According to the International Organization for Standardization (ISO), an “influence quantity” is a “quantity that is not the measurand but that affects the result of the measurement” [the measurand being the particular quantity subject to measurement (1)]. The effect of an influence quantity on the measurement process is an interference that generates a systematic error. In clinical chemistry, depending on the molecular entity responsible for an interference, influence quantities may be classified as endogenous or exogenous.

Concentrations of bilirubin, hemoglobin, and triglyceride in plasma (or serum) are generally studied by the in vitro diagnostic industry in the development of measurement systems as potential endogenous influence quantities. However, depending on the criteria that the reagent manufacturer uses to decide whether the systematic error caused by an influence quantity is significant, influence quantities may be the most important component of the uncertainty of a patient’s result. Let me illustrate this statement using the measurement of urate substance concentration in plasma as an example.

In this example, the substance concentration (subst. c.) of urate [uric acid and urate ion in equilibrium (2)] in plasma (P) is measured using a procedure based on an uricase/peroxidase method. The measurement system is calibrated daily with a calibrator traceable to the reference material SRM 909b from NIST. Let a patient’s result [according to the IFCC-International Union of Pure and Applied Chemistry (IUPAC) recommendation (3)] be:

\[ P = 275 \, \mu \text{mol/L} \]

According to the ISO, the numeric part of this result is incomplete because a complete statement of a measurement result must include information about the dispersion of the values that could reasonably be attributed to the measurand (i.e., the uncertainty of measurement) (1,4). This information usually is given as a standard deviation or the half-width of an interval having a stated level of confidence.

To estimate the uncertainty of measurement in our example, we assume that the sources of uncertainty are only premetrological variability, uncertainty of the calibrator assigned value, day-to-day imprecision, and endogenous influence quantities.

Premetrological variability. For blood quantities, the premetrological phase
(preexamination or preanalytical phase, when a broader sense is necessary) begins when the needle is first inserted into the vein and lasts until the sample enters the measurement system. The CV observed in this phase for the quantity measured is 0.8% (5), which in our example corresponds to a standard deviation, or standard uncertainty, of 2.2 μmol/L.

Uncertainty of the value assigned to the calibrator. The manufacturer of the calibrator does not declare the uncertainty of the assigned value. Because the uncertainty of the assigned value of the reference material SRM 909b, to which the calibrator is traceable, expressed as relative standard deviation is 1%, we can (optimistically) assume the same uncertainty for the calibrator. Thus, because the assigned value of calibrator is 301 μmol/L, the standard uncertainty attributable to the calibrator is 3.0 μmol/L.

Day-to-day imprecision. The measurement procedure of this example has an heteroscedastic behavior with a day-to-day CV within the measurement range equal to 1.1%. This imprecision applied to the patient’s result (275 μmol/L) corresponds to 6.6 μmol/L, but because there are three influence quantities studied by the reagent manufacturer, the estimated standard uncertainty should be multiplied by 3:

\[ u = \left[ 3 \times (6.6)^2 \right]^{0.5} = 11.4 \text{ μmol/L} \]

When the standard uncertainties of every uncertainty component have been estimated, the combined standard uncertainty \( u_c \) attributable to all of these components may be estimated (4, 5):

\[ u_c = (2.2^2 + 3.0^2 + 11.4^2 + 3.0^2)^{0.5} = 12.4 \text{ μmol/L} \]

Finally, we will estimate the expanded uncertainty \( (U) \) with a confidence level 1 − α = 0.95, multiplying the combined standard uncertainty by a coverage factor \( k \) equal to 2 (4, 6):

\[ U = u_c \times k = 12.4 \times 2 = 24.8 \text{ μmol/L} \]

Thus, the complete patient’s result, after rounding the value of the expanded uncertainty as is usually done for the measurement result, will be:

P–Urate; subst. c. (SRM 909b) = (275 ± 25) μmol/L

Keeping all of the above in mind, it seems clear that more effort should be devoted to improve the metrological specificity of the measurement procedures used in clinical laboratory sciences, because in many cases, influence quantities, in spite of being not significant, may be, quantitatively, the more important component of the uncertainty of a patient’s result.

References
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Serendipitous Detection of Umbilical Venous Catheter Displacement by Cardiac Troponin I Measurement

To the Editor:

The measurement of cardiac troponin I (cTnl) is pivotal in the biochemical diagnosis of myocardial damage in adults and in infants as well (1). cTnl could also be used in other pathologies that may affect the neonatal heart, such as birth asphyxia, primary pulmonary hypertension, sepsis, and multiple organ system failure (2, 3).

A newly born term male suffered a