

Sameness of the Reliance Mechanism: From guidelines to practical implementation



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Presentation Outline

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Introduction

02

FRP Guideline – key
features & tools

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From guidelines to practical
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Challenges in practicing reliance
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Best Practices: Recommendations for
implementing reliance



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Best Practices: Recommendations for
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Facilitating Approval to innovative medicines/generics/biosimilars

Full Evaluation (Standard Pathway)

1

- 245 WD* (NCE & Biologics)
- 210 WD (Generic)
- Validity: 5 years

Full Evaluation (Conditional Registration (CR))

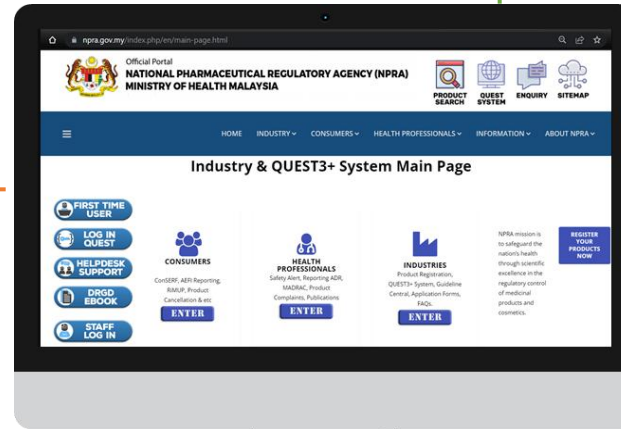
2

- Registered by at least 1 DCA reference agency
- 245 WD (NCE & Biologics)
- Upon request based on early clinical data (i.e. Phase II data)
- Confirmatory trials (Phase III) can be submitted when available
- Validity: 2 years

Conditional Registration of Pharmaceutical Products During Disaster

3

- Fulfills the pre-defined criteria
- Priority Review is automatically granted
- 70 WD
- Validity: 1 year



4

Orphan Medicines (For Rare Diseases)

- Designated as orphan medicine based on the list of rare diseases in the Malaysian Orphan Medicines Guideline
- 120 WD
- Validity: 5 years

5

Priority Review

- Unmet medical needs, life-saving medicine, interest of public health, emergency supply, first generic/first biosimilar/first local generics/biosimilars
- 120 WD (NCE & Biologics)
- 100 WD (Generic)
- Validity: 5 years

6

Facilitated Registration Pathway (FRP)

- Approved by the DCA reference agencies: such as EMA, US FDA, TGA, UK MHRA, Health Canada, PMDA, SwissMedic/WHO CRP/ASEAN Joint Assessment
- Abbreviated: 90 WD
- Verification: 30 WD (ASEAN Joint Assessment)
- Assessment reports and list of Q&As to be provided
- Validity: 5 years
- NCE, Biologic, Generics

Understanding Reliance Practice



RELIANCE: The act whereby a national regulatory authority (NRA) in one jurisdiction may take into account and give significant weight to work performed by another NRA or trusted institution in reaching its own decision - WHO

Concept

- Leveraging assessments from trusted regulators to expedite local approvals
- Trust in reference agency expertise and processes
- Focus on local context and population needs

Benefits

Reduces redundant reviews, reduced timeline - accelerates market access, and optimizes resource allocation

Global Trend

Adopted by leading regulatory bodies worldwide for worldwide for enhanced efficiency



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Strategic Evolution of FRP in Malaysia: A Timeline of Progress



3

2024: Major Enhancements

Expanded scope, shorter timelines, and a broader list of reference agencies, including PMDA and procedures (WHO CRP & ASEAN Joint Assessment), reflecting Malaysia's commitment to global regulatory convergence and capacity building.

2

2020: Integration with WHO Collaborative Registration Procedure (CRP)

1

2019: FRP Inception

Introduced to streamline drug registration, focusing on limited product categories (NCE & Biologics) and reference agencies (EMA & US FDA) to enhance regulatory efficiency and accelerate patient access to essential medicines.

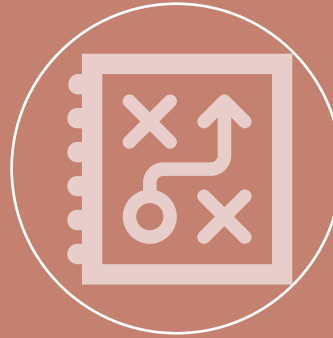
Facilitated Registration Pathways (FRP): First guideline, 2019



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)



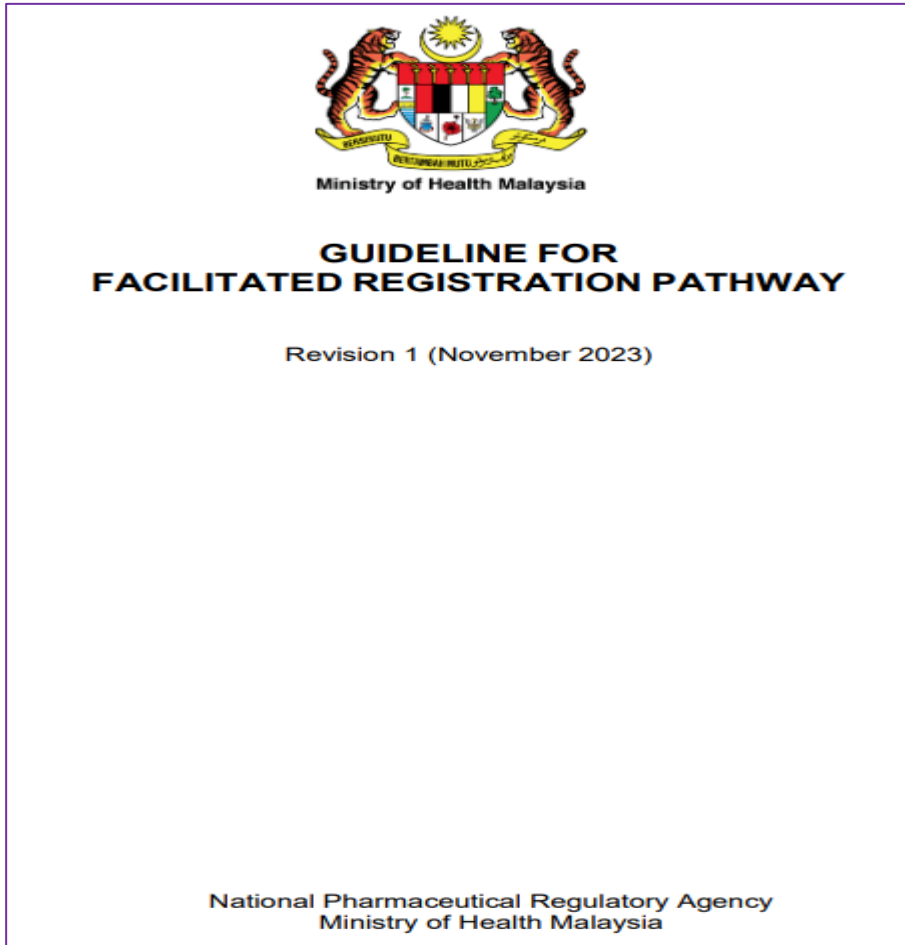
Route

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

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

Submitted within 2 years from the date of approval by the chosen reference agency/procedure

Updates and Improvements of the New FRP Guidelines



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

Expansion : Category of products & reference Agencies/ procedures

Increased number of products eligible for participation under the FRP

Clearer Procedures and requirements

Enhanced guidelines - provide unambiguous eligibility criteria and procedural steps (flow chart) and tools

Faster Timelines

Reduction in approval times, with NPRA aiming for median approval times under FRP significantly shorter than standard pathways.

FRP guideline, Revision 1 (November 2023) – key features



Expansion

Scope of products

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



Addition

Reference agencies &

- 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 & timelines

- 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

Introduction of Regulator Tools:

Dossier Checklist – applicant to highlight differences
Evaluators' Guide/SOP

Introduction of Regulator & Applicant Tools:

Flow chart (FRP process)
FAQ (NPRA website)

Regulatory requirements & tools

Full Dossier

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

Assessment Report

- *Complete assessment report (unredacted)*
- *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*

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)

Regulator Tools



Dossier Checklist

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

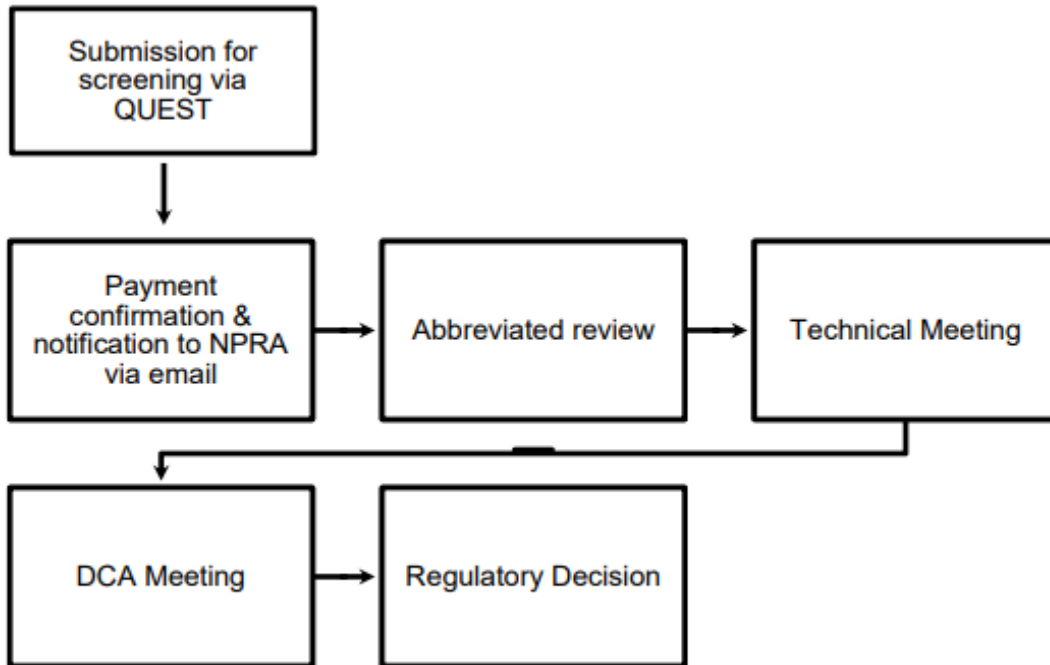
EVALUATORS' GUIDE FOR PRODUCTS SUBMITTED VIA A FACILITATED REGISTRATION PATHWAY

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 valid long?** no)?

AMV data : aw

2. **Is th the a** ent by ion?

Yes, secti r

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Reco

Item	agency		
Drug Substance			
Manufacturer(s) S2.1	<u>Initial assessment report</u> Name & address of Manufacturer A <u>XXX variation report</u> Addition of Name & address of	1) Name & address of Manufacturer A 2) Name & address of Manufacturer B	



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Step-by-Step Process

1

Screening/ Validation (Dossier Completeness Check)

- ✓ Ensure eligibility criteria are met
- ✓ Verify that a complete dossier and all additional documentation for reliance has been submitted.

2

Verification of sameness

- ✓ Begin with dossier checklist – note the differences
- ✓ Rely on quality, non-clinical, and early clinical data from reference agency. Cross check AR, Q&As, PAC –when necessary.

3

Risk-Based Evaluation

- ✓ Focus on locally critical
- ✓ Assess benefit-risk profile in local context.

4

Specific Review

- ✓ Examine quality differences, country-specific labelling requirements, and risk minimization measures to be implemented locally.

Step 1: Screening/ Validation (Dossier Completeness Check)

No.	Screening Package	Remarks
1.	A cover letter to describe the application	Mandatory to be submitted during screening - to be attached under E14 and S10
2.	Screening Checklist (Dossier checklist)	Mandatory for all, except products submitted via the Facilitated Registration Pathway - to be attached under E14 and S10 - to provide applicant remarks only for the relevant fields, with further details as briefly outlined in the Cover Letter
3.	Annex 2b	Mandatory for products submitted via the Facilitated Registration Pathway - to be attached under E14 and S10
4.	Relevant forms	
	a) Applicant Declaration on Post-Marketing Commitments	Mandatory for all products - to be attached under E12
	b) ACTD Part III: Non Clinical Documentation - Good Laboratory Practice (GLP) Compliance Form	Mandatory for all products, except Hybrids (Generic) - to be attached under E14
	c) Bioequivalence Study Report Submission Checklist	Mandatory for Hybrids only (oral dosage form) - to be attached under P9 - other application forms and checklist relevant to bioequivalence studies can be found here .

Screening Package -

to be prepared and submitted by the applicant aside from the complete dossier + a complete assessment report

Step 2: Verification of Sameness- Checklist vs submitted dossier vs assessment report including Post Approval Changes Document



- Confirmation Process**
Rigorous checks to ensure product matches reference agency approval
- Critical Information Analysis**
Compare application details with assessment report. Conduct gap analysis to spot discrepancies. Cross-reference dossier information as needed.
- Key Aspects Verification**
Scrutinize indication, dosage, administration route, formulation, and manufacturing processes, specifications. Ensure alignment with reference agency approval.

Steps 3 & 4: Risk-Based Evaluation—focusing on locally critical elements—and specific review

Quality-related:

Focus on differences: quality parameters, especially in relation to the product stability under different climatic conditions

Country-specific information:

Administrative data documents (PI/labelling)

Product's post-approval life-cycle management:

Cross check post approval changes document vs the dossier

Benefit–risk assessment:

Applicability of the reference agency's assessment in the Malaysian context – **indication, target population**, epidemiology, clinical relevance of an endpoint, etc.

Risk management plan

Risk-minimisation measures specific to the local context

Assessment and verification – important points to consider

- Not evaluating the full dossier but ‘evaluating’ the report to ensure the product meets our local context

- Unlikely to be the same across applications/products - flexible view of ‘reliance’ is required
- What might require little effort for one application may not be the same for the next
- The general principles are the same

Key point: Trust in evaluation process and agency decision making should be maintained



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Staffing
Challenges

**Capacity &
Resource
Constraints**

Develop expertise,
ensure consistency,
risk-based approach

Challenges

**Technical &
Procedural
Challenges**

Adapting new process, complexity of
comparisons- verification of the sameness

**Data
Interpretation**

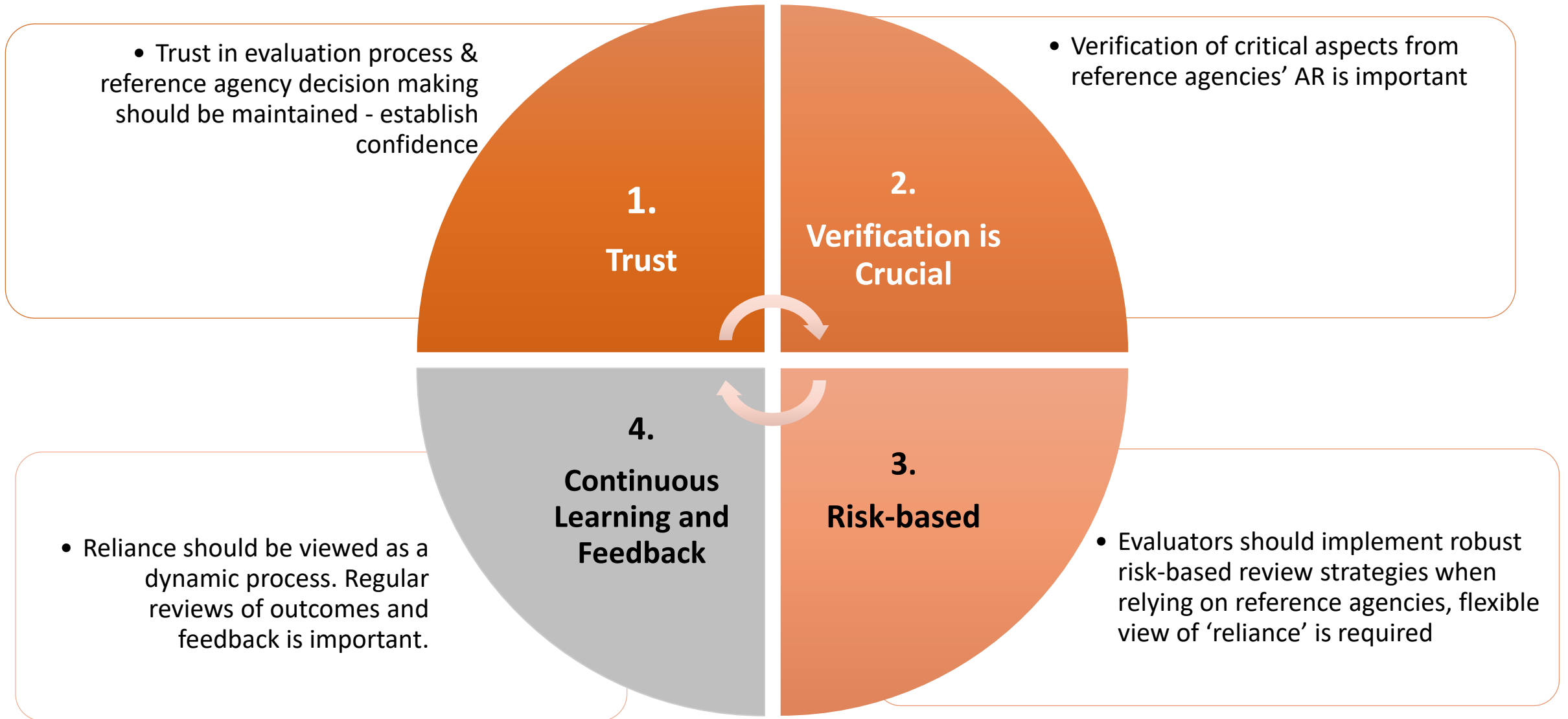
Different format of
assessment report
between reference
agencies

**Inconsistencies
of data**

Dossier checklist vs dossier
submitted to NPRA vs
assessment report by the
chosen reference agency

**Training &
Capacity
Building**

Reliance- Lesson learnt





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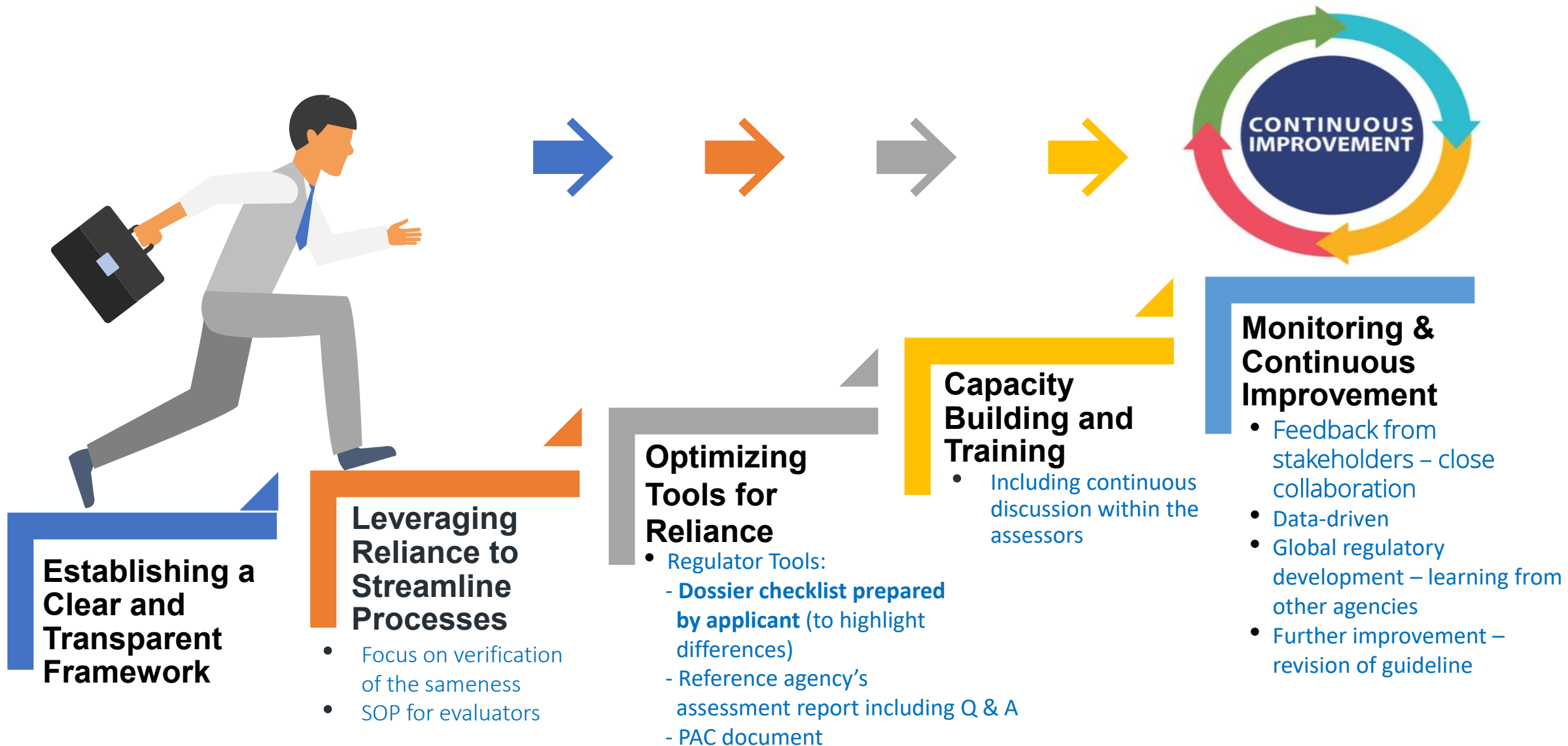
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**Best Practices: Recommendations for
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Best practices: Recommendations for implementing reliance



**Thank you for your
kind attention**

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