Translation of Leitfaden für die Massebestimmung bei Referenzmessprozeduren in medizinischen Referenzlaboratorien, PTB-Mitteilungen 109 (1999) No. 5, pp. 379-383

Guide for the determination of the mass within the scope of reference measurement procedures in medical reference measurement laboratories

Foreword

This Guide was drawn up by the working group "Measuring Devices" of the Technical Committee "Medical Quantities" of the Deutscher Kalibrierdienst (DKD, German Calibration Service) and the Advisory Council for Metrology in Medicine at the Physikalisch-Technische Bundesanstalt (PTB). After a testing period the Guide will be revised, if necessary, and probably published as a DKD Guidance Publication.

1 Purpose

1.1 Fields of application

This Guide establishes metrological requirements for the calibration of measuring devices used to determine the mass within the scope of reference measurement procedures in medical reference measurement laboratories (also referred to as medical target value laboratories).

The Guide is to enable the bodies concerned to prove a given relative expanded uncertainty by suitable procedures.

The Guide gives examples which prove compliance with a relative expanded uncertainty $U/m \leq 0{,}1$ % (coverage factor $k = 2$) assigned to a value of the mass m. The Guide may also be used analogously to prove a greater relative expanded uncertainty fixed in accordance with the requirements of the reference measurement laboratory.

The Guide is intended for operators of calibration laboratories accredited for measurands significant in the field of medicine.

Note

The method specified in this Guide for the determination of the relative expanded uncertainty cannot be applied to determine the mass of any product to be weighed. Contributions to the uncertainty of mass determinations can also result from the properties of the product to be weighed, such as hygroscopicity, evaporation, electrostatic charging and others. They must be reduced by suitable measures, for example by weighing of the product in a closed container, use of evaporation traps and ionization blowers. The contributions to the uncertainty of measurement must be determined and taken into account when the uncertainty of measurement is calculated. In view of the specific nature of this problem, the Guide does not go into details.

2 Standard

2.1 Traceability to the national mass standard

Calibrated weights must be used as standards to ensure traceability to the national standard which realizes the unit of mass in compliance with the International System of Units (SI).

These weights must be accompanied by a calibration certificate issued by an accredited calibration laboratory or a national metrology institute (e.g. PTB), or by a verification certificate stating the conventional masses and the uncertainties of measurement. All certificates must be kept for the whole period of use (service life) of the weights.

The weighing instruments used are to be tested and calibrated according to sections 3 and 5 using these weights.

2.2 Selection of the standards and relative standard uncertainty $u_{rel,N}$ determined upon calibration

The relative standard uncertainty $u_{rel,N}$ assigned to the conventional mass of the standards is to be equal to or smaller than one sixth of the relative expanded uncertainty U/m, i.e. $\leq 0{,}015$ %. This requirement is met for the accuracy classes of the weights shown in Table 1. The conventional mass stated in the certificate must usually be taken into account.

Table 1: Requirements to be met by the weights

Nominal value m_0	Accuracy class according to OIML Recommendation R 111 [1]
≤ 5 mg	E_1
10 mg, 20 mg	E_2
≤ 50 mg	F_1

The relative standard uncertainty $u_{rel,N}$ must be calculated from the uncertainty of measurement U_N stated in the certificate of the weight, applying the coverage factor k and the nominal value m_0:

$$u_{rel,N} = \frac{U_N}{k \cdot m_0} \quad . \tag{1}$$

Note: The nominal value m_0 may be used instead of the mass m_N of the weight (standard) (only) for the calculation of the uncertainty of measurement, as the difference between m_N and m_0 is negligible here.

If, in the exceptional case, more than one weight is used as a standard, the uncertainties assigned to the conventional masses of the individual weights must be added because correlations exist between them:

$$u_{rel,N} = \frac{\sum_{i=1}^{n} u_{Ni}}{\sum_{i=1}^{n} m_{0i}} \text{ , where } u_{Ni} = \frac{U_{Ni}}{k_i} \; . \tag{2}$$

Example: m_0 = 500 mg; U_N = 0,08 mg; k = 2. From this results: $u_{rel,N}$ = 0,008 %.

2.3 Recalibration period

The period until new weights are recalibrated for the first time should not exceed two years. This period may be prolonged to maximally four years when there is agreement with previous results. If the deviations exceed the uncertainty of measurement U_N, the period must, however, be reduced to one year, other standards of better stability must be used or the conditions of use must be improved.

2.4 Handling and cleaning

Prior to each use, the weights must be checked for visible changes and impurities, and they may be used only if no significant mass changes must be assumed.

The weights must be handled carefully, using suitable tweezers with plastic surfaces. Before each use, dust possibly adhering to them should be removed with a soft brush.

3 Calibration of the weighing instrument

3.1 Selection of a suitable weighing instrument and relative standard uncertainty $u_{rel,w}$ determined upon calibration

The relative standard uncertainty $u_{rel,w}$ assigned to the value indicated by the weighing instrument usually furnishes the greatest uncertainty contribution to mass determinations within the scope of reference measurement procedures in medical laboratories. It must be smaller than half the relative expanded uncertainty of 0,1 %, i.e. < 0,05 %. The relative standard uncertainty $u_{rel,w}$ results from the ratio of the standard deviation s_w (see 3.2) to the mass m_N of the weight used for the calibration of the weighing instrument, taking into account the resolution of the indication (rounding error) and the relative uncertainty from the calibration of the weight:

$$u_{rel,w} = \sqrt{\frac{1}{m_N^{\,2}}\left(s_w^{\,2} + \frac{d^2}{12}\right) + u_{rel,N}^{\,2}} \tag{3}$$

Table 2 shows some examples of actual scale intervals (d) of electronic weighing instruments which usually meet the above requirements. Guidance publication DKD-R 7-1, sheet 1 [2] gives further details of the evaluation model for a weighing instrument and of influence quantities to be taken into account in addition when the requirements are higher.

Table 2: Actual scale intervals of electronic weighing instruments

Mass m of the weighed-in quantity	Example of the actual scale interval d of the weighing instrument
0,5 mg to < 5 mg	0,0001 mg
5 mg to < 30 mg	0,001 mg
30 mg to 250 mg	0,01 mg
> 250 mg	0,1 mg

Example: s_w = 0,16 mg; d = 0,1 mg; m_N = 500 mg; $u_{rel,N}$ = 0,008 %. From this results: $u_{rel,w}$ = 0,033 %

3.2 Determination of the standard deviation s_w of the indications of the weighing instrument

The method described here for the determination of the standard deviation s_w of the weighing instrument's indications is not generally applicable, but it has been adapted to the concrete measurement tasks in medical laboratories. The measurement sequence followed to determine s_w must be in compliance with the measurement sequence followed in practical application.

s_w must be determined by ten weighings with the greatest total mass occurring. The measurement sequence should be in compliance with the weighing process performed to determine the weighed-in quantities: The difference between tare container (e.g. 67 g) and tare container plus standard (using, for example, 200 mg + 100 mg + 50 mg weights or a 500 mg weight for a weighed-in quantity of 350 mg) is determined several times. Each time the tare container is placed on the weighing instrument, the instrument's indication is set to zero (I is the indication with weights placed on the weighing instrument, and n is the number of weighings).

$$\bar{I} = \frac{1}{n}\sum_{i=1}^{n} I_i \tag{4}$$

$$s_w = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}\left(I_i - \bar{I}\right)^2} \,. \tag{5}$$

The load must be applied to the load receptor in the same way as in actual weighings. This means that in particular great deviations form the central position of the loads on the load receptor must be avoided to keep the uncertainty contribution due to eccentric loading negligibly small. The influence of the remaining positional error, which cannot be avoided, is comprised in the standard deviation determined.

3.3 Correctness of the weighing instrument's indication

The measurement sequence to be followed for the determination of the correctness of the weighing instrument's indication should also be in compliance with the weighings carried out to determine the weighed-in quantities (cf. 3.2). In the range of the maximum weighing difference (e.g. 350 mg), the deviation of the weighing instrument's indication from the conventional mass of the weights should be smaller than the standard deviation s_w determined for the weighing. Otherwise, the deviations would have to be corrected upon mass determination or be taken into account by an additional uncertainty component.

3.4 Time of weighing instrument calibration

The weighing instrument must be calibrated before a campaign for the calibration of reference materials is started or at least once a year. Calibration must be documented.

4 Environmental conditions

As far as the environmental conditions are concerned, the values stated in Table 2 and the requirements of the weighing instrument manufacturer should be met.

Table 3: Environmental conditions to be complied with

Environmental condition	Tolerance
Air temperature	18 °C to 25 °C
Maximum change of the air temperature per hour	± 0,7 K
Maximum change of the air temperature during twelve hours	± 1,0 K
Relative humidity of the air	35 % to 65 %
Maximum change of the relative humidity of the air during four hours	± 10 %

In the case of mass values which are small compared with the nominal value of the adjustment weight, changes of the room temperature exert a negligibly small influence on the weighing results. For greater mass values, this uncertainty component may be avoided by re-adjustment of the weighing instrument after each temperature change.

Air streams, vibrations and heat radiation from one side as well as dusts which may influence the weighings should be prevented in the measurement rooms. Constructional measures should be taken for heat insulation and to prevent heat transmission by solar radiation through the windows. If necessary, the measurement rooms should be air-conditioned.

5 Mass determination

5.1 General condition

Uncertainty components of the weighing may also result from the properties of the product to be weighed (e.g.: evaporation, hydroscopic behaviour, see 1.1). It is, however, assumed that the product to be weighed is stable within the scope of the accuracy requirements and that it is, therefore, not necessary to take it into account when the uncertainty of the mass determination is calculated.

5.2 Determination of the mass

Each day the weighing instrument is used it should be adjusted in accordance with the manufacturer’s instructions.

Gross deviations from centric application of the load to the load receptor must be avoided during weighing.

Table 4: Determination of the mass

Sequence	Step to be taken
1	One hour before the weighing process is started, tare container and weights are placed on the load receptor to reach temperature stabilization
2	Zero setting of the weighing instrument / taring with tare container
3	Calibration of the weighing instrument in the measuring range used (e.g. 350 mg) with calibrated weights; the deviations of the weights’ masses from their respective nominal value should be smaller than the standard deviation s_w of the weighing
4	Zero setting of the weighing instrument / taring with tare container
5	Weighing of the substance to be determined and determination of the weighing result m_w
6	Calculation of the mass m

5.3 Calculation of the mass *m*

The mass m is calculated according to equation (6) below, where m_w is the weighing instrument’s indication for the weighed-in quantity. The conventional reference value of the air density is ρ_L = 1,2 kg/m^3 and the density of the standard is ρ_N = 8000 kg/m^3; the density ρ of the product to be weighed must be known or assumed:

$$m = m_{\mathrm{w}}\left[1+\rho_{\mathrm{L}}\left(\frac{1}{\rho}-\frac{1}{\rho_{\mathrm{N}}}\right)\right] \quad (6)$$

Example: m_{w} = 349,9 mg; ρ = 1150 kg/m^3. From this results m = 350,2 mg.

5.4 Calculation of the relative expanded uncertainty *U*/*m* of the mass determination

The relative standard uncertainty $u_{\mathrm{rel},\rho}$ of the density of the product to be weighed results from the uncertainty u_ρ of the density of the product to be weighed. The uncertainty u_ρ is calculated from the limiting values of the uncertainty of the density, assuming rectangular probability density. The limiting value a_ρ is half the known or assumed density range of the product to be weighed.

$$a_\rho = \frac{1}{2}\left(a_{\rho,\max} - a_{\rho,\min}\right) \quad (7)$$

$$u_\rho = \frac{a_\rho}{\sqrt{3}} \quad (8)$$

The following is obtained, for example, for a density range between 900 kg/m^3 and 1400 kg/m^3: a_ρ = 250 kg/m^3, ρ = 1150 kg/m^3 and u_ρ = 144 kg/m^3.

The relative standard uncertainty of the density of the product to be weighed is:

$$u_{\mathrm{rel},\rho} = \frac{u_\rho}{\rho} \quad (9)$$

The relative expanded uncertainty *U*/*m* is determined from the relative standard uncertainties $u_{\mathrm{rel,w}}$ of the weighing instrument's calibration (see equation (3)), the density of the product to be weighed $u_{\mathrm{rel},\rho}$ (see equation (9)) and the coverage factor k = 2 according to the "Guide to the Expression of Uncertainty in Measurement" (ISO, 1995) [3], [4]. Equation (6) serves as a model for evaluation. (Equation (10) does not include portions which are negligibly small compared with $u_{\mathrm{rel,w.}}$)

$$u_{\mathrm{rel}} = \sqrt{u_{\mathrm{rel,w}}^{\;2} + \left(\frac{\rho_{\mathrm{L}}}{\rho}u_{\mathrm{rel},\rho}\right)^2} \quad (10)$$

$$\frac{U}{m} = k \cdot u_{\mathrm{rel}}\,. \quad (11)$$

Example: $u_{\mathrm{rel,w}}$ = 0,033 %, ρ = 1150 kg/m^3, $u_{\mathrm{rel},\rho}$ = 12,5 %. From this results u_{rel} = 0,0355 % and *U*/*m* = 0,071 %.

5.5 Statement of the weighing result

The measurement result is to be stated in one of the following forms (example: *m* = 350,21 mg; *U*/*m* = 0,071 %):

a) *m* = 350,2 (1 ± 0,0007) mg
b) Complete measurement result for the mass of the weighed-in quantity: 350,2 (1 ± 0,0007) mg
c) *m* = 350,2 mg ± 0,3 mg
d) Complete measurement result for the mass of the weighed-in quantity: 350,2 mg ± 0,3 mg
e) *m* = 350,2 mg; *U*/*m* = 0,0007
f) *m* = 350,2 mg; *U*/*m* = 0,07 %

The statement of the measurement result is to be supplemented by the following explanation:
"The expanded uncertainty stated is the product of the standard uncertainty and the coverage factor *k* = 2. For a normal distribution it corresponds to a coverage probability of approx. 95 %."

Note

The numerical value of the uncertainty of measurement must be stated with maximally two significant digits. As far as rounding of the numerical value of the uncertainty of measurement is concerned, the value must be rounded up whenever rounding down would change the uncertainty of measurement by more than 5 %.

The numerical value of the measurement result must be rounded to the last significant digit which corresponds to the expanded uncertainty of measurement. The usual rules valid for the rounding of numbers (see ISO 31-0, Annex B [5]) also apply to the rounding of the measurement result.

References

[1] OIML R 111: Weights of classes E1, E2, F1, F2, M1, M2, M3

[2] DKD-R 7-1: 1998-11: Kalibrierung elektronischer nichtselbsttätiger Waagen (Calibration of electronic non-automatic weighing instruments); Blatt 1 (sheet 1): Allgemeiner Teil (General part)

[3] Guide to the Expression of Uncertainty in Measurement, first edition 1993, corrected and reprinted 1995, International Organization for Standardization (Geneva, Switzerland)

[4] DKD-3: 1998: Angabe der Messunsicherheit bei Kalibrierungen (German version of EA-4/02 (EAL-R2): 1997: Expression of the Uncertainty of Measurement in Calibration

[5] ISO 31-0: 1992-08: Quantities and Units; Part 0: General Principles