Clinical perspective on developing a DBS assay for daily routine

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Scope of the lecture:
Building further upon the previous lecture, this lecture will discuss the different clinical aspects that are important during the development of a dried blood sample-based method for routine use, designed to quantitate small molecules using liquid chromatography tandem mass spectrometry.

Learning objectives:
1. How to ensure a dried blood sample-based method is fit for purpose?
2. Which clinical aspects should be taken into consideration during method development and evaluation?
3. How to perform the clinical validation of a dried blood sample-based method?

Extended abstract:
This presentation follows up on the previous lecture, in which the analytical strategy to set up a robust method for the analysis of dried blood samples was outlined. It is generally accepted that a DBS method can only be implemented in routine care for the purpose of TDM (and thereby replacing the standard venous whole blood sampling, with analysis of blood, plasma or serum) after it has been successfully validated in a clinical study. In a clinical validation, paired DBS and venous blood (plasma/serum) samples are obtained and analyzed. The analytical results obtained from DBS and conventional sampling are then compared and statistically evaluated. The purpose of a clinical validation is to demonstrate that results from DBS are interchangeable with and/or can be converted reliably to those obtained using the standard method for TDM, i.e. a blood, serum or plasma analysis.

Current guidelines on bioanalytical method validation, extended by the recommendations as outlined in the previous presentation, do not cover all aspects of the clinical validation of DBS assays. Therefore, the aim of this presentation will be to provide recommendations on how to fully validate a DBS assay for TDM in clinical practice.

Topics covered will encompass:
1. the concentration range that should be covered;
2. the number of clinical samples and patients to be included;
3. how to compare DBS concentrations to plasma concentrations;
4. what statistical methods can or should be applied;
5. how to interpret the outcome of the method comparisons.

In addition, attention will be paid to:
1. the type of card, paper or device used;
2. sampling method and spot quality;

3. incurred sample reanalysis;
4. clinical validation of automated analysis methods;
5. how to set up and implement quality controls;
6. the aspect of cross-validation, when a DBS assay is altered in terms of punch size, filter paper, or sampling method

During this presentation, examples from literature will be used to illustrate the different points made.

This presentation, together with the presentation on the analytical perspective on developing a DBS assay for clinical routine, should allow the attendees to gain insight into how a DBS study should be set up and validated before clinical implementation. The success of further implementation of DBS-based methodologies for the follow-up of patients in the future will largely depend on the data quality these methodologies offer. For the patient's safety, it is of utmost importance that no concessions are made in this respect. Therefore, the careful set-up of analytical and clinical validation studies (and the correct interpretation thereof) is an aspect that cannot be emphasized enough.