Summary - In-Process and Bulk Drug Product Holding Times

This Guidance sets out guidelines for the determination and validation of in-process and bulk product holding times.

When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product." .This regulation could be interpreted to include the time for holding bulk product as part of the production process. "holding times (includes storage times) studies may be conducted during development or carried out in conjunction with process validation lots and shall be representative of full scale holding conditions.

- For current marketed products, a historical review of product lot release and stability data may be used to substantiate hold times if hold times were not established as part of validation. The longest hold time used for the lots reviewed will become the validated hold time.

The product bracketing or matrixing approach may be used to group products with same/similar formulations or combination strength products. For multiple strengths of the same formula, use of lots with the highest and lowest dosage only may be justified for the study. Reasons for excluding a product from a bulk holding study should be justified. Typically, one lot is recommended for bulk holding studies.

Typically, if these in-process products are used within 24 hours of manufacturing, no bulk holding time studies are deemed necessary. An in-process product that is held for longer than 24 hours should be monitored for physical characteristics and microbial contamination. A solution/suspension should be held for the defined hold period. At the test points, a sample should betaken from the storage container and tested. Results obtained should be compared with the initial baseline data of the solution/suspension control sample results.

Typical tests include the following: Microbial count; Yeast/Mould count; Specific Gravity; and Viscosity.

Read More