

Experience in Implementing Reliance Pathways for NDA and PAC

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PRESENTATION OUTLINE

- I. Introduction and Regulatory Framework
- II. Implementation of Reliance in the Philippines
- III. Experience with NDA vs PAC reliance
- IV. Framework vs Operational Reality
- V. Operational Challenges in PAC Reliance
- VI. Conclusion and Way Forward

I. Introduction and Regulatory Framework

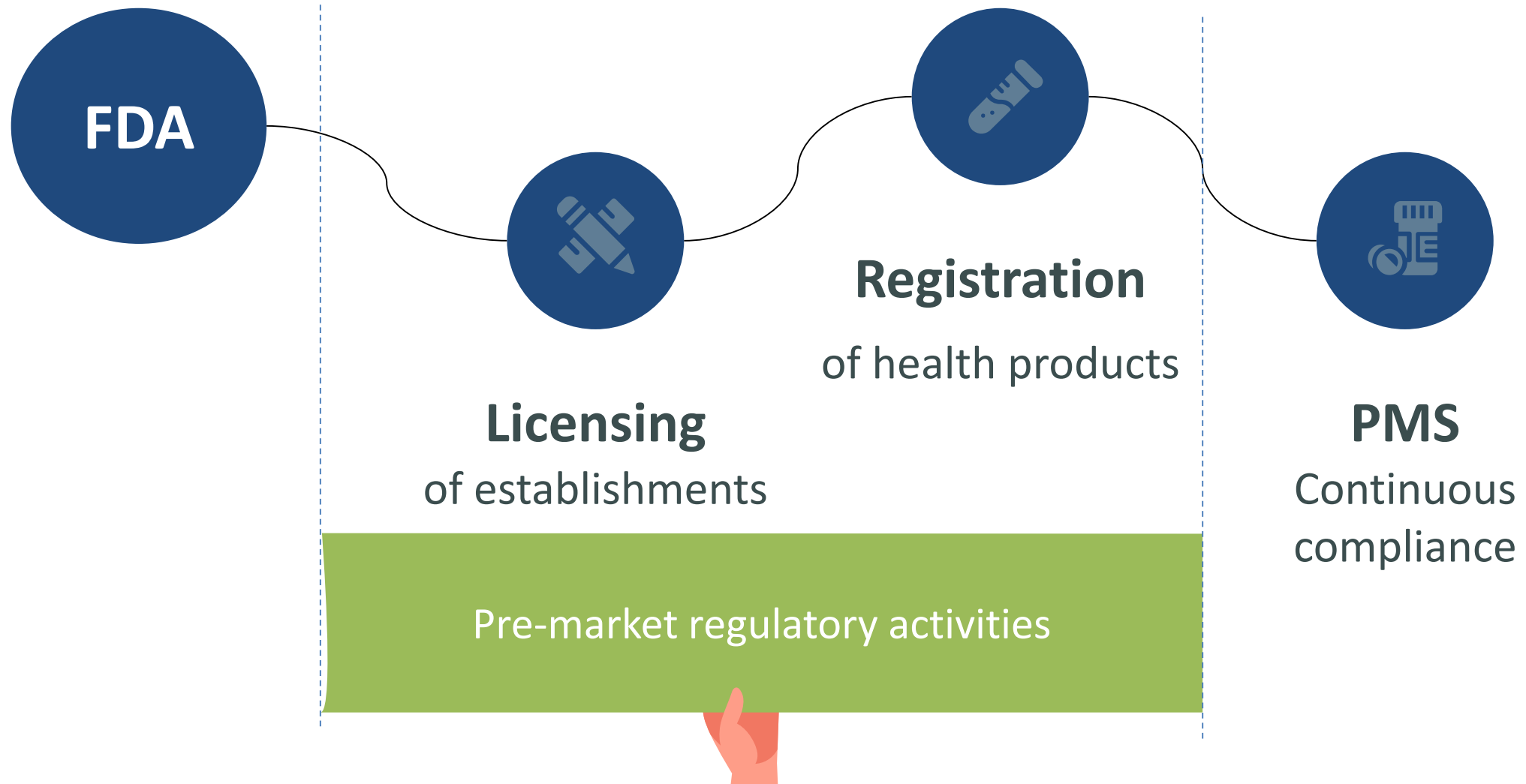


LEGAL BASES: RA 3720 and RA 9711

“To guarantee the **safety, quality, purity, efficacy** of health products in order to protect and promote the right to health of the general public.”



Regulatory Framework



II. Implementation of Reliance in the Philippines

II. Implementation of Reliance in the Philippines

A. Administrative Order No. 2020-0045

- **Subject: Establishing Facilitated Registration Pathways for Drug Products, including Vaccines and Biologicals**
- Issued on 22 September 2020
- Purpose
 - Accelerate access to medicines while ensuring quality, safety, and efficacy
 - Enable regulatory reliance (RDRAs)
 - Support efficient FDA processes (Ease of Doing Business)
- Mechanism: Reliance Pathways
 - Abridged Review
 - Verification Review
 - Collaborative Procedure

II. Implementation of Reliance in the Philippines

B. FDA Circular No. 2022-004

- **Subject: Implementing Guidelines on the Abridged and Verification Review Pathways for New Drug Registration Applications in accordance with AO No. 2020-0045**
- Issued on 16 June 2022
- Purpose
 - Operationalizes AO 2020-0045 for reliance pathways
 - Covers abridged and verification review (NDA and PAC)
 - Institutionalizes regulatory reliance using RDRA assessments

II. Implementation of Reliance in the Philippines

B. FDA Circular No. 2022-004

- **Subject: Implementing Guidelines on the Abridged and Verification Review Pathways for New Drug Registration Applications in accordance with AO No. 2020-0045**
- Implementing Guidelines Summary
 - Must apply within 3 years from RDRA approval
 - Only one pathway per application
 - Product must be identical to RDRA-approved product (formulation, manufacturing, specs, indications)
 - Requires complete and unredacted RDRA assessment reports
 - FDA may still request additional data if needed

II. Implementation of Reliance in the Philippines

B. FDA Circular No. 2022-004

- **Subject: Implementing Guidelines on the Abridged and Verification Review Pathways for New Drug Registration Applications in accordance with AO No. 2020-0045**
- Core Documentary Requirements/Review Approach
 - Formal request + identification of RDRA/s
 - Assessment reports (completed/unredacted)
 - CPP or equivalent
 - ICH CTD/ACTD dossier + stability data (Zone IVB)
 - Labeling aligned with RDRA (+PH requirements)
 - Sworn assurance confirming full compliance
 - Risk-based reliance + limited independent assessment
 - FDA PH evaluates suitability to PH context and benefit-risk using submitted data
 - May consult clinical experts if needed

II. Implementation of Reliance in the Philippines

B. FDA Circular No. 2022-004

- **Subject: Implementing Guidelines on the Abridged and Verification Review Pathways for New Drug Registration Applications in accordance with AO No. 2020-0045**
- Timelines

Type of Application / Pathway	Timeline
Abridged Review	not more than 45 working days
Verification Review	not more than 30 working days
Post-approval change/s	

II. Implementation of Reliance in the Philippines

B. FDA Circular No. 2022-004

- **Subject: Implementing Guidelines on the Abridged and Verification Review Pathways for New Drug Registration Applications in accordance with AO No. 2020-0045**
- List of Reference Drug Regulatory Agencies

List of Reference Drug Regulatory Agencies (RDRAs)*

1. Therapeutic Goods Administration (TGA) – Australia
2. Federal Agency for Medicines and Health Products (FAMHP) – Belgium
3. Health Canada (HC) - Canada
4. European Medicines Agency (EMA) - European Union
5. French National Agency for Medicines and Health Products Safety (ANSM) - France
6. Federal Institute for Drugs and Medical Devices (BfARM) – Germany
7. Paul-Ehrlich-Institut (PEI) – Germany
8. Italian Medicines Agency (AIFA) – Italy
9. Pharmaceuticals and Medical Devices Agency (PMDA) – Japan
10. Medicines Evaluation Board (MEB) – Netherlands
11. Health Sciences Authority (HSA) – Singapore
12. Swiss Agency for Therapeutic Products (Swissmedic) - Switzerland
13. Medicines and Healthcare Products Regulatory Agency (MHRA) - United Kingdom
14. US Food and Drug Administration (USFDA) – United States of America

II. Implementation of Reliance in the Philippines

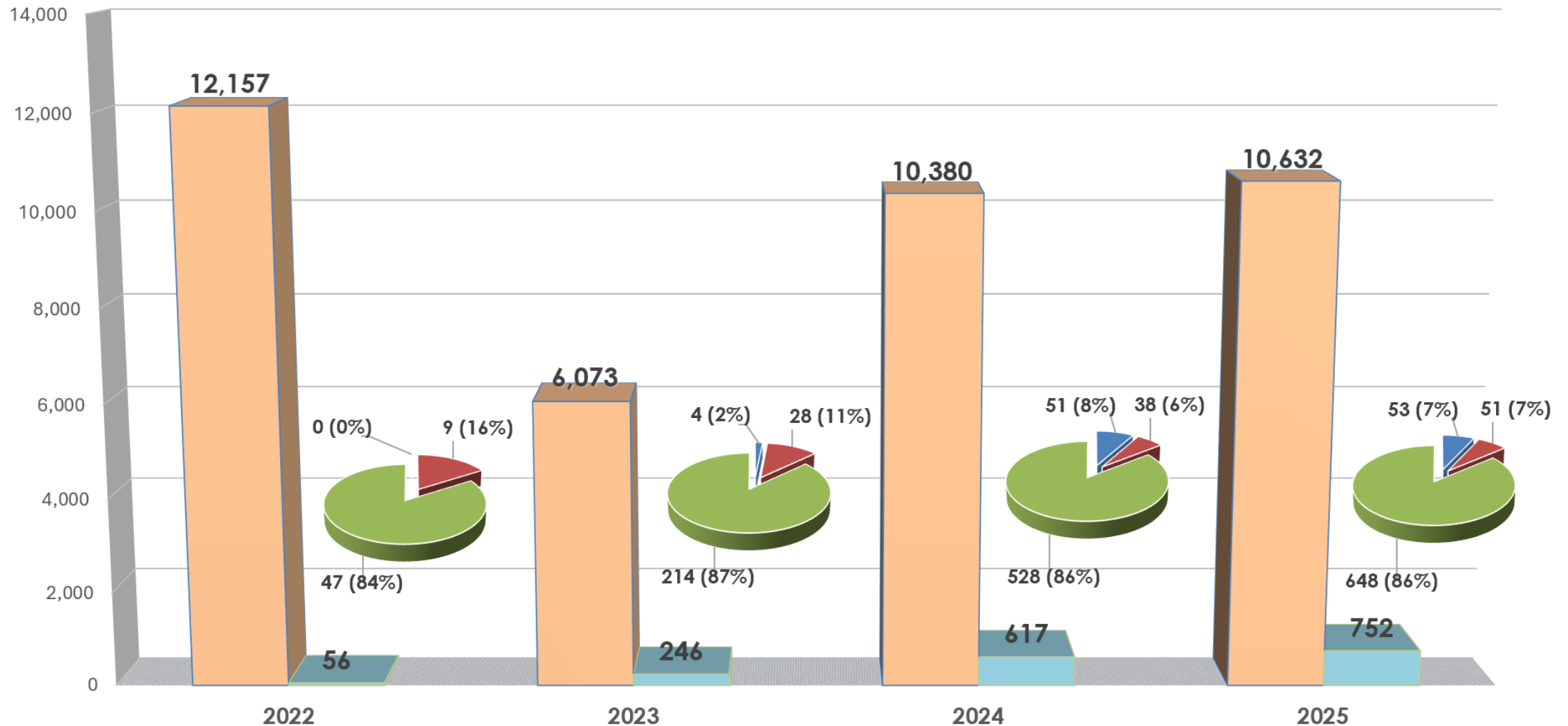
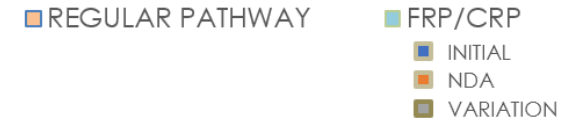
C. FDA Circular No. 2022-004-A

- **Amendment to FDA Circular No. 2022-004**
- Issued on 15 February 2024
- Purpose of Amendment
 - Expands implementation reliance pathways under AO No. 2020-0045
 - Addresses gaps from initial rollout of FDA Circular No. 2022-004
 - Enhances coverage, RDRA list, and applicability
 - Extends reliance pathways to GENERIC DRUGS
 - Maintains eligibility criteria, documentary requirements, sworn assurance requirement
 - Removes the 3-year validity requirement from RDRA approval
 - Updated RDRA list (+MFDS Korea, SFDA Saudi Arabia)

II. Implementation of Reliance in the Philippines

Reliance Pathway Utilization

TOTAL APPLICATION FOR YEAR 2022 - 2025



II. Implementation of Reliance in the Philippines

Reliance Pathway Utilization

- Regular pathway remains dominant across all years
- Volumes throughout the years suggest operational adjustments, backlog shifts, and transition to reliance
- Adoption of reliance pathways – steady and significant growth throughout the years
- Indicates increasing confidence and uptake over time
- Reliance is primarily used for post-approval changes
- FRP/CRP remains small vs regular pathway
- Reliance is complementary, not yet dominant

III. Experience with NDA vs PAC Reliance

III. Experience with NDA vs PAC Reliance

A. NDA Reliance

- More structured and well-defined pathway
- Clearer scope of reliance
- Greater alignment with reference authority decisions
- Generally more predictable timelines
- Still requires local review/verification for:
 - Labeling
 - Administrative requirements
 - Critical quality aspects

III. Experience with NDA vs PAC Reliance

B. PAC Reliance

- More complex and variable in nature
- Differences in variation classification across jurisdictions
- Limited clarity on scope of reliance
- Greater dependence on:
 - Complete documentation
 - Specificity of reference approval
- Less predictable timelines due to:
 - Need for additional clarification
 - Local requirements

IV. Framework vs Operational Reality

IV. Framework vs Operational Reality

Framework (Expected Outcomes)	Operational Reality (Observed in Practice)
Streamline review process	Continued need for local verification/review
Reduced duplication of effort	Variability in application of reliance
Clear reliance scope	Ambiguity in PAC classification and scope
Faster and more predictable timelines	Inconsistent and less predictable timelines

V. Operational Challenges in PAC Reliance

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Observations in Implementation

1. Reliance framework is established and in use.
2. However, operational implementation remains challenging.
3. Challenges are more pronounced in PACs.
4. Key factors affecting implementation include:
 - Handling of reference information
 - Documentation and explanation requirements
 - Variability in review timelines

V. Operational Challenges in PAC Reliance

Handling of Reference Information

- Limited access to complete or unredacted assessment reports
- Reliance on publicly available or partial information
- Need for additional verification and clarification

V. Operational Challenges in PAC Reliance

Documentation and Explanation Requirements

- Incomplete or inconsistent submissions
- Lack of alignment between submitted changes and reference approvals
- Additional information requests to support evaluation

V. Operational Challenges in PAC Reliance

Variability in Review Timelines

- Dependence on completeness and quality of data
- Additional time required for local verification
- Inconsistencies due to classification and scope issues

To better demonstrate how these factors translate into operational challenges, we present selected examples based on evaluator experience in handling reliance applications.

V. Operational Challenges in PAC Reliance

Observed Challenges from Evaluator Experience

1. Variation classification misalignment
 - Differences in classification of post-approval changes between the PH and RDRAs (e.g., minor vs major variations) create inconsistencies in reliance application.

2. Mismatch between approval and submitted change details
 - RDRA approvals are sometimes generalized, while applicant submissions contain more detailed or expanded post-approval changes, requiring additional clarification.

V. Operational Challenges in PAC Reliance

Observed Challenges from Evaluator Experience

3. Limited access to complete assessment information
 - Approval documents may contain redacted information (e.g., contact details or key data), which limits verification and is inconsistent with the expectation for complete, unredacted assessment reports.

4. Lack of specificity in approval letters
 - Some approval letters do not clearly specify the exact changes approved, making it difficult to determine the scope of reliance.

V. Operational Challenges in PAC Reliance

Observed Challenges from Evaluator Experience

5. Insufficient supporting documentation
 - In some cases, only email confirmations are submitted without clear documentation of the approved changes, leading to challenges in validation.

6. Changes outside of the scope of reference approval
 - Applications may include post-approval changes that are not covered by the reference authority approval, requiring reclassification to the standard/regular regulatory pathway.

V. Operational Challenges in PAC Reliance

Observed Challenges from Evaluator Experience

7. Additional local requirements affecting efficiency
 - Additional data requirements (e.g., holding-time studies in line with the ASEAN Variation Guidelines such as MaV-4) may still be required locally, even if not required by the reference authority, leading to delays and reduced efficiency of the reliance pathway.

VI. Conclusion and Way Forward

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Conclusion

- ✓ Framework established, but operational gaps remain
- ✓ Challenges in reference information handling, documentation, timeline predictability
- ✓ Challenges more pronounced in PAC reliance

VI. Conclusion and Way Forward

Way Forward

- ✓ Enhance clarity on scope of reliance (PAC)
- ✓ Improve access to complete reference information
- ✓ Strengthen documentation and submission standards
- ✓ Promote consistency in application of reliance
- ✓ Capacity-building and knowledge sharing
- ✓ Establish dedicated reliance unit (ongoing initiative)

VI. Conclusion and Way Forward

Way Forward: Dedicated Reliance Unit

- ✓ Establish dedicated unit for reliance applications
- ✓ Focused handling of NDA and PAC reliance
- ✓ Improve consistency and expertise
- ✓ Expected benefits:
 - Better handling of reference information
 - Improved documentation assessment
 - More consistent application of reliance principles
 - Faster and more predictable timelines

END

THANK YOU!



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