Recommendations of criteria for development and validation of analytical methods for estimating concentrations of drugs in blood to be used in 24/7 clinical toxicology

Clinical Toxicology Committee GTFCh and Quality Control Committee GTFCh

The majority of emergency methods for clinical toxicological purpose are not quantitative in nature. They are usually used to identify and to estimate the blood concentration of drugs in blood in the context of a fast 24/7 analysis. The estimated amount may then be classified as "within therapeutic level", "above therapeutic level" or "within the toxic range".

The estimation can be based on different approaches such as one-point calibration or an electronically stored multi point calibration.

During validation, the following recommended aspects should be evaluated and the given specifications should be obtained, when such a method is developed.

a) The calibration model (usually linear) has to be established using multiple calibration levels and should include therapeutic up to toxic concentrations of the analytes
b) If linearity has been verified one-point calibration is possible, provided the requirements for accuracy and precision are fulfilled
c) Analytical Limits (lower and upper end of estimated concentration and limit of detection) should be known
d) Bias (within ±30%) of two QCs at upper (80%) and lower (20%) end of the measurement range, determined on 5 different days in duplicate
e) Precision (<30%) of two QCs at upper (80%) and lower (20%) end of the measurement range, determined on 5 different days in duplicate
f) Accuracy, expressed as 95% ß-tolerance interval, should be within ±50% for low and high QC concentrations
g) Matrix effects of LC-MS methods (suppression/enhancement should be within 70-130% at low and high QC concentrations)
h) In case of multi-analyte procedures, effects of co-eluting analytes on other analytes and/or internal standards should be within ±30% at lower therapeutic and higher toxic concentrations
i) Storage stability of extracted calibrator and QC samples has to be shown in case of reinjection instead of fresh preparation
j) Selectivity using at least n = 6 different blank matrix samples
k) Analyte carry-over (signal of <10% of the lowest calibrator after injection of high QC)

LOD= Limit of detection
LLOQ= Lower limit of quantification
QC= Quality control