European Federation of Pharmaceutical Industries and Associations

Current Achievements and Areas of Improvement in the Post Approval Change Management for Safety Labelling Updated in the Middle East Region (September 2023)

This document is aligned with and builds on the principles of the EFPIA position paper:

- Optimising Post-Approval Change Management for Timely Access to Medicines Worldwide https://www.efpia.eu/media/25953/efpia-post-approval-change-position-paper_final_feb2017.pdf
- Optimising Post Approval Change Management for Safety Labelling Updates in the Middle East Region https://www.efpia.eu/media/413097/optimising-post-approval-change-management-for-safety-labelling-updates-in-the-middle-east-region.pdf

1. Introduction

Safety labelling updates (SLUs) are changes made by pharmaceutical manufacturers to the labelling or package insert of a medication to communicate new safety information to healthcare providers and patients. SLUs are important because they help to ensure that patients and healthcare providers are aware of any new risks or side effects associated with the medication, allowing them to make informed decisions about its use and take appropriate precautions to avoid potential harm. They are an essential tool for keeping patients and healthcare providers informed about the latest safety information regarding medications, which can help to reduce the risk of adverse events and improve patient outcomes.

In the previous position paper entitled “Optimising Post Approval Change Management for Safety Labelling Updates in the Middle East Region”, we identified the limiting factors to rapid implementation of a safety update in the region and provided recommendations to accelerate approvals of SLU.

In this position paper, we will explore the milestones already achieved in the middle east region and will identify the areas which requires improvement for the safety labelling updates process according to the results of a survey conducted on June 2022 by EFPIA Middle East Regulatory Network (MERN). The paper also provides recommendations to ensure an efficient and timely safety labelling update process.

2. Current Achievements in the Middle East Region

Over the past few years, several milestones have been attained in the Middle East region in order to improve and accelerate the implementation of safety labelling updates. In this survey, our primary focus was directed towards the electronic submission, the legalisation of CPP, the possibility of acceptance of eCPP and the review timelines.

The results of the survey emphasize that some countries in the region have already implemented electronic systems for the submission of regulatory applications, including SLUs. In addition, the CPP is no longer requested for submission, or its legalization is currently waived in some countries in the region. Moreover, the eCPP is accepted in most countries in Middle East.

In terms of timelines, according to the survey, the approval of SLUs is granted within few days and the timelines are accelerated (within one month from submission) in few Gulf countries. While some countries expect immediate implementation, a grace period of 6-9 months is automatically granted in some countries and can be extended if needed.
Also, few countries currently accept the parallel submission of variations. However, within the survey results, not all companies are ensuring the same information due to technical challenges of the parallel submission.
To conclude, while significant strides have been made in recent years, further improvements are necessary to fully maximize the effectiveness of the post-approval change management process for safety labelling updates in the Middle East region.

3. Areas for improvement / Limiting factors to rapid implementation in the region:

Until the present time, all SLU submissions are not immediate notifications based on reference country approval, and approval is requested from National Regulatory Authorities (NRAs) for implementation in most countries. This is not optimal for patient safety in the region and it is noted and highly recognized that few NRAs already use notification process, and some have taken necessary actions to accelerate approvals of SLU.
Some countries in the region still do not have online portals for submission and an appointment is required to submit safety updates. Moreover, the parallel submissions are not accepted in some countries which leads to delay in submissions, approvals, and implementation. Approval timelines remain a challenge for some countries. The reasons for such delays can differ from country to country, but reflect the difficulties faced by industry and regional health authorities
Furthermore, it should be noted that, in contrast to other countries in the region, eCPP legalisation is still requested in several countries, and waiving of legalisation may be accepted on a case-by-case situation. In the same context.
Finally, the extension of grace period is not accepted in some Middle East countries.

4. Recommendation

EFPIA recommends a set of actions to facilitate SLUs management, noting that some of these are already enacted in some Middle East NRAs' guidance.

Prioritization of safety labelling update with prior approval by reference agency using facilitated pathways

- Using the concept of reliance and simplifying the review procedure.
- Approval procedures for submission of SLUs, after reference country approval, should be:
    - Do & Tell or notification to support alignment with reference label. Otherwise inconsistencies will drive complex dependency issues and confusion to Health Care Professionals (HCP) and patients.

Classification of SLUs and procedural guidance

- Converge of requirements through the adoption of international standards for risk-based classification of SLUs, consequent procedure approval type should be Do & Tell.
- In specific cases where NRA will still need to conduct a review, then to consider a reasonable review timeline (e.g., max. 1-3 months).
- To streamline the process of implementation and shared pack management across the Middle East.

The recommendation would be to follow the principles outlined in:

- **EU Variation guideline** (2013/C223/01) (for small molecules – see WHO guidelines below for other products) : LexUriServ.do (europa.eu)
- **WHO guideline on procedures and data requirements for changes for approved vaccines :** Guidelines on procedures and data requirements for changes to approved vaccines, Annex 4, TRS No 993 (who.int)
- **WHO Guidelines on procedures and data requirements for changes to approved biotherapeutic products, Annex 3, TRS No 1011 :** annex_3_extract_who_trs_1011_web.pdf

Strategic management of changes or activities

- Submission and review of SLUs should not be limited by ongoing other variations such as CMC, renewals, or baseline eCTD application.
- Encourage exchange of knowledge between the review and inspection departments to prevent drug shortages.

Dossier Content

- Minimize the number of country-specific requirements such as local artworks.
- Harmonize requirements across ME.
- Content to be limited to:
  - Notification Letter with SLU description
  - Approved Reference Country Label
  - Document showing the updated label.
  - Comparison of new and existing label
- Remove the need for the legalization of documentation.
- Leverage use of Reference Agency website for verification of approved labels.
- Consider commitments (post-approval) to allow for timely approval and implementation of SLU.

5. Conclusion

In conclusion, comparing to the previous position paper entitled "Optimising Post Approval Change Management for Safety Labelling Updates in the Middle East Region", and after reviewing the current regulatory landscape in the Middle East region in terms of Safety Labelling Updates Management, several high priorities were already achieved including the reduction of the country specific requirements such as legalised CPP, and the prioritisation of safety labelling update with prior approval by reference agency using facilitated pathways (for, eg, considering SLUs as a notification in Lebanon), but inconsistencies between countries continue to be a challenge in the region.

Equally important, some high priorities remain pending including but not limited to the use of reliance to simplify the review procedure, the streamlining of the implementation process and shared pack management across the Middle East, in addition to considering the post-approval commitments to allow timely approval and implementation of SLUs.

EFPIA MERN has identified opportunities for simplification and harmonization of the Review-Approval-Implementation Process in alignment with WHO recommendations for good regulatory practice trs1033-annex11-good-practices-for-regulation-of-medical-products.pdf (who.int), global convergence and processes simplification that ensures continuous patient access to safe, well tolerated, high quality and compliant medicines. The EFPIA MERN recognizes and welcomes the efforts undertaken by many NRAs of the Middle East region that yielded simplified, faster procedures through notification process and reliance on

reference agency label approval. Not only will this ensure timely safety labeling updates, but also ensures faster implementation and access of the most updated label to Health Care Professionals and patients.