

Analytical Order, its Figures of Merit, and their Authentication*

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The evaluation of any developed chemical analytical method has to be preceded by a defined analytical order (request) that is derived from the social order defined by the fundamental aim of the analytical activity. The validation of the performance and efficiency of an analytical method is based on the comparison of tolerance parameters, defined in advance with parameters derived from experimental measurements. Therefore analytical chemistry becomes a basis for obtaining chemical information.

The analytical order [1] is formulated hierarchically by means of parameters defined in advance. These numerical values express the required performance of the analytical method. The choice of the parameters needs, at the same time, to take into account the ISO standards [2], and general validation principles [3]. From the point of view of analytical importance it is necessary to divide the considered parameters into three groups. They are: the primary fundamental parameters, the secondary additional parameters, and finally the tertiary parameters which support the elucidation of performance parameters, as well as the parameters with specific nature [4]. The hierarchy and classification of the used tolerance and experimental values of the analytical order are presented in Table 1.

The subscript T marks the chosen parameters of the analytical order, because they are simultaneously the tolerance values, the attainment of which is required for an actual analytical method.

These tolerance values are in the course of validation process compared with the equivalent experimentally obtained values. The values obtained from the experimental measurements as well as the derived values, are conventionally marked by the mark $\hat{\cdot}$ above the symbol defining the given parameter. By comparison of the tolerance and experimental values it is possible to test not only the degree of fulfillment of the analytical order but also the information efficiency [5] of the tested method.

THEORETICAL

The primary input parameters of the analytical order are the following tolerance values: the desired maximum concentration of the analytical determination $c(X)_{\max,T}$, the minimum concentration $c(X)_{\min,T}$,

Table 1. Hierarchy and Classification of the Input Data and the Validation

Fundamental data	Additional data	Elucidation data
<i>A. In advance chosen tolerance input data</i>		
$c(X)_{\max,T}$	$c(X)_{st}$	$c(X)_{\max,lin,T}$
$c(X)_{\min,T}$	$c(X)_{rec}$	$c(X)_{\min,lin,T}$
$c(X)_{L,T}$		$c(X)_{LOQ,T}$
<i>B. Calculated tolerance values</i>		
$\bar{c}(X)_{p,T}$	$\Delta c(X)_{st}$	$\Delta c(X)_{lin,T}$
$\Delta c(X)_T$	$\Delta c(X)_{rec}$	
$s(c)_{X,T}$		
$\hat{s}(c)_{X,T,r}$		
Primary parameter	Secondary parameter	Tertiary parameter
<i>A. Experimentally obtained input data</i>		
$\hat{c}(X)_{\max}$	$\hat{c}(X)_{st}$	$\hat{c}(X)_{\max,lin}$
$\hat{c}(X)_{\min}$	$\hat{c}(X)_{rec}$	$\hat{c}(X)_{\min,lin}$
$\hat{c}(X)_L$		$\Delta \hat{c}(X)_{LOQ}$
<i>B. Calculated experimental values</i>		
$\hat{\bar{c}}(X)_p$	$\Delta \hat{c}(X)_{st}$	$\Delta \hat{c}(X)_{lin}$
$\Delta \hat{c}(X)$	$\Delta \hat{c}(X)_{rec}$	
$\hat{s}(c)_X$		
$\hat{\hat{s}}(c)_{X,r}$		

and the absolute value of standard deviation $s(c)_{X,T}$ of the determined analytical element (X). In the following step, it is necessary to calculate the half sum $\bar{c}(X)_{p,T}$ which represents the arithmetical centre of the given concentration range $\Delta c(X)_T$

$$\bar{c}(X)_{p,T} = \frac{1}{2}(c(X)_{\max,T} + c(X)_{\min,T}) \quad (1)$$

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the value of the concentration range $\Delta c(X)_T$

$$\Delta c(X)_T = c(X)_{\max,T} - c(X)_{\min,T} \quad (2)$$

the absolute standard deviation $s(c)_{X,T}$, and the relative standard deviation $s(c)_{X,T,r}$

$$s(c)_{X,T} = \sqrt{\frac{1}{N-1} \sum_i^N (c(X)_i - \bar{c}(X))^2} \quad (3a)$$

$$s(c)_{X,T,r} = (s(c)_{X,T} / \bar{c}(X)_{p,T}) \times 100 \quad (3b)$$

By verification of an analytical order, the above-mentioned tolerance values need to be compared with the adequate experimentally determined values: $\hat{c}(X)_{p,T}$, $\Delta \hat{c}(X)$, $\hat{s}(c)_X$ or $\hat{s}(c)_{X,r}$. It is reasonable to derive these experimental values from analytical calibration [6, 7].

The fulfillment of an analytical order with regard to the concentration range is expressed by the inequality

$$\Delta c(X)_T \leq \Delta \hat{c}(X) \quad (4a)$$

The fulfillment of the analytical order is valid only in case when both boundary conditions defined by the following relations are fulfilled

$$\bar{c}(X)_{p,T} \approx \hat{c}(X)_p \quad (4b)$$

$$s(c)_{X,T,r} \geq \hat{s}(c)_{X,r} \quad (4c)$$

However, if the inequalities

$$\Delta c(X)_T > \Delta \hat{c}(X) \quad (5a)$$

and

$$\bar{c}(X)_{p,T} < \hat{c}(X)_p \quad (5b)$$

are confirmed, the analytical order is fulfilled only partially [8], and the analytical method requires additional optimization. In the case of multielement analytical determination, if the optimization condition by the majority of elements is not fulfilled, the method needs additional optimization. The determining fact is that the optimization condition is fulfilled for the most significant elements [9].

The agreement of the absolute and relative standard deviations is also necessary to analyze. If the inequalities

$$s(c)_{X,T} \geq \hat{s}(c)_X \quad (6a)$$

and

$$s(c)_{X,T,r} \geq \hat{s}(c)_{X,r} \quad (6b)$$

are confirmed, it is an unambiguous evidence of a fulfillment of the demands on the precision of the concentration determination. If the priority is the detectability, the method has to be optimized further.

The last primary parameter is connected with the detectability (LOD) of the analytical method. This parameter is expressed by the tolerance limit of detection $c(X)_{L,T}$. If the inequality

$$c(X)_{L,T} \geq \hat{c}(X)_L \quad (7)$$

is confirmed, the analytical order is also fulfilled. This assessment is particularly important in trace analysis.

The most significant parameter among secondary parameters of the analytical order is trueness of the analytical results (expressing accuracy and reliability). This evaluation, however, is dependent on the existence of certified standards of the analyzed matrix with the declared concentrations $c(X)_{st}$ of the actual analytical elements. The condition for the attainment of true results is expressed by the equation

$$\hat{c}(X)_{st} - c(X)_{st} = \Delta c(X)_0 \approx 0 \quad (8)$$

The concentration value $\hat{c}(X)_{st}$ of the analytical element (X) has to be obtained by an attested analytical method using the certified standard. The equality of the values in eqn (8) has to be confirmed by the statistical test (9) involving the standard deviation $s(\hat{c})_X$

$$t_{\text{calc}} = (\hat{c}(X)_{st} - c(X)_{st}) / \left(s(\hat{c})_X \cdot \frac{2\tau}{\sqrt{N}} \right) \quad (9)$$

If the inequality $t_{\text{calc}} \leq t_{\text{tab}}$ is valid, then the agreement of the tested values is confirmed. In the opposite case when $t_{\text{calc}} > t_{\text{tab}}$ the agreement is rejected [10]. The value t_{tab} may be obtained for the degree of freedom $F = N - 1$ and the significance level α . Here N represents the actual number of measurements used for the determination of standard deviations and τ is the value of Student's test. In the case that certified standards are not available, it is necessary to use artificially prepared reference samples. In this very frequent case, only the test of recovery effect takes place. This test may be represented by the equation

$$\Delta \hat{c}(X) = \hat{c}(X) - c(X)_{\text{rec}} \quad (10)$$

For the test of recovery the equation for testing of trueness is valid.

Among other parameters of the analytical order the value of the linear concentration range of the analytical straight line is also important

$$\Delta c(X)_{\text{lin},T} = c(X)_{\max,\text{lin},T} - c(X)_{\min,\text{lin},T} \quad (11a)$$

The fulfillment of this analytical order is given by inequalities

Table 2. The Experimental Input Data and their Validation

A. Experimental input and calculated data		
$w(\text{Co})_{\max, \text{T}} = 500 \text{ ppm}$ $\hat{w}(\text{Co})_{\max} = 500 \text{ ppm}$	$w(\text{Co})_{\min, \text{T}} = 1 \text{ ppm}$ $\hat{w}(\text{Co})_{\min} = 8 \text{ ppm}$	$\bar{w}(\text{Co})_{\text{T}} = 250.5 \text{ ppm}$ $\hat{w}(\text{Co}) = 254 \text{ ppm}$
$w(\text{Co})_{\max, \text{lin}, \text{T}} = 500 \text{ ppm}$ $\hat{w}(\text{Co})_{\max, \text{lin}} = 500 \text{ ppm}$	$w(\text{Co})_{\min, \text{lin}, \text{T}} = 10 \text{ ppm}$ $\hat{w}(\text{Co})_{\min, \text{lin}} = 50 \text{ ppm}$	$\bar{w}(\text{Co})_{\text{lin}, \text{T}} = 255 \text{ ppm}$ $\hat{w}(\text{Co})_{\text{lin}} = 275 \text{ ppm}$
$\Delta w(\text{Co}) = 499 \text{ ppm}$ $\Delta \hat{w}(\text{Co}) = 492 \text{ ppm}$	$s(w)_{\text{Co}, \text{T}} = 20.6 \text{ ppm}$ $\hat{s}(w)_{\text{Co}} = 27.2 \text{ ppm}$	$w(\text{Co})_{\text{L}, \text{T}} = 0.1 \text{ ppm}$ $\hat{w}(\text{Co})_{\text{L}} = 0.3 \text{ ppm}$
$w(\text{Co})_{\text{st}} = 32 \text{ ppm}$ $\hat{w}(\text{Co})_{\text{st}} = 37 \text{ ppm}$	$\Delta w(\text{Co})_{\text{lin}} = 490 \text{ ppm}$ $\Delta \hat{w}(\text{Co})_{\text{lin}} = 450 \text{ ppm}$	
B. Validation data		
$\Delta w(\text{Co})_{\text{T}} ? \Delta \hat{w}(\text{Co})$ 499 ppm > 492 ppm V.N.C.	$\bar{w}(\text{Co})_{\text{T}} ? \hat{w}(\text{Co})$ 250.5 ppm < 254 ppm V.N.C.	$w(\text{Co})_{\text{L}, \text{T}} ? \hat{w}(\text{Co})_{\text{L}}$ 0.1 ppm < 0.3 ppm V.N.C.
$s(w)_{\text{Co}, \text{T}} ? \hat{s}(w)_{\text{Co}}$ 20.6 ppm < 27.2 ppm V.N.C.	$\Delta w(\text{Co})_{\text{st}} ? 0$ 5 ppm > 0 V.N.C.	$\Delta w(\text{Co})_{\text{lin}} ? \Delta \hat{w}(\text{Co})_{\text{lin}}$ 490 ppm > 450 ppm V.N.C.

Remarks: The abbreviation V.N.C. means that the validation is not confirmed.

$$\Delta c(\text{X})_{\text{lin}, \text{T}} \leq \Delta \hat{c}(\text{X})_{\text{lin}} \quad (11b)$$

$$\tilde{c}(\text{X})_{\text{lin}, \text{p}, \text{T}} \approx \hat{c}(\text{X})_{\text{lin}, \text{p}} \quad (11c)$$

Extraordinarily favourable conditions are represented by the inequalities

$$\hat{c}(\text{X})_{\max, \text{lin}} \geq c(\text{X})_{\max, \text{T}} \quad (12a)$$

$$\hat{c}(\text{X})_{\min, \text{lin}} \leq c(\text{X})_{\min, \text{T}} \quad (12b)$$

The limit of the quantification (LOQ), called also the limit of determination, is defined very doubtfully. It is the concentration of analytical element (X), which is possible to be determined with the acceptable standard deviation and accuracy [2, 10]. The procedure of the determination of LOQ-value requires in advance to define the precision $s(c)_{\text{X}, \text{T}}$ and trueness $\Delta c(\text{X})_{\text{o}}$ values, and the concentration value $\hat{c}(\text{X})_{\text{LOQ}}$, it is accepted when the following inequalities are both fulfilled.

$$s(c)_{\text{X}, \text{T}} \geq s(\hat{c})_{\text{X}} \quad (13a)$$

$$c(\text{X})_{\text{st}} \approx \hat{c}(\text{X})_{\text{st}} \quad (13b)$$

DISCUSSION

On the one hand, the fundamental, additional and elucidation tolerance input values, the calculated values footing in this input values, and on the other hand the complex of experimentally obtained data was used

for the illustration of the suggested validation procedure. The concentration values are given in the weight ratios and therefore are marked as w values. In the given case as input data are used the figures of merit (Table 2) of Co analytical element [11, 12].

The remarkable difference between the tolerance and experimentally obtained values is in the minimal observed content value, $w(\text{Co})_{\min}$, in the values of the arithmetical means $\bar{w}(\text{Co})$, in the content ranges $\Delta w(\text{Co})$, and at last in the values of the limits of detection of $w(\text{Co})_{\text{L}}$. The differences between $\Delta w(\text{Co})_{\text{T}}$ and $\Delta \hat{w}(\text{Co})$ values allowed to express only the approximate agreement and therefore the fulfilling of the equality is not confirmed. The judgement of agreement of $\bar{w}(\text{Co})_{\text{T}}$ and $\hat{w}(\text{Co})$ values unambiguously demonstrated the shifting of the experimental arithmetic mean value to the higher concentrations. Similarly the values of standard deviations $s(w)_{\text{Co}, \text{T}}$ and $\hat{s}(w)_{\text{Co}}$ confirmed that the precision of the concentration determination of experimental values is remarkably worse. In the same manner it was confirmed that the linear segment of the analytical straight line is evidently shorter. Lastly the testing of the trueness confirmed that the determination of Co did not give a sufficient accuracy.

CONCLUSION

The evaluation of the parameters of analytical order presents the fundamental procedure of the verifying of all analytical methods. The tolerance parameters of the analytical order are urgent in advance to defining. It is necessary to compare these values to the equivalent experimental values.

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REFERENCES

1. Flórián, K., Matherny, M., and Danzer, K., *GIT Fachzeitschrift* 42, 693 (1998).
2. EUROCHEM/WELAC Guide 1. *Welac Guidance Document No. WGD 2*. Eurochem, 1998.
3. Günzler, H., *Accreditation and Quality Assurance in Analytical Chemistry*. Springer-Verlag, Berlin, 1998.
4. Flórián, K., Matherny, M., and Danzer, K., *GIT Fachzeitschrift* 42, 787 (1998).
5. Matherny, M., *Chem. Pap.* 56, 228 (2002).
6. Matherny, M. and Ondáš, J., *Anal. Chim. Acta - Comp. Techn. Optim.* 133, 137 (1981).
7. Matherny, M. and Eckschlager, K., *Talanta* 41, 1113 (1994).
8. Matherny, M. and Eckschlager, K., *Chemom. Intell. Lab. Syst.* 32, 67 (1996).
9. Burington, R. S. and May, D. C., *Handbook of Probability and Statistics*. McGraw-Hill, New York, 1970.
10. EURACHEM/CITA Guide: *Quantifying Uncertainty in Analytical Measurement*. Eurochem, 1999.
11. Flórián, K., Matherny, M., and Pliešovská, N., *Microchem. J.* 51, 26 (1995).
12. Filo, O. and Matherny, M., *Acta Chim. Acad. Sci. Hung.* 98, 13 (1978).