani Ismail
Senior Principal Assistant Director
National Pharmaceutical Regulatory Agency
Ministry of Health Malaysia

Presentation Outline

- Introduction
- Facilitated Registration Pathway (FRP) Guideline: Key features & tools
- Practices in Implementing Reliance
- Challenges in Practicing Reliance
- Reliance: Lesson Learnt
- Best Practices: Recommendations for Implementing Reliance

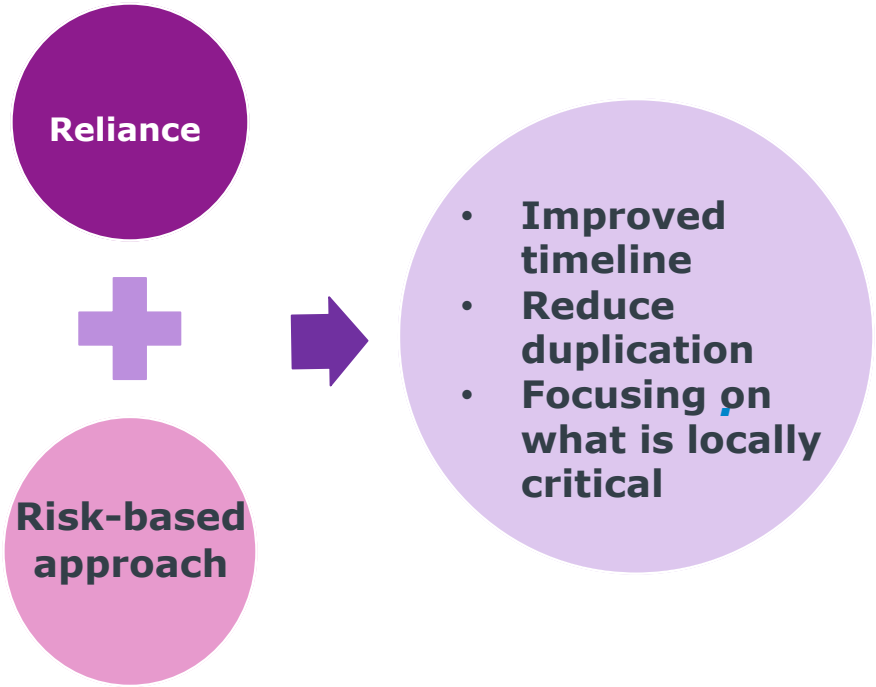
INTRODUCTION

APAC
Asia Partnership Conference
of Pharmaceutical Associations

"RELIANCE….an act whereby a regulatory authority in one jurisdiction may take into account/give significant weight to work performed by another regulator or other trusted institution in reaching its own decision"

"In applying reliance in daily practice, NRAs maintain independence, sovereignty and accountability in regulatory decision-making"

Annex 10, WHO Technical Report Series, No.1033, 2021



#Regulatoryreform

Asia Partnership Conference of Pharmaceutical Associations

"RISK-BASED….focuses on those areas which present the greatest risk, assist in prioritizing & determining the appropriate regulatory response…"

Reliance & Recognition : NPRA previous approach

NPRA has implemented partial reliance (in various forms) for > 20 years

Pre-marketing assessment – partial reliance & recognition

Public assessment report of the reference agencies
EDQM certificate of suitability (CEP) for DS
GMP inspection reports/certificate for overseas manufacturing sites (PIC/S)
Certificate of Pharmaceutical Product
Batch Release Certificate

Post-market activities

Safety alert
Variations

APAC
Asia Partnership Conference of Pharmaceutical Associations

Preparing for the FRP framework - step by step

Political will – direction by the top management to mandate the establishment of a new pathway

2018

Culture change: The benefits were explained to all staff expected to implement reliance approaches

Investment of resources & time – task force: preparation of guideline

Stakeholder engagements

List of questions, clarifications

Finalising and endorsement of the guidance and supported by appropriate regulations

2019

APAC
Asia Partnership Conference of Pharmaceutical Associations

FACILITATED REGISTRATION PATHWAY (FRP)

APAC
Asia Partnership Conference of Pharmaceutical Associations

Facilitated Registration Pathways (FRP): First guideline, 2019

- First Guideline was issued in 2019
- Limited scope & reference agencies - to sensitize the evaluators with new procedure
- Application must be submitted within 2 years from the date of approval by the chosen reference agency/procedure

Monitoring the impact: how many products were registered, timeline

Scope

New Drug Products including NCEs

Biologics including Biosimilars

Reference Agencies

US FDA & EMA

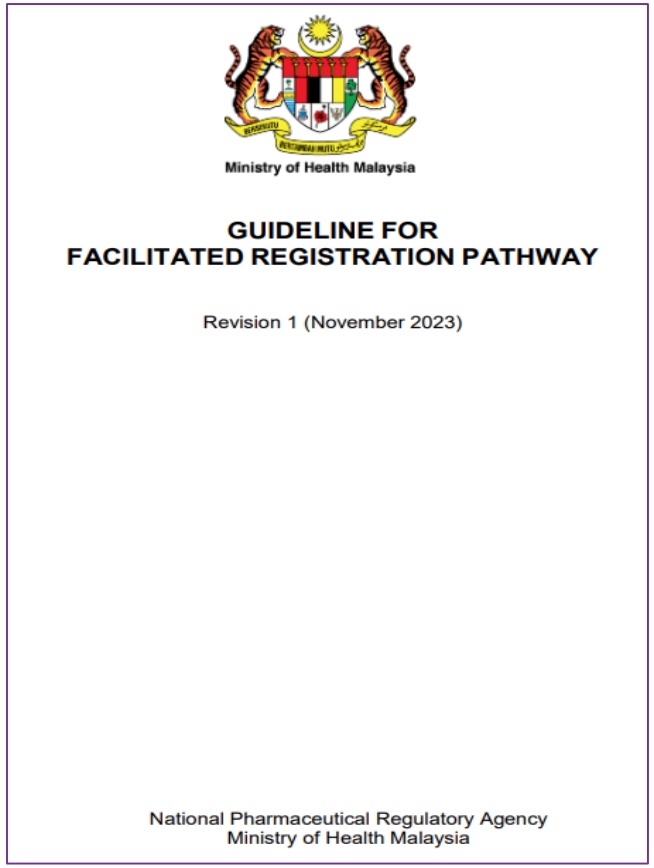
WHO Pre Q Medicinal Products covered by the alternative listing procedure (approved by US FDA & EMA)

Route

Abbreviated review: approved by at least 1 reference agency (120 WD)

Verification review: approved by 2 reference agencies (90WD)

Revised FRP guideline, November 2023 (effective implementation 1st Jan 2024)


Ministry of Health Malaysia

GUIDELINE FOR
FACILITATED REGISTRATION PATHWAY

Revision 1 (November 2023)

National Pharmaceutical Regulatory Agency
Ministry of Health Malaysia

Key features

- *Expansion of the scope of products*
- *Addition of more reference agencies/ procedures*
- *Redefine the abbreviated and verification review*
- *Extension of time limited from date of reference country approval*
- *Revision of the timeline*
- *Addition of a template for the declaration statement by the applicant, dossier template and flow charts*

APAC
Asia Partnership Conference of Pharmaceutical Associations

Revised FRP guideline – key features

Expansion

Scope of products

- New drug products (NCEs)
- **Generic medicines**
- Biologics including **cell and gene therapy products**

Addition

Reference agencies & Procedures

- EMA, US FDA, **Health Canada, PMDA, Swiss Medic, TGA, UK MHRA**
- **WHO Collaborative Registration Procedure (CRP)- SRA & PreQ**
- **ASEAN Joint Assessment (JA)**

Shorter timeline

Routes

- **Abbreviated review (90 WD):** Product approved by any of the reference agencies or approved via WHO CRP
- **Verification Review (30WD):** Product approved via ASEAN JA

Eligibility criteria:

- submitted within 3 years from the date of approval by the chosen reference agency/procedure
- approved/reviewed via a full evaluation process (standalone)
- all aspects are the same as approved by reference agencies (except CCS, manufacturing sites if clearly justified)

Not eligible:

- product that has been approved under exceptional circumstances e.g. Conditional marketing authorization or via reliance pathway
- product requiring a more stringent assessment as a result of differences in local disease patterns and/or medical practices

1
1

Regulatory requirements

Full Dossier

- *Complete Common Technical Document -stability study complies with ASEAN stability guideline (where relevant)*

Assessment Report

- *Complete assessment report*
- *Q&A documents between the PRH and reference agency*
- *Documents pertaining to post approval changes*

Proof of Approval

- *Proof of approval from the chosen reference agency/procedure*

Declaration Letter & statement

- *All aspects - identical to the currently approved by the reference agency*
- *Information and documents submitted in this application are true and authentic*

1
2

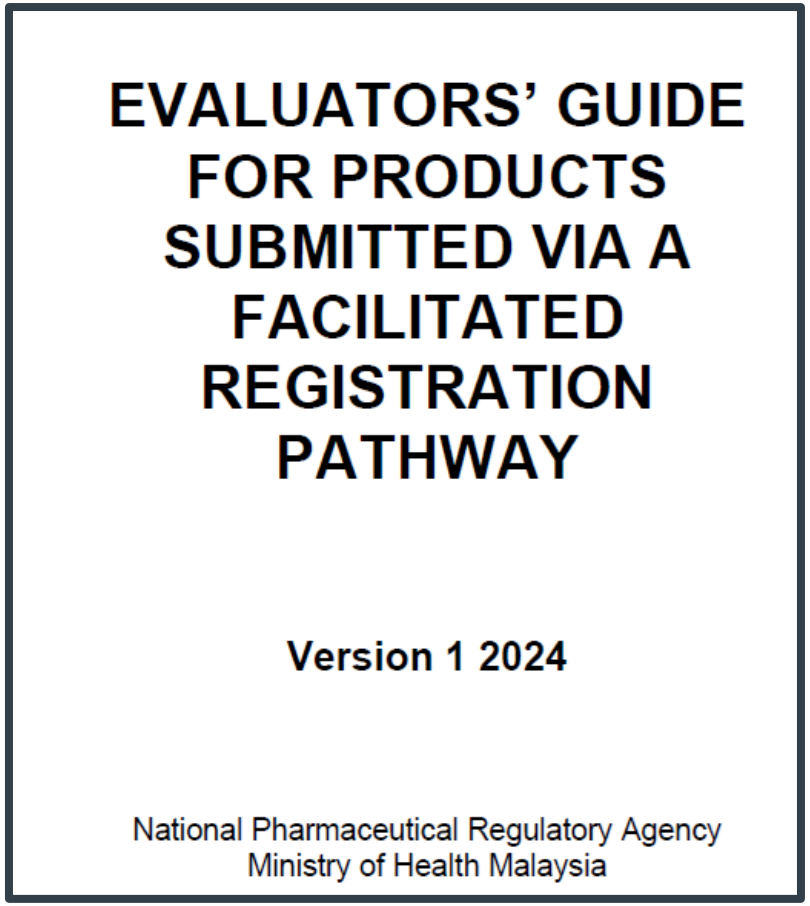
Regulator Tools

APAC
Asia Partnership Conference of Pharmaceutical Associations

Dossier Checklist

Item	Data approved by reference agency	Data submitted to NPRA	Comments
Drug Substance			
Manufacturer(s) **S2.1**	Initial assessment report Name & address of Manufacturer A XXX variation report Addition of Name & address of Manufacturer B	1) Name & address of Manufacturer A 2) Name & address of Manufacturer B	
Specification **S4.1**	Document (specific filename), version, and page number	Document (specific filename), version, and page number	Same as reference agency
Drug Product			
Stability Data **P8**	Stability data according to Zone III Document (specific filename), version, and page number	Stability data according to Zone IVb Document (specific filename), version, and page number	To comply with the ASEAN stability requirements

Evaluators' Guide/SOP

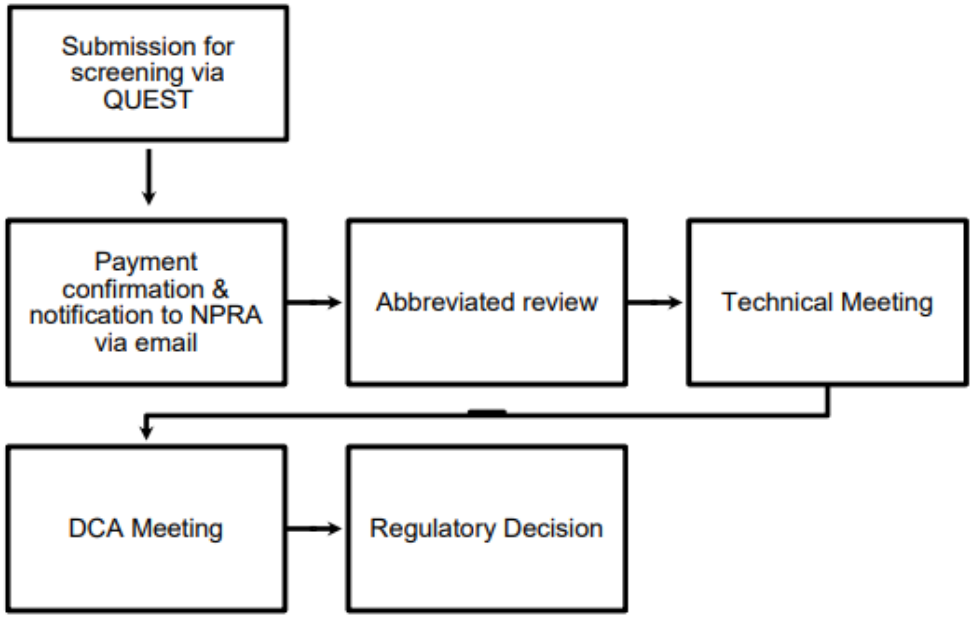

EVALUATORS' GUIDE FOR PRODUCTS SUBMITTED VIA A FACILITATED REGISTRATION PATHWAY

Version 1 2024

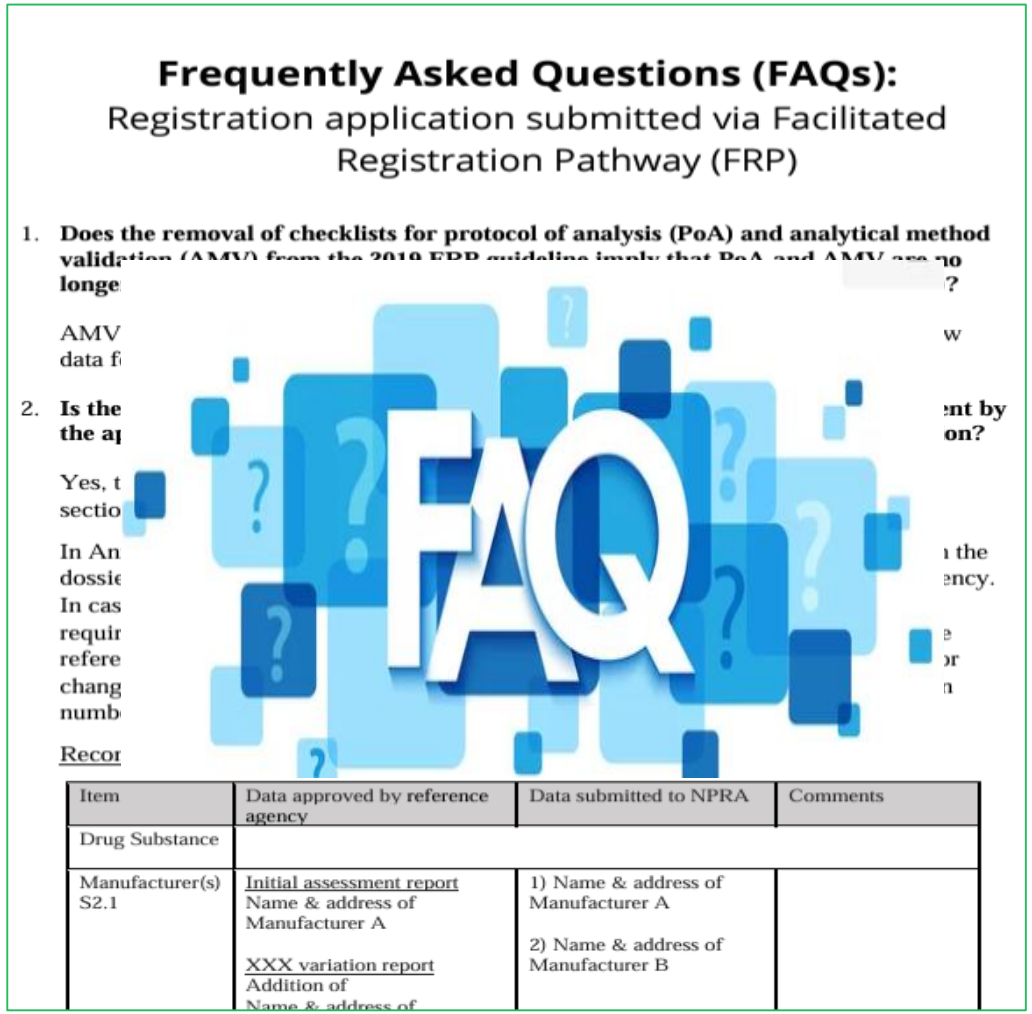
National Pharmaceutical Regulatory Agency
Ministry of Health Malaysia

Other Tools for Regulator & Industry

Flow chart
e.g. Product approved by reference agencies



FAQs (NPRA website)



Frequently Asked Questions (FAQs):
Registration application submitted via Facilitated Registration Pathway (FRP)

1. **Does the removal of checklists for protocol of analysis (PoA) and analytical method valida... longe... ?**

AMV... w
data f...

2. **Is the... the ap... ent by on?**

Yes, t...
sectio...

In An... the
dossie... ency.
In cas...
requir... e
refere... or
chang... n
numb...

Recor...

Item	Data approved by reference agency	Data submitted to NPRA	Comments
Drug Substance			
Manufacturer(s) S2.1	Initial assessment report Name & address of Manufacturer A XXX variation report Addition of Name & address of	1) Name & address of Manufacturer A 2) Name & address of Manufacturer B	

Asia Partnership Conference of Pharmaceutical Associations

PRACTICES IN IMPLEMENTING RELIANCE

APAC
Asia Partnership Conference of Pharmaceutical Associations

APAC
Asia Partnership Conference of Pharmaceutical Associations

Step-by-Step Review Process

1

Initial Dossier Checklist/QIS Review

Begin with applicant-prepared dossier checklist/QIS. Note the differences and justifications provided.

2

Sameness Verification

Confirm product identity. Rely on quality, non-clinical, and early clinical data from reference agency. Cross check reports - Q&As, PAC –when necessary

3

Risk-Based Evaluation

Focus on locally critical factors. Assess benefit-risk profile in Malaysian context.

4

Specific Review

Examine quality differences, country-specific labelling requirements, and risk minimization measures.

Verification of Product Sameness-

Checklist vs submitted dossier vs assessment report

APAC
Asia Partnership Conference of Pharmaceutical Associations

1 Confirmation Process

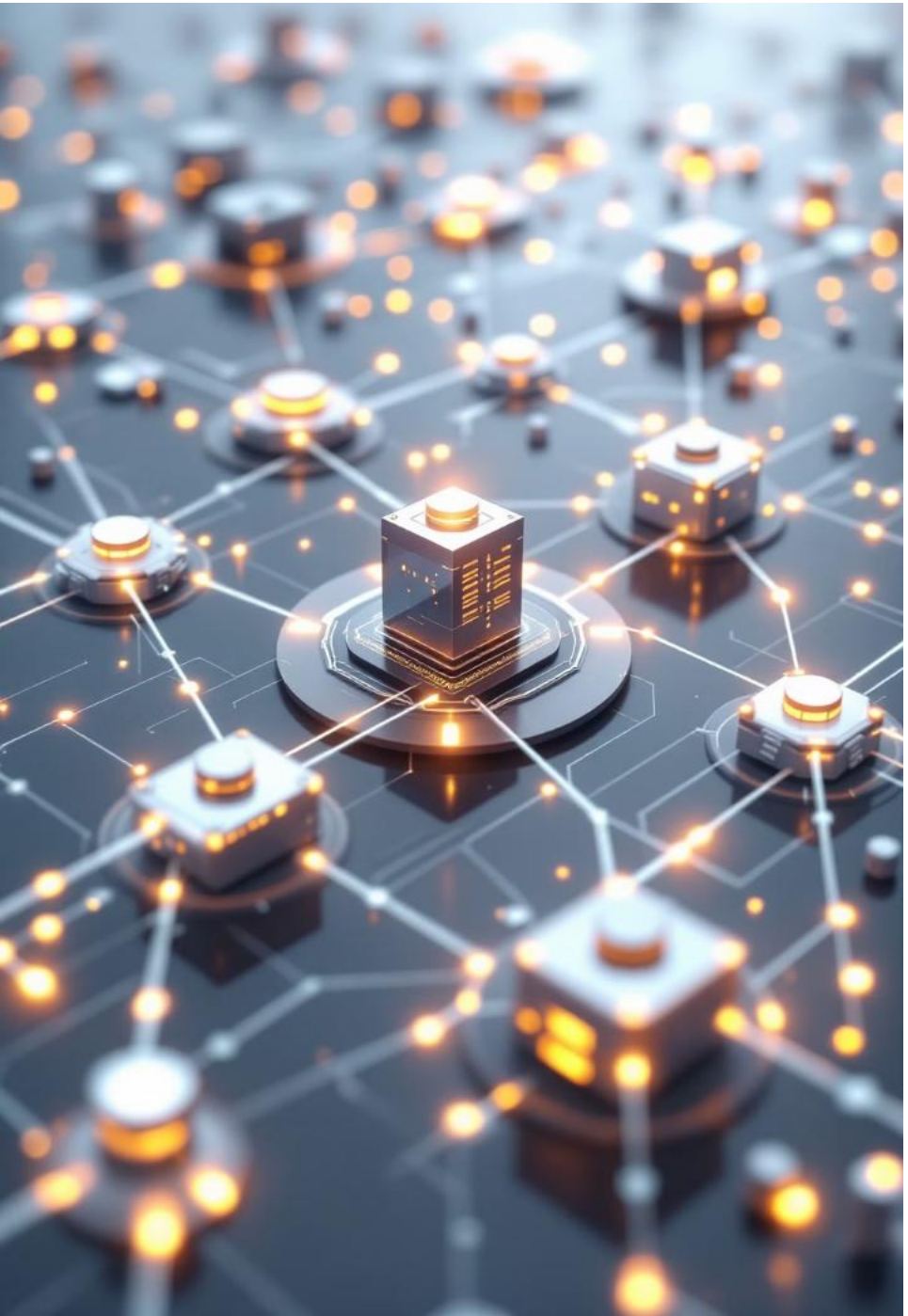
Rigorous checks to ensure product matches reference agency approval

2 Critical Information Analysis

Compare application details with assessment report. Conduct gap analysis to spot discrepancies. Cross-reference dossier information as needed.

3 Key Aspects Verification

Scrutinize indication, dosage, administration route, formulation, and manufacturing processes, specifications. Ensure alignment with reference agency approval.



APAC
Asia Partnership Conference of Pharmaceutical Associations

Areas for Leveraging Reference Agency Information

Quality

Rely on reference agency's evaluation of product quality - CMC

Non-Clinical Studies

Utilize pre-clinical data and safety assessments.

Clinical Studies

Leverage clinical trial results and efficacy data.

Product-Specific Approach

Adopt flexible reliance strategies based on individual product characteristics and risk profiles.

Risk-Based Assessment & Specific Review

APAC
Asia Partnership Conference of Pharmaceutical Associations

1

Benefit-Risk Assessment

Evaluate applicability of reference agency's assessment to Malaysian context. Consider local epidemiology and clinical relevance.

2

Quality Differences

Focus on variations in quality parameters including stability data Zone IVb (if applicable)

3

Country-Specific Information

Review administrative documents, including product information and labelling for local relevance.

4

Risk Management Plan

Review risk minimization measures specific to Malaysia.

Note that all situations are unlikely to be the same and a flexible view of 'reliance' is required

BEST PRACTICES – RECOMMENDATIONS IN IMPLEMENTING RELIANCE

APAC
Asia Partnership Conference of Pharmaceutical Associations

Establishing a Clear and Transparent Framework:

Comprehensive guideline & defined review pathways

Leveraging Reliance to Streamline Processes:

Focus on sameness verification, SOP for evaluators

Optimizing Tools for Reliance –

e.g. Digital :Quest system; Regulator Tools: Dossier checklist

Capacity Building and Training

Monitoring & Continuous Improvement:

Data-driven, global regulatory development: updating guideline

Best practices in implementing reliance

APAC
Asia Partnership Conference of Pharmaceutical Associations

Thank you for your kind attention

APAC
Asia Partnership Conference of Pharmaceutical Associations