Pharmacy

MASS MEASUREMENT GUIDE

radwag.com

Radom 2025
Issue I
RADWAG Wagi Elektroniczne
26-600 Radom, ul. Toruńska 5
Tel. 48 48 38 48 800, fax 48 48 385 00 10
e-mail: radom@radwag.pl
http://www.radwag.com

CONTENTS

1. Introduction

In numerous laboratories, mass measurement is the first step for further qualitative or quantitative analyses. Therefore it must be precise, regardless of its application. Mass measurement errors may have a significant influence on security and precision of production processes as well as quality of the final product. There is no doubt that safety in pharmacy is one of the major aspects, also strictly related to micro- and macro-scale mass measurement. From the metrological point of view, measuring accuracy is a qualitative notion defined through the value of a systematic error, i.e. correctness (trueness) and random error value (precision). The value of the systematic error is influenced by the linearity, sensitivity and centricity deviation. This test can be conducted only with the use of certified mass standards, as performed in the Radwag's QC department (fig. 1). The measure of random error is the standard deviation from the series of measurements. The method of assessing these parameters is strictly defined in such discipline-specific documents as USP section 41 Balances, 1251 Weighing on an Analytical Balance, Ph. Eur. Section 2.1.7 Balances for analytical purposes, JP XVIII section 9.62 Measuring Instruments, Appliances G1-6-182. Please note that unification of requirements of the American, European or Japanese pharmacopoeia with regard to correct operation of balances is a guarantee of not only safe production but also transfer of weighing methods and systems that may be adapted to the nature of the workplace.

Figure 1. Quality Control Department – AS 220.R2 balance, correct value assessment

AS 220.R2, Maximum load 220g, elementary reading unit d=0.1mg
automatic adjustment, OIML certificate

2. Quality Management System

Supervising balances and weighing systems is the primary requirement of every quality management system, i.e. ISO 9001, ISO 17025, QMS, IS0 22000, HACCO, GMP, GLP. However the first step in putting the balance into service should always be installation qualification and operational qualification. During these processes, metrological capabilities of the balance are verified with respect to desired parameters. In stable ambient conditions, measurement results are compared with expected limits, taking into consideration methods and guidelines specified for example in USP 41, Ph. Eur. 2.1.7.

One of the most important aspects of balance supervision is calibration that allows maintaining metrological traceability to SI units. On the other hand calibration provides information on actual deviations in balance indications related to systematic and random errors. Such a procedure is performed by Radwag Measuring Laboratory – accreditation AP 069 with regard to mass measurements and single- and multi-channel pipette volume measurements.

Figure 2. Mass comparator calibration using manual method

Maximum load 500 g, electrical compensation range - 10g to + 20 g
Internal ballast weights, automatic control

Quality Management Systems also require scheduling and periodical inspections, the so-called SOP, with regard to the parameters that prove essential for the procedure in question. Preparing for the tests, it is necessary to remember that working environment fluctuations related to temperature and humidity may substantially hinder mass measurements. Another harmful effect may result from vibrations caused by machines and excessive air movement. Bearing these in mind, Radwag balances have been equipped with sensors for detection of the aforesaid phenomena, which is one of the aspects of application of Digital Weighing Auditor (DWA). DWA function has been showed in the figure 3.

Figure 3. Digital Weighing Auditor application

Key: 1 – weighing quality monitor (shocks), 2 – Digital Weighing Auditor status,
3 – temperature control, 4 – humidity control, 5 – floor vibration detection.

One of the aspects of the Quality Management System in every organisation, including Radwag, is accreditation and certification of balances and weighing systems. It is of paramount importance for such fields as pharmacy, where legal metrology supervision is required too. Therefore all Radwag's balances hold type approval certificates issued by the Notified Body, European (CMI, GUM), American (NTEP), or other adequate body for the country of use. The result of European certification is the so-called OIML certificate that confirms proper quality of the balance.

3. Mass measurement accuracy as per USP/Ph. Eur./JP

As mentioned before, accuracy is a qualitative notion. Therefore measurement must be considered as precise only when the value of systematic and random errors falls within acceptable limits. The systematic error of the balance depends on changes to balance sensitivity, linearity deviation and centricity deviation. It is assumed that the total of errors of these factors must not exceed 0.10%, but they are unlikely to occur simultaneously and have the same algebraic sign. For this reason acceptance criterion for each of them is set at 0.05%. The figure 4 shows a graphic interpretation of this phenomenon.

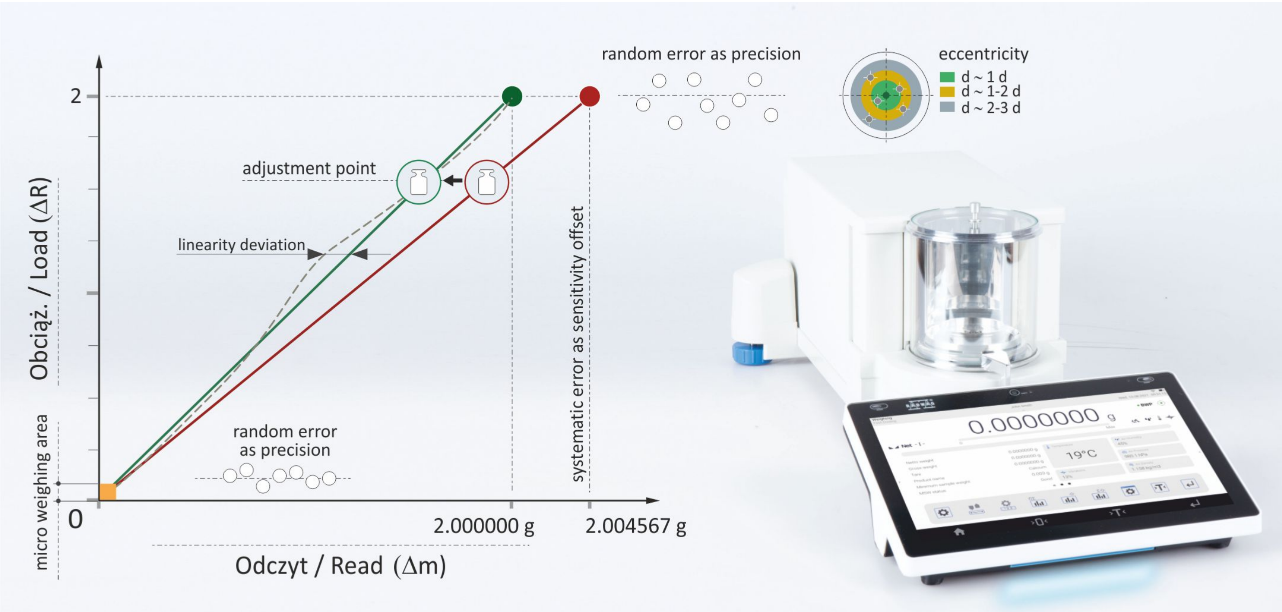

Figure 4. Systematic and random errors

As showed in the figure 4, balance accuracy, particularly in the upper weighing range, is strictly dependent upon changes to sensitivity. Sensitivity deviation rises approximately linearly with the balance load, and this is why it may be critical to measurements in which load mass is higher than 50% of the lifting capacity of the balance. It must be noted that balance adjustment performed in automatic and manual (operator's intervention) cycles eliminates these deviations. All Radwag laboratory balances (X2, X7, 5Y series) provide such adjustment possibilities.

The lower part of the diagram demonstrates in turn that potential sensitivity deviations are negligible when the load mass is minor; it is assumed that it is fewer than 5% of the maximum lifting capacity of the balance (micro weighing area). The accuracy of weighing such lightweight samples only depends on the value of the random error. This is the basis for determination of the starting point for the weighing range, the so-called Minimum Sample Weight.

The view of adjustment masses integrated into the design of balances of various resolution is showed in the figure 5. Please be informed that the adjustment mass is in fact a mass standard, but contrary to other mass standards does not hold the calibration certificate.

Figure 5. Adjustment mass of balances with various resolutions

3.1. Periodical inspection of balance sensitivity

The sensitivity deviation must be determined using a single mass standard whose nominal value ranges from 5 to 100% of the maximum lifting capacity of the balance. As a rule the test is conducted with a standard whose mass is close to the maximum load limit. The standards used to test sensitivity must comply with OIML R-111-1 or ASTM E-617 standard requirements, where standard mass determination uncertainty must not be higher than accuracy limit, i.e. 0.05%.

The test must be conducted once the balance has managed to acclimatise, in stable ambient conditions. The acclimatisation period is defined in the technical documentation dedicated to every balance and is significant with regard to measurements made with a resolution of 0.001mg (microbalances) and 0.0001mg (ultra-microbalances).

1. Load the weighing pan twice using a mass standard used to perform the test, remove the mass standard from the weighing pan,
2. Close the weighing chamber, if applicable,
3. Zero (reset) the balance indication
4. Put the mass standard on the weighing pan and record the value when stable.
5. Calculate the sensitivity deviation as per the following equation (1),

$$m - I \vee \frac{}{m} \times 100 \leq 0.05 \quad (1)$$

where:

m – standard nominal mass or its conventional mass specified in the calibration certificate,

I – indication, e.g. in grams.

Example

- AS 220.X7 balance, maximum load Max = 220g
- elementary reading unit d=0.1mg
- 200-g mass standard control, mass standard set number K-1485/18, calibration certificate 14366/4786/24
- conventional mass of mass standard 199,99987g, standard mass determination extended uncertainty, U = 0.06mg
- I weighing result = 199.9999g

$$\frac{|199.99987 - 199.9999|}{199.99987} \times 100 \leq 0.05 \tag{2}$$

$$0.000015 \leq 0.05$$

Figure 6. Balance sensitivity deviation control using a mass standard

The balance sensitivity deviation is lower than the limit defined in USP 41, Ph. Eur 2.1.7 and JP XVIII section 9.62. The balance is suitable for mass measurements in the entire measuring range.

According to Ph. Eur 2.1.7, it is usually sufficient to use a nominal mass of the weight or standard while assessing the sensitivity deviation as long as the maximum permissible test weight error (i.e. maximum permissible error for weight or test standard divided by the nominal mass) is not higher than one third of the sensitivity test specification, i.e. 0.05%. If this relation cannot be achieved, the standard mass value specified in the calibration certificate must be adopted. This being the case, the operator must make sure the standard mass determination uncertainty divided by its nominal mass is not higher than one third of 0.05%.

$$\frac{U}{M} \leq \frac{1}{3} 0.05\% = \frac{U}{M} \leq 0.00016 \tag{3}$$

where:

U – standard mass determination uncertainty,
M – standard nominal mass

Example – inspection of mass standard suitability for balance sensitivity testing

- Standard nominal mass = 200g,
- Standard mass determination extended uncertainty = 0.06mg $\rightarrow$ 0.00006g
- U/M = 0.0000003
- Limit = 0.00016
- Mass standard may be used for sensitivity deviation assessment

From the metrological point of view, the value of extended uncertainty during calibration is a distinctive feature of each laboratory that proves dependent upon accuracy of balances used for calibration and upon higher-order mass standard uncertainty.

Figure 7. XA 82/220.5Y analytical balance with control thermometer and mass standards

XA 82/220.5Y Maximum load 220g, elementary reading unit d=0.1/0.01mg
Internal adjustment, OIML certificate, interfaces: USB-A ×2, USB-C, HDMI, Ethernet, Wi-Fi®, Hotspot

It is possible to reduce measurement uncertainty while calibrating mass standards in case of adoption of automatisation. This is what happens in the Radwag's Measuring Laboratory.

4. Minimum mass USP/Ph. Eur./JP

While weighing lightweight samples, e.g. measuring the amount of powder, only the random error is essential for the measuring accuracy. Such an assessment of the mass measurement quality is presented in documents of USP 41, Ph. Eur. 2.1.7, JP XVIII section 9.62.

For determination of the random error value, it is necessary to perform a series of at least 10 measurements, and then use the final results to calculate the standard deviation. The purpose of this test is to check if the random error value (indication repeatability) is acceptable (dependency 3). The lowest possible standard deviation as per USP/Ph.Eur., may be 0.41d. If the standard deviation obtained from the series of measurements is lower than 0.41d, it must be replaced with 041d.

$$R = \frac{2 \cdot S}{m} \leq 0.10\% \rightarrow \frac{2 \cdot S}{m} \leq 0.001 \qquad (3)$$

where: S – standard deviation for values (e.g. in grams);
m – lowest net mass of the sample to be weighed.

The example of calculating the standard deviation for several various potential balances is showed in the table 1.

Table 1. Random error of balances with various values of the elementary reading unit

No.	W-1	W-2	W-3	W-4
1	20.001	0.1001	0.50001	5.0001
2	20.000	0.0999	0.50002	5.0004
3	20.001	0.1000	0.50003	5.0005
4	20.001	0.1002	0.49998	4.9997
5	20.001	0.1001	0.49998	4.9992
6	20.001	0.1000	0.50002	5.0003
7	20.001	0.0999	0.50002	5.0010
8	20.001	0.1001	0.49998	4.9992
9	20.001	0.1001	0.49998	5.0001
10	20.001	0.1000	0.50001	5.0006
St. dev. (S)	0.00032	0.00010	0.00002	0.00059
S_{MIN} = 0.41d	0.00041	x	x	x

In another step, the value of the standard deviation is used to calculate the starting point of the weighing range → the so-called Minimum Sample Weight, dependence (4).

$$MSW = 2000 \cdot S \qquad (4)$$

Weighing below the MSW threshold usually does not meet the condition 3. As per requirements of USP, Ph. Eur., JP, they cannot be considered as „accurate" and virtually should not be performed. The starting point of the weighing range for balances 1-4 is demonstrated in the table 2.

Table 2. MSW values depending on random error value

No.	W-1	W-2	W-3	W-4
d (g)	0.001	0.0001	0.00001	0.0001
St. dev. (S)	0.00032	0.00010	0.00002	0.00059
S_{MIN} = 0.41d	0.00041	x	x	x
MSW	0.82g	0.2g	0.04g	1.18g

It must be noted that MSW value is not determined by the balance resolution (number of decimal places) but by the random error value, which can be seen while comparing MSW of the balance no. 2 and 4.

In practice, measuring precision for the so-called „lightweight masses" is assigned a fixed value, assuming the test conditions are stable. Unfortunately also the operator's skills play a crucial role in testing the measuring accuracy. It refers to weighing without shocks and other measurement-hindering factors, such as vibrations or excessive air movement. While testing, it is essential that standards slightly heavier than anticipated MSW threshold must be used, mainly for practical reasons.

It is a way easier to grab the standards with forceps and place them onto the weighing pan if their surface is larger.

Figure 8. Testing filter mass changes after filtration, measuring the amount of substance

MYA 5.5Y.FA microbalance – filter mass measurement, Maximum load 5g, elementary reading unit d=0.001mg
XA 82/220.5Y analytical balance, Maximum load 220g, elementary reading unit d=0.01mg

The lowest MSW values for balances of various resolutions are showed in the table 3, yet in reality, these values are obtainable only with regard to balances with a resolution of 1mg and 0.1mg.

Table 3. Minimum MSW values, depending on elementary reading unit of the balance

Elementary reading unit (d)	Formula	MSW	Type of balance
1 mg	0.41 · 1mg ·2000	820 mg	PS 1000.X2
0.1 mg	0.41 · 0.1mg ·2000	82 mg	AS 220.5Y
0.01 mg	0.41 · 0.01mg ·2000	8.2 mg	XA 82/220.5Y
0.001 mg	0.41 · 0.001mg ·2000	0.82 mg	MYA 5.5Y
0.0001 mg	0.41 · 0.0001mg·2000	0.082 mg	UYA 2.5Y

Please note that the determined random error value is only an experimental estimation of the value that may in fact vary in view of variability of the working environment. For this reason it is advisable to perform weighing above MSW threshold.

Determination of the MSW value is only a part of the achievement as now it is necessary to consider these requirements in everyday work. MSW program function available in Radwag's AS, XA, MYA, UYA.5Y balances provides substantial support in this respect. The value of MSW threshold and its validity period are defined by the balance administrator. The weighing procedure status, regarding MSW, is clearly showed in the display unit of the balance.

Figure 9. MYA 5.5Y microbalance with an active MSW function

MYA 5.5Y, Maximum load 5g, elementary reading unit d=0.001mg
Internal adjustment, OIML certificate

5. Adjustment

The task of adjustment is to correct indications (read) of the balance. To do so, the standard weighing result (the so-called adjustment mass) is compared with its known value. These comparison are automatic → temperature change, time expiration, or semi-automatic before testing is initiated → balance operator's intervention. As opposed to external standards, the adjustment mass is not calibrated. Calibration as a procedure proving „accuracy" of indications is performed for the balance as a whole, so in fact also with reference to the internal value of the adjustment mass. The adjustment principle has been showed in the figure 9; it is identical to each balance, and correct operation of this unit is verified by the QC Department in Radwag.

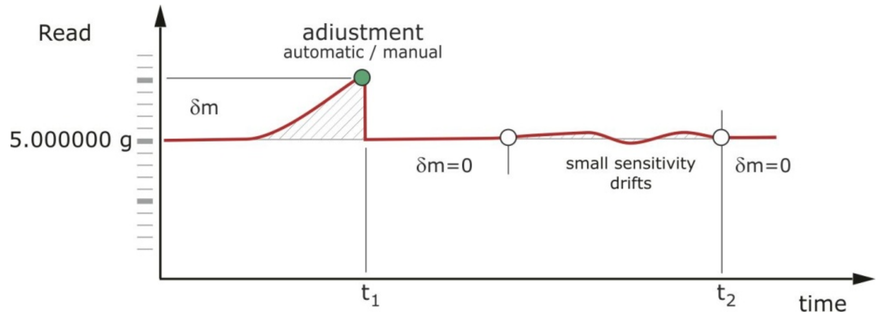

Figure 10. General principle of electronic balance adjustment

The balance adjustment is concerned with a typical weighing of the load. From the metrological point of view, the quality of this procedure may be defined through the precision of measurement. It is a common knowledge that measurement precision is widely dependent upon measuring conditions as well as operator's skills. It must be emphasised that adjustment automation and integration of the adjustment mass inside the balance substantially increases precision of measurement when compared to manual measuring. It is highly important and desired as the balance sensitivity is corrected on the basis of the adjustment mass weighing result.

As mentioned before, the qualitative parameter of adjustment is precision of measurement that can be determined through the Autotest GLP diagnostic function. It is available in the menu of Radwag's most laboratory balances. The principle of operation of the GLP Autotest is based on determination of the standard deviation → measure of measuring precision, based on a series of 10 weighing cycles of the internal adjustment mass. The final value of the standard deviation is usually lower than the value of the elementary unit of the balance in question.

6. Measuring methods

As a rule, the weighing method is defined through PN-EN, ASTM standards, ISO guidebooks or other renowned and adopted-for-use discipline-specific documents, internal or external documents. The requirements may concern the sample mass, method of sample collection, storage and weighing tolerance. Please remember that samples are not neutral and may prove unstable in view of moisture sorption, unbalanced electrostatic charges and thermal instability. The working environment may also have an influence on weighing, when its variability with regard to temperature, humidity and air movement as well as vibrations is too high.

Figure 11. XA 82/220.5Y balance, filter mass measurement,
MYA 2.5Y microbalance, capsule mass measurement - uniformity of medical preparation mass (USP)

XA 82/220.5Y analytical balance, Maximum load 220g, elementary reading unit d=0.01mg, OIML certificate
MYA 2.5Y microbalance, Maximum load 2g, reading unit d=0.001mg, OIML certificate

The variable working environment is monitored by internal sensors installed in 5Y-series balances → green icons in the display unit, figure 10. It is a professional solution for every laboratory in terms of variable working conditions supervision. It is also possible to connect additional temperature and humidity sensors to the balance USB port in order to monitor the working environment.

The accuracy of measurement in the micro scale may be disturbed by numerous factors that interact with one another. In spite of this, it is possible to specify the potential mass measurement accuracy by checking the precision of measurement in the place of using the device. This test is usually conducted using a standard whose mass is similar to the mass of weighed samples. The standard deviation (S) from a series of measurements is a measure of imprecision; the lower the value (S), the better the series result consistence → higher precision of measuring. As we know, precision of measurement is a random error, and the measuring accuracy is also affected by the systematic error. It may be significant only when the mass of weighed samples exceeds 50% of the maximum lifting capacity limit of the balance.

7. Metrological inspection of balances and weighing systems

From the metrological and regulatory[1] point of view, there is no doubt that every measuring instrument, including a balance, must be subject to periodical inspection as per the adopted schedule. With respect to balances, such a procedure is carried out using one or several mass standards, and is concerned with comparing the balance indication with the known certified standard value. As a rule the permissible tolerance (+-) applicable to the standard weighing result or limit, i.e. weighing threshold, MSW, is determined.

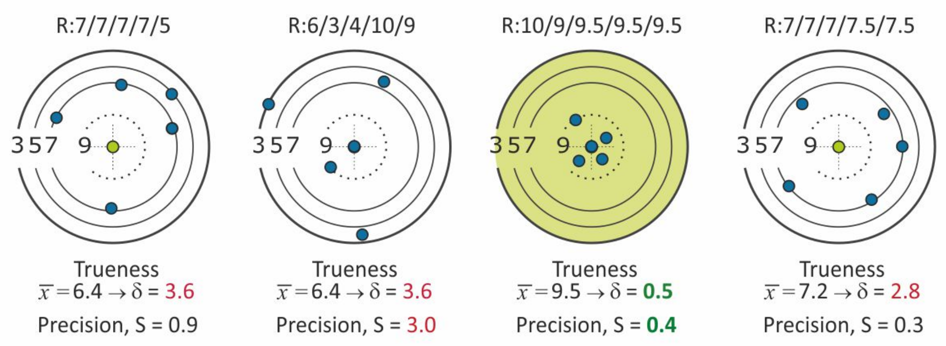

Figure 12. Trueness and precision in mass measurement

As part of the metrological inspection, mass standards are used to assess accuracy of measurement → systematic error. It is the normative approach, recommended by OIML, with reference to all non-automatic balances. It must be noted that in reality the mass measurement is performed for completely different items than steel standards. Therefore one may assume that precision of measurement will be different, especially when the weighed item has a way larger surface → filter.

Figure 13. Balance metrological inspection, filter mass measurement

[1] ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories, EN ISO 9001:2015 Quality management systems – Requirements)

LIST OF FIGURES

LIST OF TABLES

Radwag

Toruńska 5 Street
26-600 Radom, Poland
Tel. +48 48 386 60 00
e-mail: office@radwag.com

radwag.com