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International Federation
of Pharmaceutical
Manufacturers & Associations

Post-approval change management and its impact on vaccine supply

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Agenda

1. Complexity of Global Vaccine Post-Approval Change (PAC) Management.
2. 2025 IFPMA-Clarivate PAC Assessment for Biological Products – Viet Nam
3. Current PAC Framework for Vaccine in Viet Nam
4. Example of Further Convergence Opportunity
5. Regulatory Reliance for PACs
6. Considerations for Efficient PAC Management

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The lifecycle of vaccines is more complex compared to small-molecule drugs due to their inherent biological complexity.

Vaccines are biological products often formulated with multiple antigens, with or without adjuvants, provided in liquid or freeze-dried presentations.

Why Are Changes Needed in Lifecycle?

- New knowledge on safety and effectiveness
- Innovation in manufacturing and controls
- Ensure compliance with new regulatory requirement / pharmacopoeia updates
- Maintain and expand supply

Complex Environment – Challenges Post-Approval

Regulatory Authority Perspective

Post-approval change

One change

One submission
One assessment

Vaccine Companies Management

Post-approval change

Multiple submissions
Multiple assessments

Lack of harmonization / convergence in the management of Post-Approval Changes (PACs)

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Global Complexity for Vaccine PAC Management

Siloed Regulatory Approach

- Each change can potentially impact 50-100 licenses worldwide [1]
- **Divergence** in change categorization, review/approval timelines (3 months to 48 months) [1]
- Different data requirements ☾ multiple dossier versions

Supply Chain Implication

- Delayed Implementation of Improvements
- **Supply Chain Fragmentation**: Varying approval timelines
- **Increased Shortage Risk:** Multiple product versions ☾ logistical challenge!
  - Example: In one year, 83 batches of a Vaccine product were produced according to **55** different variations[2].

Ref:
1. Case Studies to Illustrate IFPMA Position Paper on the Handling of Post-Approval Changes to Marketing Authorizations, Nov 2018, IFPMA
2. Anders V. et.al., Approaches to Design an Efficient, Predictable Global Post-approval Change Management System that Facilitates Continual Improvement and Drug Product Availability. Therapeutic Innovation & Regulatory Science (2024) 58:433–442

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Global regulatory approaches to PAC in biotherapeutic products

- A comparative analysis against WHO guidelines

IFPMA - Clarivate, October 2025

Region	ICH RA Members	ICH Observers	Non-ICH Members
APAC (8)	China, South Korea, Singapore, Taiwan	India, Malaysia, Thailand	**Viet Nam**
LATAM (5)	Brazil, Mexico, Argentina	Peru, Colombia	
MEA (8)	Egypt, Saudi Arabia, Turkey, Jordan	Nigeria, South Africa	Ghana, Rwanda
Europe (1)	European Union (EC)		

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3. PAC CMC Scenarios in APAC

Viet Nam

Vietnam - CMC changes	Drug substance	Drug product
1. Manufacturing Facility changes		
2. Manufacturing Process changes		
3. Pharmacopoeia standard/monograph changes		
4. Specification and/or Analytical methods changes		
5. Shelf-life extension/changes		

Parameters analysed: Categorization, Requirements and Timeframes.
Convergence level of country vs WHO guidance:
Low convergence (1 or none of the 3 parameters aligned)
Medium convergence (2 parameters aligned)
High convergence (all 3 parameters aligned)

References

1) Circular No. 12/2025/TT-BYT: Regulations on the Registration of Drugs and Medicinal Ingredients
2) ASEAN Variation guideline for pharmaceutical products

Convergent

It has regulation on variations (Q1)

It is applicable to other modalities (Q3)

It has risk-based categorization (Q4)

It has timelines for approval of changes (Q5)

It has grouping of changes (Q6)

It has submission format in CTD (Q7)

It has grace periods for PAC (Q10)

Non-Convergent

It does not have specific guidance for biotherapeutics (Q2)

It does not have scientific advice (Q8)

It does not have reliance for PAC (Q9)

Putting Vaccine PAC into Context - Convergence

- Vaccines PAC framework available in Registration circular 12/2025/TT-BYT, Appendix II (Section C, III Vaccines).
- **Convergence on PAC supporting documents -** Appendix II (Section C, III Vaccines) refer to WHO vaccine PAC guidelines TRS 993 and EMA for dossier requirements.
- Grouping of changes are allowed.

Considerations for Further Improvement

- **Greater convergence with WHO/EMA on risk-based categorization of quality, safety, efficacy changes** (e.g., minor quality changes such as specification tightening, etc.)
- **Greater convergence of approval timelines for quality changes (WHO/EMA: 3-6 months) ☾ Predictability is key**
- In addition to high level principles in Annex II, consider to outline **clear guidance on criteria and supporting data requirement** to avoid misalignment in interpretation and understanding.
- **Reliance for PAC** are being adopted in ASEAN region (e.g., Singapore, Malaysia, etc.), opportunity for Viet Nam to further optimize PAC process.

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Example of Further Convergence Opportunity

Example: Manufacturing facility for the final product (including formulation/ filling and primary packaging)

	WHO (same applicable for EMA / US FDA)	**Viet Nam**
Categorization	Major / Moderate	Application for new certificate of registration (new MAA)
Dossier Requirement	Affected CMC section (M3) and supporting documents demonstrating quality post-change	Entire CTD from M1 to M5
Timeline	3-6 months	>12 months

- Delayed supply from new site.
- Update needed for Innovative Pharmaceutical Product (IPP) and Prescribing Bidding for Supply of Drugs for Public Health Facilities.
- Duplication of license in life-cycle maintenance.

References:

1) WHO Guidelines on procedures and data requirements for changes to approved vaccines TRS993
2) US FDA Guidance for Industry: Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products
3) Guidelines on the details of the various categories of variation, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 (Official Journal of the European Union, C/2025/5045)
4) Circular No. 12/2025/TT-BYT: Regulations on the Registration of Drugs and Medicinal Ingredients

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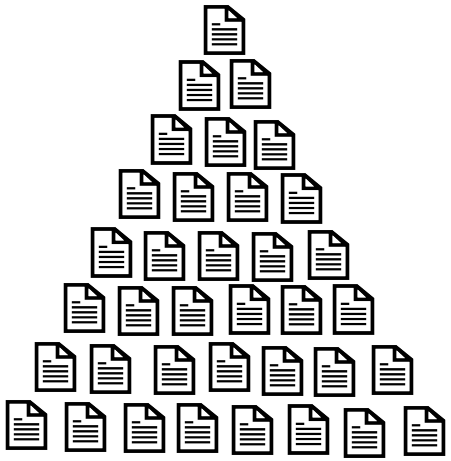
Strategic Benefits of Applying Regulatory Reliance for Lifecycle PACs

Reliance implemented for New Certificate of Registraion

Post-Approval Lifecycle Phase



Significant Optimization Opportunity with Reliance

New Certificate of Registration

- Relatively fewer in number but higher complexity in data review
- Example: EMA in 2024 – 114 positive opinions (46 new active substances)

Post Approval Changes

- Much higher volume compared to new certificate of registrations
- Example: EMA alone - >8000 in 2023 expected to rise >9K in 2026

References – (1) EMA – Human Medicines in 2024 https://www.ema.europa.eu/en/documents/report/human-medicines-2024_en.pdf (2) EMA Final Programming Document 2025-2027 pp 57/223 https://www.ema.europa.eu/en/documents/report/final-programming-document-2025-27_en.pdf

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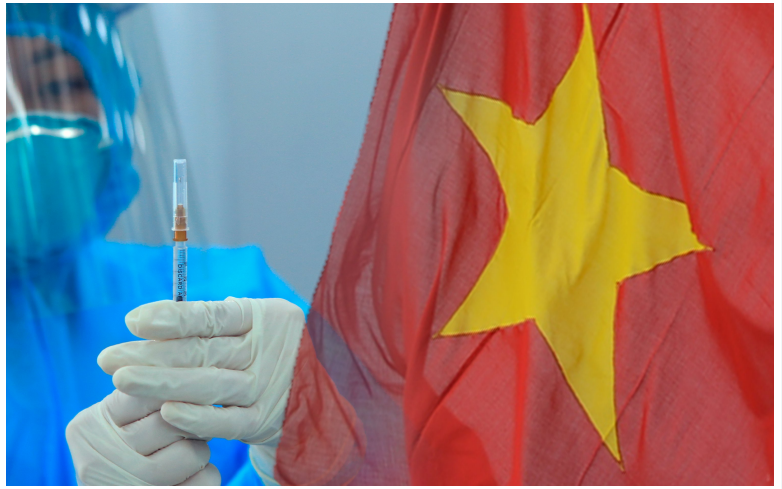
Considerations for Efficient Vaccine PAC Management

1. Convergence with WHO/EMA on risk-based change categorization
2. Clear guideline with categorization criteria and required data
3. Consistent and predictable approval timelines
4. Reliance

Predictable and Efficient PAC management

Robust and Stable Supply of Vaccines for Viet Nam



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Thank you!

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