Post-approval Changes for Biologics in Latin American Markets

EFPIA LATAM Network
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Overview

Global life-cycle management of biologic products, including biotherapeutics, biosimilars, and vaccines, is complex and there is a lack of harmonization/ alignment among the global drug regulatory agencies.

Not only post-approval change regulations vary globally, but also the time it takes for the drug regulatory agency to review and approve the changes differs from country to country. This creates challenges for the regulated biopharmaceutical industry, as the change cannot be implemented globally. The result is complexity for the manufacturer and co-existence of 'variants' of the product in the market. More importantly, this complexity results in delayed access to innovation, increased costs of the medicines and eventually supply constraints.

The 16th International Conference of Drug Regulatory Authorities (ICDRA) recommended that WHO assist Member States in ensuring regulatory oversight throughout the lifecycle of biotherapeutic products.

Summary of Industry Position

EFPIA believes in one global standard for post approval changes to facilitate innovation, continuous improvement and enhance availability of safe and effective medicines and vaccines for patients.[1]

EFPIA suggests that the Latin American market's drug regulatory agencies follow the 'WHO guidelines on procedures and data requirements for changes to approved biotherapeutic products'[2] in order to assure their continued quality, safety and efficacy, as well as continuity in supply and access. And for vaccines, follow the 'WHO guidelines on procedures and data requirements for changes to approved vaccines'.[3]

The WHO guidelines classify the changes based on the potential effect of the quality change (for example, manufacturing change) on the quality attributes (that is, identity, strength, purity and

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[1] EFPIA Post-Approval Change Position Paper

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[2] WHO Guidelines on procedures and data requirements for changes to approved biotherapeutic products
http://www.who.int/biologicals/areas/biological_therapeutics/Annex_3_WHO_TRS_1011_web-7.pdf?ua=1

[3] WHO Guidelines on procedures and data requirements for changes to approved vaccines (Annex 4, TRS 993, 2015)

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potency) of the biotherapeutic product, and on the potential impact on the safety or efficacy of the product. A post-authorization change might be categorized as:

- a major quality change
- a moderate quality change
- a minor quality change

In addition, there are administrative changes with no impact on safety, efficacy and quality of the finished product. Therefore, no assessment is needed, and the company can implement the change. GMP documents (if impacted) can be reviewed during GMP inspections.

Some of the principles to be applied are:

- Reliance on post-approval changes already approved by reference regulatory agencies such as FDA and EMA/EC
    - EFPIA recommends consulting the WHO good regulatory practices as a guide for regulatory reliance between national regulatory authorities
- Short timelines of assessment should be considered for labeling changes especially those linked to safety variations that would ensure the safe use of the medicine
- Short assessment timelines also for new innovative applications of the product such as new therapeutic indications for unmet needs, or new formulations for population groups like pediatrics
- Establish clear procedures and mechanisms, including timeline, for the review of a submission or notification for a proposed post-approved change, taking into account technological changes
- Possibility of combining different related changes in the same package
- Possibility of combining different administrative changes in the same package
- Allow flexibility in terms of procedure and data requirements when scientific justified

EFPIA contributed to and is also supportive of the position being developed by ICH (guideline ICH Q12).[4] Although draft ICH Q12 guideline is a different approach to the WHO guideline, they are not incompatible, they are complementary.

EFPIA emphasizes the importance of training to ensure consistent interpretation and implementation of WHO guidelines, and suggest collaboration with academia and industry to accomplish this goal. If well understood and implemented, the concepts and tools in the WHO guidelines would reduce regulatory uncertainty and result in a more efficient post-approval chemistry, manufacturing, and control changes.

[4] ICH Q12 - Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management
https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q12/Q12_Draft_Guideline_Step2_2017_1116.pdf