USP new regulation

Compliance with the **NEW USP** requirements... It's simple

radwag.com

The mass measurement is one of the most simple measurements that are executed in the laboratory.

Weighing, which is a seemingly simple measuring process, is characterized by quite complicated mechanisms. To understand, what these mechanisms really are and how they work, lets to improve the work but also to use the scale optimally.

Our technological solutions ensure full accordance with legal requirements, no matter what country the scales is to be used.

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New regulations concerning the scales are to be found in two chapters, <General Chapters, Apparatus forTests and Assays <41„BALANCES"> and <General Information, <1251„WEIGHING ON AN ANALYTICAL BALANCE">

TERMS OF PARTICULAR IMPORTANCE

The main parametre which decides about the scales accuracy is its repeatability.
Other parametres such as centricity, linearity or stability of the sensitivity are of lesser importance.

ACCURATE

The measurement is „accurate" if its relative uncertainty is not higher than 0.0010 (0.10%}.
Tests include parameters such as:

- Sensitivity,
- Linearity,
- Eccentricity,
- Repeatability

ABOUT

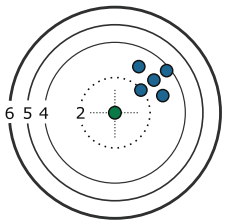
This term refers to the measurements, for which the relative uncertainty is not higher than 0.1 (10%).

ASSAY

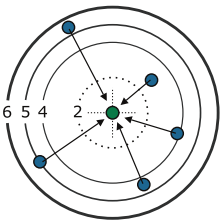
This term refers to the active ingredient of the medicine. The tests (Assays) are „accurate" by assumption unless it has been stated the other way round.

TEST

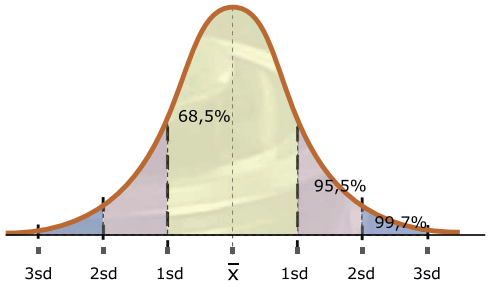
This term refers to the inactive ingredients of the medicine. The tests are not „accurate" by assumption unless it has been stated the other way round.

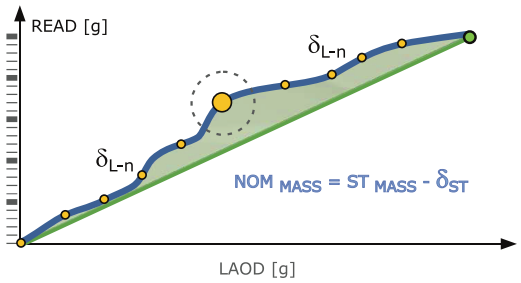


The precision of measurement does not mean accuracy



Inaccurately Imprecisely measurement





Sensitivity, linearity, and eccentricity all accountfor systematic deviations; i.e., they limit the accuracy of the bolonce. Because deviations are targety independent from each other, it is not likely that all deviations occur simultaneously and have the same a/gebraic sign. Therefore the arithmetic addition of all individua/ deviations to assess the bolonce accuracy wou/d constitute a rather conservative approach {USP 1251).

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CHANGES IN REGULATORY USP

A term for a „correct" weighing of the substance has been modified. It has been done by introduction of a new condition for the repeatability.This allowed for an elimination of possibility to make big mistakes when determining the input value of the weighing range. The tolerance and mass range have been established duringthe accuracy test.

REPEATABILITY <41 balances>	**11.2013** (finish) old regulations	**12.2013** (start) NEW regulations
Tolerance	0,1% (0,149%)	0,10%
Expansion factor	3	2
Quantity measurements	10	10
Acceptance criterion	$\frac{3 \times sd}{m} \leq 0,1\ \%$	$\frac{2 \times sd}{m} \leq 0,10\ \%$

Repeatability is satisfactory if two times the standard deviation of the weighed value, divided by the nominał value of the weight used, does not exceed 0.10%. If the standard deviation obtained is less than 0.41d , where d is the scale interval, re place this standard deviation with 0.41d.

REPEATABILITY <41 balances>	**11.2013** (finish) old regulations	**12.2013** (start) NEW regulations
Tolerance	---------	≤ 0,10 % (Rw)
Reference weight	---------	m = 5% ÷ 100% Max

RW - reference weight

The accuracy of a balance is satisfactory if its weighing value, when tested with a suitable weight(s), is within 0.10% of the test weight value.
A test weight is suita ble if it has a mass between 5% and 100% of the balance's capacity

Test for balances

Repeatability, Accuracy, stability ... SOP RADWAG

Applying the scales into a new reality {New USP) requires their parametres to be verified through the evaluation of the results or through metrology research.

REPEATABILITY

Do the repeatability test by weighing the same mass 10 times in a row. Calculate the standard deviation of the measuring series. Check if the relationship is fulfilled.

(2 x sd)/m ≤ 0,0010

(2 x 0,00085)/ 5 = 0,00034

TEST IS APPROVED

1. 5,040 mg
2. 5,041 mg
3. 5,040 mg
4. 5,041 mg
5. 5,041 mg
6. 5,042 mg
7. 5,041 mg
8. 5,040 mg
9. 5,039 mg
10. 5,040 mg

sd = 0,00085 mg

MYA 5Y

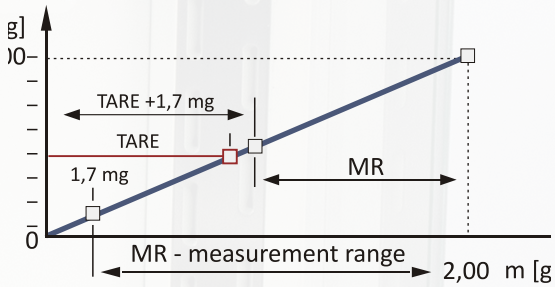
MINIMUM SAMPLE WEIGHT

Calculate the value for MSW- starting point of the measurement range.

MSW = 2000 x sd

MSW = 2000 x 0,00085 = 1, 7 mg

MEASUREMENT RANGE: 1,7 mgt ÷ Max



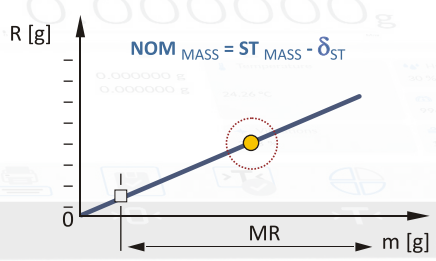
The minimum sample weight is not a term defined by normative documents, its existence stems from the USP General Chapter 41 "Balances" and 1251 "Weighing on an analytical balances", where the conditions for "accurate" weighing are given.

ACCURACY

Explore the accuracy of standard mass in the range of 5% Max ÷ Max. Compare the result of weighing the value of the reference weight. Check whether the relationship is satisfactory:

Rw - R ≤ 0,10 % (Rw)

Rw - Reference weight
R - result of weighing



MR - measurement range

Mass [mg]	δ 0,10%m
1000	± 1 mg
800	± 0,8 mg
600	± 0,6 mg
400	± 0,4 mg
200	± 0,2 mg
100	± 0,1 mg
50	± 0,05 mg
40	± 0,04 mg
30	± 0,03 mg
20	± 0,02 mg
10	± 0,01 mg
5	± 0,005 mg
1	± 0,001 mg

Minimum sample weight

determination, choice of scales for your procedure

Through the study of repeatability it is possible to determine a threshold (MSW), below which it is not recommended to weigh because of too large errors. This threshold is the beginning of the measuring range. Its value can be varia ble, depending on many factors related to the process of mass measurement.

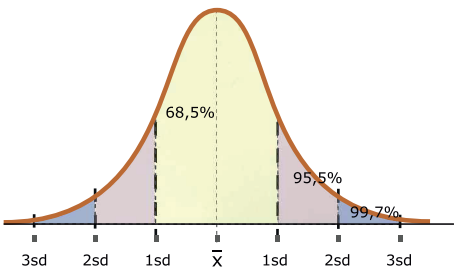
MSW - determination

Step 1. Select the test weight with a value of 5000 d

Balance readability (d)	1 mg	0,1 mg	0,01 mg	0,001 mg	0,0001 mg
Test weight	5 g	0,5 g	50 mg	5 mg	5 mg*

* - the smallest mass standard is 1 mg

Step 2. Determine the repeatability as the standard deviation of a series of 10 repetitions (m=50 mg)



1. 0,05001
2. 0,04999
3. 0,04997
4. 0,04999
5. 0,04998
6. 0,04997
7. 0,04999
8. 0,04998
9. 0,05001
10. 0,04998

$$sd = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \overline{x})^2}{n-1}}$$

sd = 0,000014 g

The repeatability of the initial weight range is not dependent on the load (a constant value).

Step 3. Calculate the value of Minimum Sample Weight

MSW = 2000 x sd

USP 1251„Weighing on an analytical balance" (guidance)

MSW = 2000 x 0,000014 g = 0,028 g = 28 mg

Step 4. Check the mass range that meet the criteria , the „correct" weighing

(2 x sd)/m ≤ 0,0010

USP 41„Balances" (mandatory)

(2 x 0,000014) / 0,05g = 0,00056 < 0,0010 (PASS)

MSW (new regulations)

Testing mass	50 mg	40 mg	30 mg	28 mg	25 mg	20 mg	15 g	10 mg	Accuracy Relationship
(2xsd)/m	0,00056	0,00071	0,00095	0,00101	0,00113	0,00142	0,00189	0,00284	**≤ 0,0010**
(3xsd)/m	0,00085	0,00106	0,00142	0,00152	0,00170	0,00213	0,00284	0,00425	**≤ 0,001**
	50 mg	40 mg	30 mg	28 mg	25 mg	20 mg	15 mg	10 mg	

Rounding problem: 0,001 [499]

MSW (old regulations)

Minimum sample weight

determination, choice of scales for your procedure

Knowing the mass of the weigh, look for a scales which meets the requirements for accurate weighing such one for which the repeatability is sufficient. Repeatability may vary, which depends on many factors related to the process of mass measurement.

Step 1. Check what is the weight of the smallest sample that is to be weighed, e.g.: m = 38 mg

Step 2. Calculate repeatability according to the relationship

$$sd = (0{,}0010 / 2) \times m$$

where:
0,0010 - accuracy of the analyssis
2 - expansion factor
m - your minimium sample mass

Step 3. Example
What repeatability shoult the balance have when 34 mg is weighed with the maintenance of accuracy of 0.10%.

$$sd = (0{,}0010 / 2) \times 34\ mg = 0{,}017\ mg$$

Step 4. Choice of balances
Balances repeatability should be less than the calculated value.

MICROBALANCES	UYA 2	MYA 2	MYA 0,8/3	MVAS	MYA II	MYA 21
Max capacity	2 g	2 g	0,8/3 g	5 g	11 g	21 g
Repeatability	0,003 mg	0,0006 mg			0,001 mg	
Verification	complies	complies			complies	

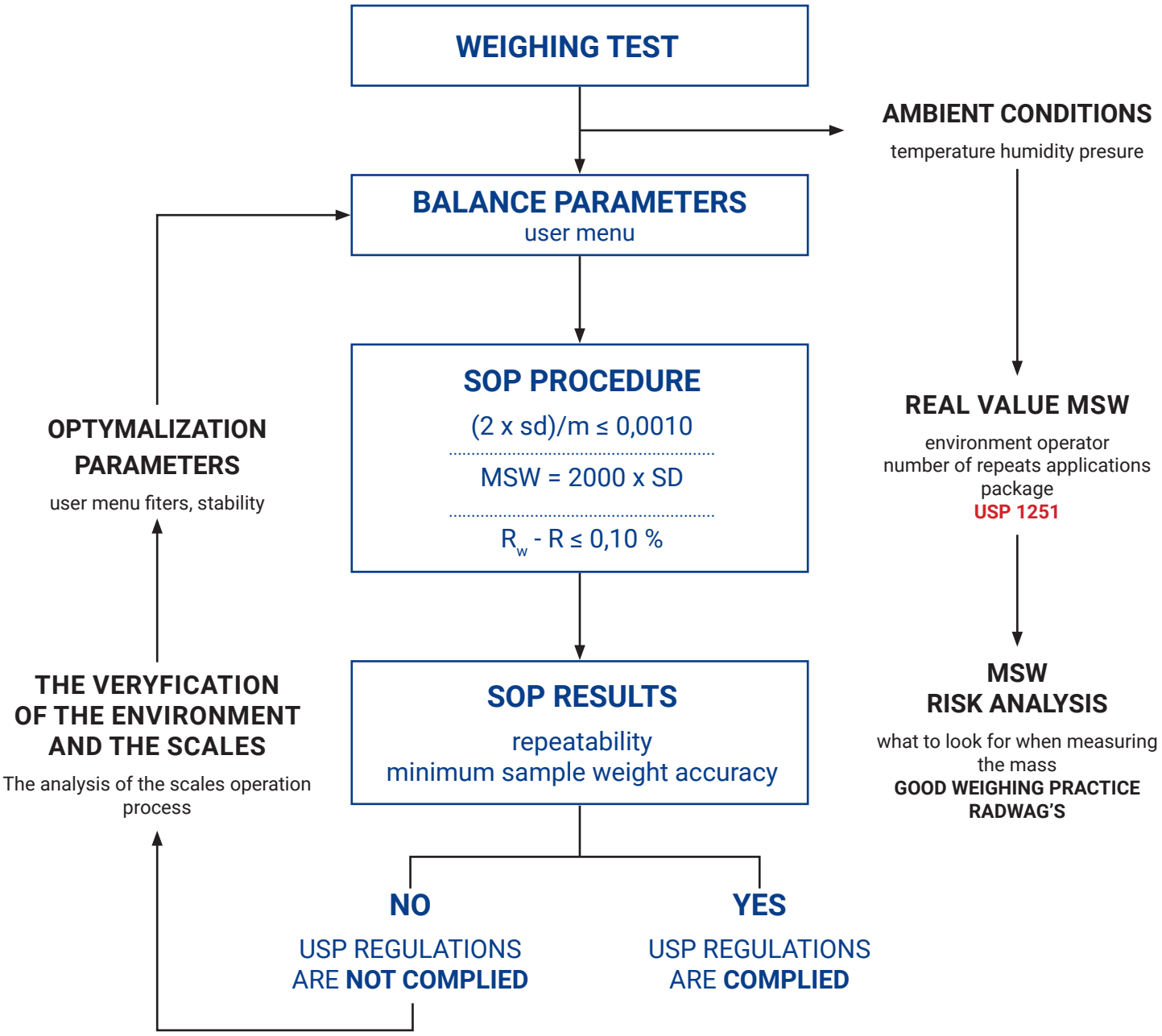
ANALYTICAL BALANCES	XA 52.5Y	XA 110.5Y	XA 210.5Y	XA 82/220.5Y
Max capacity	52 g	100 g	210 g	82/220 g
Repeatability	0,01 mg	0,02 mg		0,02/0,08 mg
Verification	complies	does not meet the requirements		

The minimum sample weight is not a term defined by normative documents, its existence stems from the USP General Chapter 41 „Balances" and 1251 „Weighing on an analytical balances': where the conditions for „accurate" weighing are given.

Test - optymalization

Repeatability, Accuracy, Stability... you can do better

The external conditions (the dynamics of change) significantly influence the measurement result. Their impact can be minimalized through the scales parametres OPTIMALIZATION.



USP new regulation in practice

Speed, precision, ergonomics ..... Radwag balances

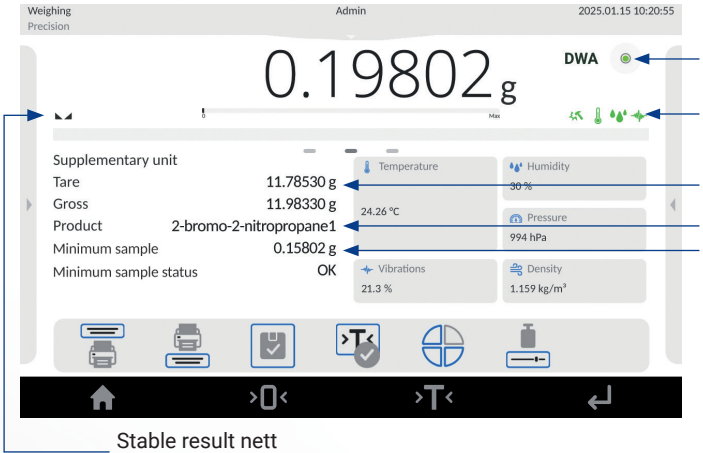
The RADWAG scales comply with all the requirements of new USP rules, therefore they can be used in laboratories (accurate weighing of the substance), on the production line (on-line time mass monitoring), in the storehouse (registration, ready products marking).

DATABASES

- Operators
- Products
- Customers
- Formulations
- Pipettes
- Pipette calibration orders database
- Minimum samples
- Packaging
- Warehouses
- Printouts / Labels
- Series
- Universal variables
- Extra variables
- Test procedures
- Manage the database

REPORTS

- Weighing record
- Formulations report
- Density reports
- Controls reports
- SQC statistics
- Pipette calibration order results
- Test results
- Ambient conditios
- Manage reports



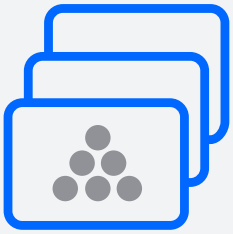
USP new regulation in practice

Radwag's Balances for accurate weighing


Easy Connect


Exchange Date


Level Sensing


Multi Modes


Multi User


Smart Menu


Touch Free


Up To Date


Weighing Transducer

Ultra-microbalances	**Max Capacity**	**Readability [d]**	**Repeatability [5%]**	**Linearity**	**Standard minimum weight (USP)**
UYA 2.5Y	2,1 g	0,1 µg	0,15 µg	± 1,5 µg	0,3 mg
UYA 6.5Y	6,1 g	0,1 µg	0,2 µg	± 1,5 µg	0,4 mg
Microbalances	**Max Capacity**	**Readability [d]**	**Repeatability [5%]**	**Linearity**	**Standard minimum weight (USP)**
MYA 0.8/3.5Y	0,8 /3 g	1 / 10 µg	0,6 µg	±3 µg	1,2 mg
MYA 2.5Y	2,1 g	1 µg	0,41 µg	±3 µg	0,82 mg
MYA 5.5Y	5,1 g	1 µg	0,6 µg	±3 µg	1,2 mg
MYA 6.5Y	6 g	1 µg	0,6 µg	±5 µg	1,2 mg
MYA 11.5Y	11 g	1 µg	0,9 µg	±6 µg	1,8 mg
MYA 21.5Y	21 g	1 µg	1 µg	±7 µg	2 mg
MYA 31.5Y	31 g	1 µg	1,2 µg	±8 µg	2,4 mg
Analytical Balance	**Max Capacity**	**Readability [d]**	**Repeatability [5%]**	**Linearity**	**Standard minimum weight (USP)**
XA 41/120.5Y.A	41 / 120 g	0,002 / 0,005 mg	0,004 mg		8 mg
XA 52.5Y.A	52 g	0,01 mg	0,005 mg	±0,03 mg	10 mg
XA 82/220.5Y.A	82 /220 g	0,01 / 0,1 mg	0,005 mg	±0,06 / 0,2 mg	10 mg
XA 110.5Y.A	110 g	0,01 mg	0,005 mg	±0,06 mg	10 mg

USP new regulation in practice

Radwag's Balances for accurate weighing

Ultra-microbalances	Max Capacity	Readability [d]	Repeatability [5%]	Linearity	Standard minimum weight (USP)
UYA 2.5Y	2,1 g	0,1 µg	0,15 µg	± 1,5 µg	0,3 mg
UYA 6.5Y	6,1 g	0,1 µg	0,2 µg	± 1,5 µg	0,4 mg
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MYA 2.5Y	2,1 g	1 µg	0,41 µg	±3 µg	0,82 mg
MYA 5.5Y	5,1 g	1 µg	0,6 µg	±3 µg	1,2 mg
MYA 6.5Y	6 g	1 µg	0,6 µg	±5 µg	1,2 mg
MYA 11.5Y	11 g	1 µg	0,9 µg	±6 µg	1,8 mg
MYA 21.5Y	21 g	1 µg	1 µg	±7 µg	2 mg
MYA 31.5Y	31 g	1 µg	1,2 µg	±8 µg	2,4 mg
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XA 52.5Y.A	52 g	0,01 mg	0,005 mg	±0,03 mg	10 mg
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XA 110.5Y.A	110 g	0,01 mg	0,005 mg	±0,06 mg	10 mg
XA 120/250.5Y.A	120 / 250 g	0,01 / 0,1 mg	0,005 mg	±0,06 / 0,2 mg	10 mg
XA 121/220.5Y.A	121 / 220 g	0,005 / 0,01 mg	0,005 mg		10 mg
XA 210.5Y.A	210 g	0,01 mg	0,005 mg	±0,1 mg	10 mg
XA 220.5Y.A	220 g	0,1 mg	0,05 mg	±0,2 mg	100 mg
XA 310.5Y.A	310 g	0,1 mg	0,05 mg	±0,3 mg	100 mg
XA 320.5Y.A	320 g	0,05 mg	0,02 mg	±0,3 mg	41 mg
XA 520.5Y.A	520 g	0,1 mg	0,07 mg	±0,7 mg	140 mg
XA 52.5Y	52 g	0,01 mg	0,005 mg	±0,03 mg	10 mg
XA 82/220.5Y	82 / 220 g	0,01 / 0,1 mg	0,005 mg	±0,06 / 0,2 mg	10 mg
XA 110.5Y	110 g	0,01 mg	0,005 mg	±0,06 mg	10 mg
XA 120/250.5Y	120 / 250 g	0,01 / 0,1 mg	0,005 mg	±0,06 / 0,2 mg	10 mg
XA 210.5Y	210 g	0,01 mg	0,005 mg	±0,1 mg	10 mg
XA 220.5Y	220 g	0,1 mg	0,05 mg	±0,2 mg	100 mg
XA 310.5Y	310 g	0,1 mg	0,05 mg	±0,2 mg	100 mg
XA 520.5Y	520 g	0,1 mg	0,07 mg	±0,5 mg	140 mg