Complexities of Life Cycle Management and the challenges for African Countries
An Industry Perspective

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Agenda

• Life Cycle Management Overview
• Post approval changes (PACs) – Variations
• Complexities & Consequences of Post Approval Changes
• Recommendations
• Conclusion
Life cycle management - Overview

Development
- Clinical
  - Phase 1, 2 & 3
  - Phase 4
  - Formulation
  - Delivery

Marketing Authorization
- CTD application
- NRAs queries management
- Labeling development and Launch plans
- Renewals

Variation Management (PAC)
- Safety Labelling updates
- Site transfers
- CMC changes
- MAH transfer
- New Indication
- Administrative change

Post Approval commitments
- Safety
- PV, PSUR,
- Safety update
- Stability
Why make Post Approval changes (PAC)?

Initial product registration is a critical milestone for the NRA and the manufacturer **BUT**, Continuous effort to improve existing medicines for sustainable supply, access to patients and Regulatory Compliance is as important.

- **New facilities(Site changes)**
- **New regulatory requirements**
- **Support Improvement of manufacturing process, analytical methods, quality etc**
- **Administrative changes (MAH address, name changes)**
- **Unplanned changes**
- **Updates to labeling information (new indications, safety updates)**
Complexities in the Management of PACs & Consequences

- **Country specific requirements** (stability studies, approval of Reference Country, Certificate of Pharmaceutical Product (CPP), commercial samples etc...)

- Difficulty in adhering to compliance.
- Complex supply, bridging stock of several versions.
- Risk of shortage or stock out for the patient.
- Delay in variation submissions following reference country approval.
- Challenges of Storage conditions for samples
- Generates additional Resources workload resulting in unpredictable timeline.

Different approval lead times worldwide denies Patients of early access to innovative medicines
Complexities in Management of PACs: Increased number of dossier versions...
Complexities in Management of PACs: Samples impact on lead time

1. Variation + artwork+ CPP
   - Preparation artwork/CPP obtention 6 months
   - Submission 1-3 months
   - Approval by NRA 0-6 months
   - Lead time for global preparation & variation approval 7-15 months

2. Variation+samples
   - Preparation artwork/CPP obtention 6 months
   - Sample manufacturing 3 months
   - Dispatch samples 3-5 months
   - Submission 1-3 months
   - Approval by NRA 0-6 months
   - Lead time for global preparation & variation approval 13-23 months
   - Industrial implementation
### Benefits of harmonized guidelines on PAC

**For Patients**
- Fast-track implementation ensures continuous access of medication to patients
- Promote patient safety by preventing stock out situation induced illicit market
- Increase patients trust in health institutions and pharma industry

**For NRAs**
- Regional rather than national assessment: Reliance will avoid duplication of effort.
- Reliance on approval of the Reference Country or WHO-Listed Authorities will reduce timelines and will optimize resources allocation.
- Reduction of work burden allowing to focus on activities with more added value (e.g. develop capabilities, tackle falsification...)

**For Pharma Industry**
- Facilitate regulatory compliance and sustainable supply
- Simplification of variations management across the globe
- Reduction of work burden allowing to focus on activities with more added value (e.g. develop new therapies, develop new technologies)
Conclusion

Recommendation for future harmonized guidelines on PACs

Convergence of regulatory requirements and/or reliance on approval of the Reference Country or WHO-Listed Authorities

WHO guidelines as reference

Harmonized requirements for variations – Regional expertise/reliance.

- **Risk Based Categorization of Changes**-Classification of variation (minor/major) based on a scientific and risk based approach-Major variation: reasonable and predictive review timelines (no more than 6 months)-Minor variation = no prior approval before implementation (notification)

- **Simplification**-artworks or mock up instead of commercial samples

- **Digitalization**- Submission of variations using electronic format ( USB Key)

- **For vaccines and biologic products**, minor variation with no impact on efficacy should be submitted as annual report after approval in the reference country located in ICH country
THANK YOU VERY MUCH !
MERCI !