Shaping the Environment

Post Approval Change Management

EFPIA position paper

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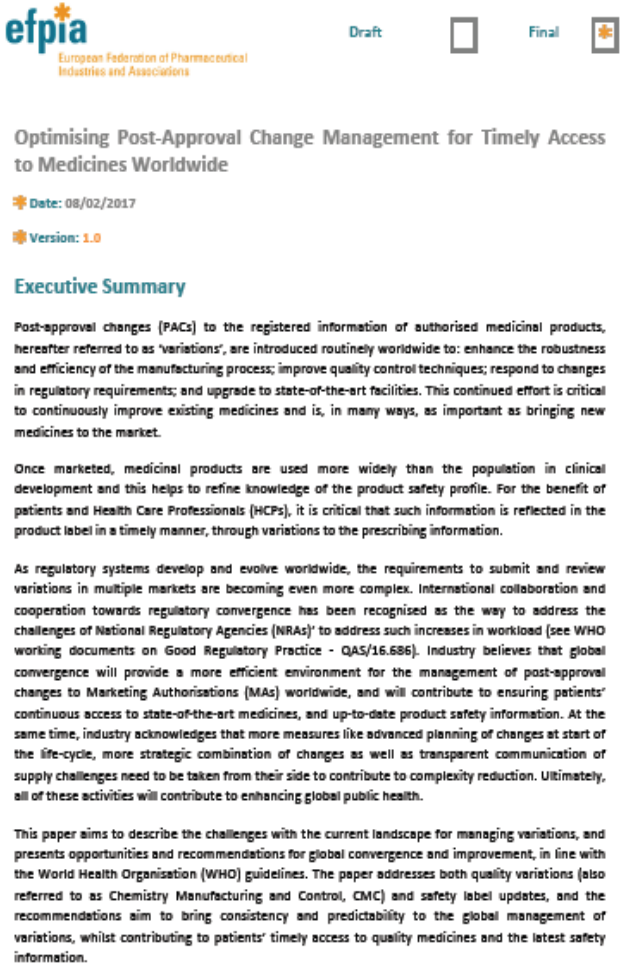
Optimising Post-Approval Change (PAC) Management for Timely Access to Medicines Worldwide - EFPIA position paper

Post Approval Changes (PAC) are essential to the Life Cycle Management (LCM) of a medicine or vaccine:

- Enhance robustness and efficiency of manufacturing process
- Improve Quality Control (QC) techniques
- Respond to changes in regulatory requirements
- Upgrade state-of-the-art facilities

This effort is critical to continuously improve existing medicines and is, in many ways, as important as bringing new medicines to market



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Optimising Post-Approval Change Management for Timely Access to Medicines Worldwide

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Executive Summary

Post-approval changes (PACs) to the registered information of authorised medicinal products, hereafter referred to as 'variations', are introduced routinely worldwide to: enhance the robustness and efficiency of the manufacturing process; improve quality control techniques; respond to changes in regulatory requirements; and upgrade to state-of-the-art facilities. This continued effort is critical to continuously improve existing medicines and is, in many ways, as important as bringing new medicines to the market.

Once marketed, medicinal products are used more widely than the population in clinical development and this helps to refine knowledge of the product safety profile. For the benefit of patients and Health Care Professionals (HCPs), it is critical that such information is reflected in the product label in a timely manner, through variations to the prescribing information.

As regulatory systems develop and evolve worldwide, the requirements to submit and review variations in multiple markets are becoming even more complex. International collaboration and cooperation towards regulatory convergence has been recognised as the way to address the challenges of National Regulatory Agencies (NRAs)' to address such increases in workload (see WHO working documents on Good Regulatory Practice - QAS/16.686). Industry believes that global convergence will provide a more efficient environment for the management of post-approval changes to Marketing Authorisations (MAs) worldwide, and will contribute to ensuring patients' continuous access to state-of-the-art medicines, and up-to-date product safety information. At the same time, industry acknowledges that more measures like advanced planning of changes at start of the life-cycle, more strategic combination of changes as well as transparent communication of supply challenges need to be taken from their side to contribute to complexity reduction. Ultimately, all of these activities will contribute to enhancing global public health.

This paper aims to describe the challenges with the current landscape for managing variations, and presents opportunities and recommendations for global convergence and improvement, in line with the World Health Organisation (WHO) guidelines. The paper addresses both quality variations (also referred to as Chemistry Manufacturing and Control, CMC) and safety label updates, and the recommendations aim to bring consistency and predictability to the global management of variations, whilst contributing to patients' timely access to quality medicines and the latest safety information.

http://www.efpia.eu/uploads/EFPIA_Post_Approval_Change_Position_paper_FINAL_Feb2017.pdf

Current regulatory landscape for PAC: major Quality and CMC* challenges ultimately have an impact on access

Observations	Impact
Heterogeneous classification systems	Multiple approved variants of a product have to be managed adding significant complexity on the supply chain and increase compliance risk
Specific local requirements	Potential impact on submissions elsewhere
Unpredictable and variable approval timelines	Resource consuming requests for regulators to have exceptions to maintain supply
Divergent decisions by regulatory bodies	Difficulty to plan submission and implementation may results in stock outs
Variable implementation periods	Reduced ability to reply to country demands, which can be sudden, in a timely and predictable manner

*CMC = Chemistry, Manufacturing and Control

Current regulatory landscape for PAC: Safety Labelling challenges ultimately have an impact on access

Observations	Impact
Approval process for safety label changes can be lengthy and unpredictable	Slower HCP and patient access to up-to-date product information resulting in increased risk to patient
Variable implementation periods	Consequences on pharmaco-vigilance surveillance based on approved product information
	Different versions of the label can be accessible on the internet (in different markets) leading to HCP and patient confusion

Proposals for improvement

Heterogeneous classification systems	- Unified risk-based variation classification system - Allow simultaneous submissions (i.e. grouping) - Stimulate NRA to work together and converge
Specific local requirements	- Converge requirements and eliminate unnecessary submission of data
Unpredictable and variable approval timelines	- Clear procedural guidance + appropriate, aligned timelines - Seek opportunities & solutions to enhance life cycle management
Divergent decision by regulators	- The above will optimise convergent decisions
Variable implementation periods	- Common implementation timings for the new change
Safety labeling review and implementation process can be lengthy &unpredictable	Independent, dedicated & expedited process for safety updates In the future, electronic labels could enable direct access to the most recent product information

Short to mid-term actions

Converge requirements through adoption of international standards (WHO) through a risk-based approach to the classification of variations, data requirements, and timelines.

Allow flexible implementation periods for technical and labelling variations

Dedicate resources for review and approval of safety labelling variations in an accelerated manner

Encourage exchange of knowledge between the review and inspection departments

Consider to focus resources to ensure that important public health aspects i.e. supervision of supply chain, counterfeits, pharmacovigilance, are in place. This may be more impactful than re-assessing a change already evaluated by other agencies.

Minimize the number of country-specific requirements

Longer term solutions

Implement best practices and principles from ICH Q12. Increasingly rely on the companies' Pharmaceutical Quality Systems (PQS) to effectively manage minor changes without the need to file variations

Stepwise Implement collaboration among regional NRAs that enables work-sharing, mutual reliance of assessments and, in the longer term, mutual recognition of approvals

Implement broad acceptance of e-labelling and progressive deletion of paper leaflets in the pack, in line with information technology capability in countries worldwide

Industry to improve planning of changes through the product life-cycle and seek to adopt new mechanisms, expected in the future, such as Post Approval Change Management Protocol

Conclusion

"A more efficient landscape for the handling of post-approval changes to MAs worldwide will contribute to enhancing global public health by ensuring patients' continuous access to state of the art medicines, and up-to-date product safety information. The potential benefits of alignment and harmonization include: reduced shortage/stockouts, faster access to product made with process improvements, and encouragement of new technologies."