

„Design Space in HPLC Method Development”

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HPLC Method robustness and Quality by Design are playing an important role in the global economy, where pharmaceutical and chemical products are distributed worldwide and the method transfer process has to be running smoothly for the same product in different countries and in different laboratories. Regulatory authorities (FDA, ICH, etc.) nowadays are promoting and requesting the application of QbD principles. The exchange of complex information about critical resolution values supports easy method transfer of specific issues about all method details. The result is a better understanding, how a method should be controlled and adjusted to a given requested performance.

Systematic evaluation of experimental parameter and instrument settings are helpful to learn about selectivity variations in HPLC. With a reduced number of meaningful experiments the so called Design Space can be elaborated and with correct peak tracking techniques, using UV and MS technologies, the movement of peaks can be studied and controlled.

The knowledge about the Design Space allows the chromatographer greater flexibility in the selection of experimental parameter settings. Computer modelling HPLC-system-selectivity enhances the easier understanding of many unexpected disturbances in previously validated methods and shed light on how to control the parameter space better.

Easy method transfer from older type columns to new submicron short columns operated at high pressures is important to ensure safe method transfer and the reduction of analysis time for a single analysis. The transfer of an HPLC method to new type of columns can be enhanced by selectivity modelling, which results in the better understanding of the factors, which are influencing critical resolution, such as flow rate, dwell volume, column dimensions, particle size and extra column effects. In this way the high quality of pharmaceutical and chemical products using high speed HPLC-methods can be maintained without loosing time for redeveloping the method for short columns with submicron particles. Industrial applications of such method transfer processes will be presented. Questions related to the automation of such method development routines will be discussed.