SPECTROGRAPHIC MONITORING OF THE RECONSTITUTION OF LYOPHILIZED HIGH CONCENTRATION PROTEIN FORMULATIONS

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Background: Traditional methods for quantifying reconstitution time of lyophilized formulations involves the visual identification of the endpoint, which has led to inconsistent values throughout the literature. The use of Deep Ultra-Violet fluorescence time-resolved spectroscopy as a novel alternative to visual quantification of the reconstitution time of lyophilised biopharmaceutical was investigated.

Methods: Spectrographic information was collected via a novel custom-made setup that allowed the measurement of the reconstitution time in a standard sealed lyophilization vial. The spectra obtained were analyzed via principal component analysis to obtain a time-based representation of the changes in a reconstituting formulation.

Results: At high protein concentration. The variability of the reconstitution time measurements was reduced from 80.4% relative standard deviation obtained via the traditional method to 8.2% for the instrumental method presented in this study.

Conclusions: The methods for reconstitution endpoint detection presented in this study provide an easy-to-use, precise, and reproducible alternative to the traditional visual observation of reconstitution protocol. The instrumental method is customizable for a wide variety of use-cases, affordable, easy to set-up, and easy to use. Increasing the viability of the measurement of the reconstitution time of lyophilised products pre-administration in a clinical environment. Furthermore, the results obtained using this method are easily cross compared, improving the usability of the reconstitution time of lyophilised product as a critical quality attribute.