Investigations on the CIP-System of the Lyophilisator GT 6750

F. Generotzky1, G. Kutz2, N. Luenz1

1 Pharmaceutical Engineering, FH Lippe und Höxter, University of Applied Sciences, Detmold, Germany
2 Baxter Oncology, Halle-Künsebeck, Germany

Introduction

Cleaning validation is the documented evidence that an approved cleaning procedure will provide equipment which is suitable for processing of pharmaceutical products. In many cases, the same equipment may be used for processing different products. To avoid contamination of the subsequent product, adequate cleaning procedures are essential. Typically three consecutive applications of the cleaning procedure should be performed and shown to be successful in order to prove that the method is validated [1].

The lyophilisator of this study is used for the production of Cytostatics. As they are highly toxic, special attention has to be taken to protect the personnel. To exclude any contamination of the operators, it has been decided to perform some validation studies in respect to the integrated cleaning system.

Because the surfaces in the lyophilisator GT6750 are as a rule not directly in contact with the product a complete cleaning validation was not necessary. In this case a verification with one cleaning cycle was carried out.

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As the surfaces in the lyophilisator are not in direct contact with the product, critical locations have to be identified. A contamination of the lyophilisator chamber is possible by turning over or bursting of the product vials. In this case the plates and the chamber walls can be contaminated over or bursting of the product vials. For the majority of calculations, information of the equipment surface, batch sizes and the therapeutic daily dose of the other drug products are necessary. These information were not available at the time of this study.

Problem: Relevant surfaces in the lyophilisator

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Problem: Definition of the limits for the pharmaceutical product

Different methods are existing to determine the limit for the allowed product residue in the equipment [3]. For the majority of calculations, information of the equipment surface, batch sizes and the therapeutic daily dose of the other drug products are necessary. These information were not available at the time of this study.

Problem: Determination of the critical locations

Method: Riboflavin study

For that purpose an aqueous/ethanolic solution of Riboflavin is sprayed onto the surfaces of the lyophilisation chamber. After drying, the established cleaning cycle is performed. Finally the surfaces are visually inspected using an UV-lamp to identify possibly adherent Riboflavin by its fluorescence.

Results: Visual Clean Criterion

This criterion is based on the fact that the human eye can see around 4µg/cm² of a white substance on a surface of steel [2]. The max. concentration of drug is 1% of the max. allowed product residue by the visual clean criterion (4µg/cm²).

Conclusion

The cleaning verification of the lyophilisator GT6750 with CIP-System has been successfully accomplished.

References