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Short communication

Change control as a key GMP process directly linked to batch release

Ana Ivceska*, Vanja Bobevska, Ana Maslarova, Brankica Petkoska Skrtov, Jasmina Kimovska, Verce Jovanovska Jankovska, Ksenija Brzilova Milenkovikj, Natasha Kronevska-Svinarska, Elizabeta Karadzinska, Olivera Paneva

Alkaloid AD Skopje, Blvd. Aleksandar Makedonski 12, 1000 Skopje, North Macedonia

Introduction

Change control, implemented as part of the Pharmaceutical Quality System (PQS), governs the evidence chain by controlling modifications to materials, processes, equipment, analytical methods, computerized systems and documentation that could influence product quality or Marketing Authorisation (MA) compliance (European Commission, n.d.).

Change control represents a critical GMP process that ensures all changes potentially affecting the safety, quality, and efficacy of a medicinal product are appropriately controlled, assessed, approved, and documented. In accordance with Annex 16, all changes must be fully assessed, implemented, documented, and approved prior to batch certification, as they directly impact the Qualified Person's decision for batch release (European Commission, 2015). Documentation requirements applicable to change control activities are further defined in Chapter 4 of the EU GMP Guide (European Commission, 2011).

Materials

Every change in manufacturing process is to ensure process optimization and to ensure batch-to-batch consistency and a product that meets specification and MA requirements. Immediate-release tablets are a common type of pharmaceutical dosage form designed to release the active pharmaceutical ingredient quickly after ingestion. The formulation of immediate-release tablets is crucial in ensuring the drug's rapid release and absorption (Pharma Tips, n.d.).For immediate-release solid oral drug products containing a high-solubility drug substance, the dissolution criteria are Q = 80% in 30 minutes (Food and Drug Administration (FDA), n.d.). Due to frequent occurrence of S2 for the dissolution parameter in drug product X, a change in the production process and formulation was introduced in order to improve dissolution.

Discussion

The formulation of immediate-release tablets involves a careful selection of excipients such as diluents, binders, disintegrants, and lubricants to achieve optimal drug performance (Formulation and Optimization of Immediate Release Tablets Using 3^2 Factorial Design, 2024).

The proposed changes involved modifications in the solvent used for the binder solution, drying temperature of the wet granulate, sieve size, and lubricant concentration. The new process parameters were tested through laboratory trials prior to process

*aivcevska@alkaloid.com.mk

validation to ensure compliance with the applicable regulatory guidelines.

A prospective process validation was performed on three consecutive manufacturing batches of the product and, based on the results, the proposed process was shown to be reproducible and capable of consistently manufacturing the product with the desired quality attributes that meet predetermined specifications. The dissolution of the API was analysed on a sample of six coated tablets taken from the middle of the coating phase in the specified medium at the 30-minute time point. All obtained results were within the specification limit of NLT 75.0% (Q) in 30 minutes.

In addition, a comparative dissolution study was performed comparing the old and new formulations. Comparison of the dissolution rate was made on one batch of the proposed formulation versus three batches of the old formulation. The obtained results support the similarity between drug product batches with minor formulation changes and the present formulation, confirming comparable drug-release characteristics. A stability study was also performed on two validation batches under ICH/VICH conditions, and all results for each parameter remained within specification throughout the approved shelf-life.

Regulatory evaluation was performed and the variation was classified as a Type IA variation since all conditions according to the Classification Guideline were fulfilled (European Commission, 2013). The change was successfully implemented.

Conclusion

In alignment with EU GMP Annex 16 requirements, such data form a critical part of the documented evidence reviewed by the Qualified Person prior to batch certification (European Commission, 2015). The completion of change control activities, including validation, comparability assessments, stability studies, and regulatory classification as a Type IA variation, ensures that the implemented changes are fully evaluated and controlled (European Commission, 2013). Consequently, this provides assurance that the affected batches comply with both GMP requirements and the marketing authorisation, thereby supporting the Qualified Person's decision for batch release to the market (European Commission, n.d.; European Commission, 2011). The quality of the medicinal product continues to be monitored through the Quality Management System (QMS), specifically via deviation management processes and ongoing process verification, which can identify any process shifts toward either improvement or deterioration.

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