Comparison of the three existing approaches for on-line calibration model transfer, update and maintenance

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In order that spectroscopic methods be an integral part of the Quality by Design approach, the main challenge is their robustness to new acceptable sources of variability on the process. To tackle different situations where the robustness of spectroscopic calibration models is challenged, a strategy for calibration model transfer, update and maintenance needs to be in place prior to implement a spectroscopic method for real-time quality measurements.

When it is possible to have a standardization set, there are existing algorithms that could be used to either correct the spectra to be predicted (e.g. PDS (Piecewise Direct Orthogonalization)) or to correct the predicted value (e.g. Bias/Slope correction (BS)). When it is impossible to obtain a standardization set, other approaches exist and consist in using a small experimental design, where the new acceptable sources of variability, disturbing the calibration model robustness, are included. Orthogonal projection is then carried out to make the model insensitive to these new acceptable sources of variability (EPO) (External Parameter Orthogonalization), OSC (Orthogonal Signal Correction), GLS (Generalized Least Squares)).

Finally, the most common case when neither a standardization set, nor a small experimental design is available, other existing methods are applicable using few in-process control (IPC) samples to update the model. These methods are: Bias/Slope correction (BS), model redevelopment (MRD) (i.e. exhaustive or global modelling) and Dynamic Orthogonal Projection (DOP). These only 3 existing methods (BS, MRD, DOP) that could be used for improvement of calibration model robustness throughout its lifecycle for on-line application, using only few IPC samples, will be discussed and compared in this paper based on the model performance for a pharmaceutical application, i.e. a drug drying process.