

# Change in the primary packaging of tablets from glass bottle to blister

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## Introduction

All medicinal products need to be appropriately protected and packaged in containers that conform to prescribed standards. It is of utmost importance that the products are protected from moisture and light and that the leaching of extractable substances into the packaging/containers is prevented. There should be no chemical interaction between the container and the product.

Primary packaging is the material that is used for the containment, protection, handling, delivery and presentation of a product that is provided to a patient at the point of sale. It is in direct contact with the product and is often referred to as retail packaging or POS (Point-of-Sale) Packaging. The main purpose of primary packaging is to preserve the product as well as provide key information to the patient.

Packaging is used in order to provide appropriate protection and containment of a medicinal product during its shelf-life. The product should be protected during storage, distribution and until it is consumed by the patient. The packaging should also provide identification information regarding the product.

Packaging must provide protection against climatic conditions biological, physical and chemical hazards and must be economical. The package must ensure adequate stability of the product throughout the shelf life. During a product's life cycle, a change in the primary packaging may be required due to various reasons. In this particular case a change was required due to disposal of equipment used for packaging in a glass bottle. The change was

documented and evaluated within the company's change management system and appropriately justified.

## Change control process

Change control is a systematic approach to all changes of the product, process or both that can have direct or indirect impact on the quality of the finished medicinal product/medical device and quality system. In order for this change to be successfully implemented a series of activities must be done such as: stability testing under ICH and long-term conditions and monitoring of the results, packaging validation, regulatory activities etc.

### *Stability testing*

Stability of a pharmaceutical product could be defined as the capability of the product to remain within its physical, chemical and microbiological specifications while contained in a specific container/closure system. (Kommanaboyina and Rhodes, 1999). Stability studies are required to be conducted in a planned way following the guidelines issued by ICH, WHO and or other agencies. (Bajaj et al., 2012). In order to change immediate packaging of the product, relevant stability studies should be started under ICH/VICH conditions and relevant stability parameters should be assessed in at least two pilot scale or industrial scale batches and the manufacturer should have at least 3 months satisfactory stability data at the disposal before submission of variation. In this particular case two industrial batches were placed under accelerated and long-term conditions for stability testing.

### *Packaging validation*

Packaging validation is establishing documented evidence, which provides a high degree of assurance that a specific packaging process, will consistently provide a product which meets regulatory approved specification criteria. For the Packaging validation process, a Blister packaging validation matrix exists, with product grouping and risk assessment, for evaluating the critical product and process parameters, and identifying representative worst-case product. Upon introduction of new product in the blister packaging process, re-evaluation of the risk assessment is performed, and decision is made for re-validation.

### *Regulatory activities and requirements*

In order to change immediate packaging of a product a variation should be submitted to all concerned regulatory agencies. This type of change entails change in the Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and mock-up as well as change in relevant parts of the dossier. Additional data that is required prior submission is appropriate data on the new packaging (comparative data on permeability e.g. for O<sub>2</sub>, CO<sub>2</sub> moisture) and proof that no interaction between the content and the packaging material occurs (e.g. no migration of components from the container into the product, as well as no loss of components from the product into the proposed container/primary packaging). (Guidelines 2013/c 223/01). Confirmation should be provided that the proposed new material complies with relevant pharmacopoeial requirements, as well as other regulatory requirements such as the legislation of the Union on plastic material and objects in contact with foodstuffs. This variation was classified as Type IB variation, meaning that the change can be implemented after approval of variation.

### **Conclusion**

In order for this change to be successfully implemented and to maintain/improve the quality of the product as well as ensure the safety of the patients, all described activities must be carried out in accordance to cGMP and regulatory requirements.

### **References**

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