

Assay of Simvastatin in Tablets by HPLC

The measurand: mean Simvastatin content of the set of 8 tablets that were taken as the sample.

The prototype of the method is based on the monographs of Simvastatin in the European Pharmacopoeia (Ph.Eur. 5th Ed.) and the United States Pharmacopoeia / the National Formulary (USP 27 / NF 22).

Scope of use and validation: Quantitative determination of Simvastatin in drug products.

Principle: The drug substance is extracted from the tablets by using solution of the 0.01M phosphate buffer pH4.0 and acetonitrile in the ratio 20:80 (V/V). The samples are filtered and the resulting solution is injected into HPLC. Separation is achieved at room temperature in a Phenomenex Prodigy 3 u ODS (end-capped) column (30 x 4.60 mm), detection wavelength is 238 nm. A Single standard solution or a series of calibration solutions (depending on the calibration procedure) of Simvastatin standard substance is used for calibration.

Model Equation:

{ The main equation

Calibration graph method (with slope b_1 and intercept b_0) is used for quantitation

The result is given Recovery-corrected (R)

The sample solution is prepared by dissolving several tablets to achieve averaging

}

$$C_{SVT} = (A_{\text{sample}} - b_0) * V_{100} / (b_1 * n_{\text{tab}} * R);$$

{ Chromatographic measurements

Peak areas are used as the basis for quantification.

We assume that the uncertainty of the chromatographic peak area of the sample solution has 4 components

- Repeatability (contained in $A_{\text{sample_rep}}$)
- Uncertainty due to detector drift ($A_{\text{sample_drift}}$)
- Uncertainty due to imperfection of peak integration ($A_{\text{sample_integr}}$)
- Uncertainty due to the slight nonlinearity of the calibration graph ($A_{\text{sample_nonlin}}$)

The $A_{\text{sample_rep}}$ carries the value and the repeatability uncertainty. The other components carry the respective uncertainty component only, their value is 0.

}

{ Sample peak area }

$$A_{\text{sample}} = A_{\text{sample_rep}} + A_{\text{sample_drift}} + A_{\text{sample_integr}} + A_{\text{sample_nonlin}};$$

{ Recovery

The value of Recovery (R_0) has been determined from spiking studies.

The R_0 also contains the sample-to-sample variability uncertainty component

The A_{R_eff} is the effective peak area during recovery determination and it takes into account the uncertainty in determining the recovery value.

The division by the const() function reforms A_{R_eff} into a coefficient with vaule 1 and uncertainty

equal to the relative uncertainty of A_{R_eff} .

}

$$R = R_0 * A_{R_eff} / \text{const}(A_{R_eff});$$

$$A_{R_eff} = A_{R_eff_integr} + A_{R_eff_nonlin};$$

{ Peak areas of the calibration standard solutions

Their areas have the same components as the sample peak area, except that the nonlinearity uncertainty contribution is not included.

}

$$A_1 = A_{1rep} + A_{1drift} + A_{1integr};$$

$$A_2 = A_{2rep} + A_{2drift} + A_{2integr};$$

$$A_3 = A_{3rep} + A_{3drift} + A_{3integr};$$

$$A_4 = A_{4rep} + A_{4drift} + A_{4integr};$$

$$A_5 = A_{5rep} + A_{5drift} + A_{5integr};$$

{ Linear regression equations (Calibration graph is used for quantitation) }

$$\Sigma AC = C_1 * A_1 + C_2 * A_2 + C_3 * A_3 + C_4 * A_4 + C_5 * A_5;$$

$$\text{AvgC} = (C_1 + C_2 + C_3 + C_4 + C_5) / n;$$

$$\text{AvgA} = (A_1 + A_2 + A_3 + A_4 + A_5) / n;$$

$$\Sigma CC = C_1 * C_1 + C_2 * C_2 + C_3 * C_3 + C_4 * C_4 + C_5 * C_5;$$

$$b_1 = (\Sigma AC - n * \text{AvgC} * \text{AvgA}) / (\Sigma CC - n * \text{AvgC} * \text{AvgC});$$

$$b_0 = \text{AvgA} - b_1 * \text{AvgC};$$

{ Preparation of standard solutions }

$$C_1 = m_1 * P_{std} / (V_{1_50} * 100);$$

$$C_2 = m_2 * P_{std} / (V_{2_50} * 100);$$

$$C_3 = m_3 * P_{std} / (V_{3_50} * 100);$$

$$C_4 = m_4 * P_{std} / (V_{4_50} * 100);$$

$$C_5 = m_5 * P_{std} / (V_{5_50} * 100);$$

{ Uncertainty of weighing

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$$m_1 = m_{1_rep} + m_{1_buoyancy} + m_{1_drift} + m_{1_round} + m_{1_electrost};$$

$$m_2 = m_{2_rep} + m_{2_buoyancy} + m_{2_drift} + m_{2_round} + m_{2_electrost};$$

$$m_3 = m_{3_rep} + m_{3_buoyancy} + m_{3_drift} + m_{3_round} + m_{3_electrost};$$

$$m_4 = m_{4_rep} + m_{4_buoyancy} + m_{4_drift} + m_{4_round} + m_{4_electrost};$$

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$$m_5 = m_{5_rep} + m_{5_buoyancy} + m_{5_drift} + m_{5_round} + m_{5_electrost};$$

$$m_{1_buoyancy} = m_{1_rep} * f_{buoyancy};$$

$$m_{2_buoyancy} = m_{2_rep} * f_{buoyancy};$$

$$m_{3_buoyancy} = m_{3_rep} * f_{buoyancy};$$

$$m_{4_buoyancy} = m_{4_rep} * f_{buoyancy};$$

$$m_{5_buoyancy} = m_{5_rep} * f_{buoyancy};$$

{ Volumes of 50 ml volumetric flask }

$$V_{1_50} = V_{1_50_cal} + V_{1_50_fill} + V_{1_50_temp};$$

$$V_{2_50} = V_{2_50_cal} + V_{2_50_fill} + V_{2_50_temp};$$

$$V_{3_50} = V_{3_50_cal} + V_{3_50_fill} + V_{3_50_temp};$$

$$V_{4_50} = V_{4_50_cal} + V_{4_50_fill} + V_{4_50_temp};$$

$$V_{5_50} = V_{5_50_cal} + V_{5_50_fill} + V_{5_50_temp};$$

$$V_{1_50_temp} = V_{1_50_cal} * \Delta t * \gamma_w;$$

$$V_{2_50_temp} = V_{2_50_cal} * \Delta t * \gamma_w;$$

$$V_{3_50_temp} = V_{3_50_cal} * \Delta t * \gamma_w;$$

$$V_{4_50_temp} = V_{4_50_cal} * \Delta t * \gamma_w;$$

$$V_{5_50_temp} = V_{5_50_cal} * \Delta t * \gamma_w;$$

{ Volume of the sample solution }

$$V_{100} = V_{100_cal} + V_{100_fill} + V_{100_temp};$$

$$V_{100_temp} = V_{100_cal} * \Delta t * \gamma_w;$$

List of Quantities:

Quantity	Unit	Definition
A ₁	AU	Peak area of the 1. calibration standard solution
A _{1drift}	AU	Drift uncertainty component of the peak area of the 1. calibration standard solution
A _{1integr}	AU	Integration uncertainty component of the peak area of the 1. calibration standard solution
A _{1rep}	AU	Value and the repeatability uncertainty component of the peak area of the 1. calibration standard solution
A ₂	AU	Peak area of the 2. calibration standard solution
A _{2drift}	AU	Drift uncertainty component of the peak area of the 2. calibration standard solution
A _{2integr}	AU	Integration uncertainty component of the peak area of the 2. calibration standard solution
A _{2rep}	AU	Value and the repeatability uncertainty component of the peak area of the 2. calibration standard solution
A ₃	AU	Peak area of the 3. calibration standard solution

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Quantity	Unit	Definition
$A_{3\text{drift}}$	AU	Drift uncertainty component of the peak area of the 3. calibration standard solution
$A_{3\text{integr}}$	AU	Integration uncertainty component of the peak area of the 3. calibration standard solution
$A_{3\text{rep}}$	AU	Value and the repeatability uncertainty component of the peak area of the 3. calibration standard solution
A_4	AU	Peak area of the 4. calibration standard solution
$A_{4\text{drift}}$	AU	Drift uncertainty component of the peak area of the 4. calibration standard solution
$A_{4\text{integr}}$	AU	Integration uncertainty component of the peak area of the 4. calibration standard solution
$A_{4\text{rep}}$	AU	Value and the repeatability uncertainty component of the peak area of the 4. calibration standard solution
A_5	AU	Peak area of the 5. calibration standard solution
$A_{5\text{drift}}$	AU	Drift uncertainty component of the peak area of the 5. calibration standard solution
$A_{5\text{integr}}$	AU	Integration uncertainty component of the peak area of the 5. calibration standard solution
$A_{5\text{rep}}$	AU	Value and the repeatability uncertainty component of the peak area of the 5. calibration standard solution
A_{R_eff}	AU	The effective peak area during the Recovery determination (difference of the peak areas of spiked and unspiked solutions)
$A_{R_eff_integr}$	AU	The value and integration uncertainty of the effective peak area during the recovery determination
$A_{R_eff_nonlin}$	AU	The uncertainty of the effective peak area due to nonlinearity of the calibration graph during the recovery determination
A_{sample}	AU	Peak area of the sample solution
$A_{\text{sample_drift}}$	AU	Drift uncertainty component of the sample peak area
$A_{\text{sample_integr}}$	AU	Integration uncertainty component of the sample peak area
$A_{\text{sample_nonlin}}$	AU	Uncertainty component of the sample peak area that takes into account the slight non-linearity of the calibration graph
$A_{\text{sample_rep}}$	AU	The value of the sample solution peak area together with its repeatability uncertainty
AvgA	AU	Interim quantity for regression statistics calculation
AvgC	mg/ml	Interim quantity for regression statistics calculation
b_0	AU	Intercept of the calibration line
b_1	AU*ml/mg	Slope of the calibration line
C_1	mg/ml	Concentration of the 1. calibration standard solution
C_2	mg/ml	Concentration of the 2. calibration standard solution
C_3	mg/ml	Concentration of the 3. calibration standard solution
C_4	mg/ml	Concentration of the 4. calibration standard solution
C_5	mg/ml	Concentration of the 5. calibration standard solution

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Quantity	Unit	Definition
C_{SVT}	mg/tab	Content of simvastatin in Simvastatin 10 mg tablets
$f_{buoyancy}$	unitless	Correction factor for air buoyancy
m_1	mg	Mass of the Simvastatin CRS taken for preparation of the 1. calibration standard solution
$m_{1_buoyancy}$	mg	Air buoyancy component of uncertainty of mass m1
m_{1_drift}	mg	Drift component of uncertainty of mass m1
$m_{1_electrost}$	mg	Electrostatic component of uncertainty of mass m1
m_{1_rep}	mg	Value of the mass of the Simvastatin CRS taken for preparation of the 1. calibration standard solution together with repeatability component of uncertainty
m_{1_round}	mg	Rounding component of uncertainty of mass m1
m_2	mg	Mass of the Simvastatine CRS taken for preparation of the 2. calibration standard solution
$m_{2_buoyancy}$	mg	Air buoyancy component of uncertainty of mass m2
m_{2_drift}	mg	Drift component of uncertainty of mass m2
$m_{2_electrost}$	mg	Electrostatic component of uncertainty of mass m2
m_{2_rep}	mg	Value of the mass of the Simvastatine CRS taken for preparation of the 2. calibration standard solution together with repeatability component of uncertainty
m_{2_round}	mg	Rounding component of uncertainty of mass m2
m_3	mg	Mass of the Simvastatine CRS taken for preparation of the 3. calibration standard solution
$m_{3_buoyancy}$	mg	Air buoyancy component of uncertainty of mass m3
m_{3_drift}	mg	Drift component of uncertainty of mass m3
$m_{3_electrost}$	mg	Electrostatic component of uncertainty of mass m3
m_{3_rep}	mg	Value of the mass of the Simvastatine CRS taken for preparation of the 3. calibration standard solution together with repeatability component of uncertainty
m_{3_round}	mg	Rounding component of uncertainty of mass m3
m_4	mg	Mass of the Simvastatine CRS taken for preparation of the 4. calibration standard solution
$m_{4_buoyancy}$	mg	Air buoyancy component of uncertainty of mass m4
m_{4_drift}	mg	Drift component of uncertainty of mass m4
$m_{4_electrost}$	mg	Electrostatic component of uncertainty of mass m4
m_{4_rep}	mg	Value of the mass of the Simvastatine CRS taken for preparation of the 4. calibration standard solution together with repeatability component of uncertainty
m_{4_round}	mg	Rounding component of uncertainty of mass m4
m_5	mg	Mass of the Simvastatine CRS taken for preparation of the 5. calibration standard solution
$m_{5_buoyancy}$	mg	Air buoyancy component of uncertainty of mass m5
m_{5_drift}	mg	Drift component of uncertainty of mass m5

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Quantity	Unit	Definition
$m_{5_electrost}$	mg	Electrostatic component of uncertainty of mass m_5
m_{5_rep}	mg	Value of the mass of the Simvastatine CRS taken for preparation of the 5. calibration standard solution together with repeatability component of uncertainty
m_{5_round}	mg	Rounding component of uncertainty of mass m_5
n	unitless	Number of points on the calibration line
n_{tab}	tab	Number of the tablets taken for preparation of the sample solution
P_{std}	%	Purity of the Simvastatin CRS
R	unitless	Recovery
R_0	unitless	The value of R and its uncertainty component that is due to the imperfection of the sample preparation procedure
V_{100}	ml	Volume of the sample solution
V_{100_cal}	ml	Value of the volume of the sample solution together with calibration component of uncertainty
V_{100_fill}	ml	Filling component of uncertainty of volume V_{100}
V_{100_temp}	ml	Uncertainty component of volume V_{100} due to temperature difference from 20°C
V_{1_50}	ml	Volume of the 1. calibration standard solution
$V_{1_50_cal}$	ml	Value of the volume of the 1. calibration standard solution together with calibration component of uncertainty
$V_{1_50_fill}$	ml	Filling component of uncertainty of volume V_{1_50}
$V_{1_50_temp}$	ml	Uncertainty component of volume V_{1_50} due to temperature difference from 20°C
V_{2_50}	ml	Volume of the 2. calibration standard solution
$V_{2_50_cal}$	ml	Value of the volume of the 2. calibration standard solution together with calibration component of uncertainty
$V_{2_50_fill}$	ml	Filling component of uncertainty of volume V_{2_50}
$V_{2_50_temp}$	ml	Uncertainty component of volume V_{2_50} due to temperature difference from 20°C
V_{3_50}	ml	Volume of the 3. calibration standard solution
$V_{3_50_cal}$	ml	Value of the volume of the 3. calibration standard solution together with calibration component of uncertainty
$V_{3_50_fill}$	ml	Filling component of uncertainty of volume V_{3_50}
$V_{3_50_temp}$	ml	Uncertainty component of volume V_{3_50} due to temperature difference from 20°C
V_{4_50}	ml	Volume of the 4. calibration standard solution
$V_{4_50_cal}$	ml	Value of the volume of the 4. calibration standard solution together with calibration component of uncertainty
$V_{4_50_fill}$	ml	Filling component of uncertainty of volume V_{4_50}
$V_{4_50_temp}$	ml	Uncertainty component of volume V_{4_50} due to temperature difference from 20°C
V_{5_50}	ml	Volume of the 5. calibration standard solution

Quantity	Unit	Definition
$V_{5_50_cal}$	ml	Value of the volume of the 5. calibration standard solution together with calibration component of uncertainty
$V_{5_50_fill}$	ml	Filling component of uncertainty of volume V_{5_50}
$V_{5_50_temp}$	ml	Uncertainty component of volume V_{5_50} due to temperature difference from 20°C
Δt	°C	Diference of solution temperature from 20°C
γ_w	1/°C	Thermal expansion coefficent of water
ΣAC	AU*mg/ml	Interim quantity for regression statistics
ΣCC	mg ² /ml ²	Interim quantity for regression statistics

A₁: Interim Result
A_{1drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 24000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the solution will be kept no longer than 2 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{1integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 18000 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to [Area(max)-Area(min)]/2. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{1rep}: Type A summarized
 Mean: 4407267 AU
 Standard Uncertainty: 12000 AU
 Degrees of Freedom: 12

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 6 injections) of a standard solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

A₂: Interim Result
A_{2drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 36000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the solution will be kept no longer than 3 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{2integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 28000 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to $[\text{Area}(\text{max})-\text{Area}(\text{min})]/2$. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{2rep}: Type A summarized
 Mean: 6436226 AU
 Standard Uncertainty: 12000 AU
 Degrees of Freedom: 12

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 6 injections) of a standard solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

A₃: Interim Result
A_{3drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 48000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the solution will be kept no longer than 4 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{3integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 38500 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to $[\text{Area}(\text{max})-\text{Area}(\text{min})]/2$. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{3rep}: Type A summarized
 Mean: 8987202 AU
 Standard Uncertainty: 12000 AU
 Degrees of Freedom: 12

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 6 injections) of a standard solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

A₄: Interim Result
A_{4drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 60000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the solution will be kept no longer than 5 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{4integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 47000 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to $[\text{Area}(\text{max}) - \text{Area}(\text{min})]/2$. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{4rep}: Type A summarized
 Mean: 10642449.5 AU
 Standard Uncertainty: 12000 AU
 Degrees of Freedom: 12

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 6 injections) of a standard solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

A₅: Interim Result
A_{5drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 72000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the solution will be kept no longer than 6 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{5integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 57500 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to $[\text{Area}(\text{max}) - \text{Area}(\text{min})]/2$. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{5rep}: Type A summarized
 Mean: 13070522 AU
 Standard Uncertainty: 12000 AU
 Degrees of Freedom: 12

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 6 injections) of a standard solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

A_{R_eff}: Interim Result

The systematic influences are practically limited to the systematic effects in peak areas (repeatability can thus be excluded). Also, it is necessary to keep in mind that calculation of Recovery by spiking experiments leads to differences of areas of peaks that have been obtained within short time intervals (the drift component can thus be excluded). Therefore the components to be included are the integration uncertainty and the uncertainty due to nonlinearity.

A_{R_eff_integr}: Type B rectangular distribution
 Value: 3000000 AU
 Halfwidth of Limits: 12600 AU

A_{R_eff_nonlin}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 40000 AU

A_{sample}: Interim Result

A_{sample_drift}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 60000 AU

The drift per hour is maximum 12 000 peak area units. Assuming that the sample solution will be kept no longer than 5 hours between preparation and measurement we arrive at this uncertainty estimate. This uncertainty estimate is essentially independent of the peak area.

A_{sample_integr}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 35000 AU

This uncertainty contribution has been obtained by integrating the peak in two ways - one somewhat underestimating (Area(min)) and the other somewhat overestimating (Area(max)) the peak area. The uncertainty contribution has been taken equal to [Area(max)-Area(min)]/2. See text for more detail. According to our data this uncertainty contribution is proportional to the peak area.

A_{sample_nonlin}: Type B rectangular distribution
 Value: 0 AU
 Halfwidth of Limits: 40000 AU

This uncertainty contribution has been estimated from the behavior of the residuals of the calibration line. The uncertainty corresponds to the maximum possible deviation (in terms of peak area) of the calibration line from the actual concentration vs peak area relationship. This uncertainty contribution is assigned only to the peak area of the sample and not to the peak areas of the standard solutions. According to this approach this uncertainty contribution is assumed to be independent of the peak area of the sample.

A_{sample_rep}: Type A summarized
 Mean: 8349089 AU
 Standard Uncertainty: 19000 AU
 Degrees of Freedom: 28

The repeatability uncertainty has been estimated using the pooled standard deviation of triplicate injections (altogether 3 x 14 injections) of a sample solution subjected to different stability tests. See the text for more detail. According to our data this uncertainty contribution is essentially independent of the sample peak area.

AvgA: Interim Result

AvgC: Interim Result

b₀: Interim Result

b₁: Interim Result

C₁: Interim Result

C₂: Interim Result

C₃: Interim Result

C₄: Interim Result

C₅: Interim Result

C_{SVT}: Result
f_{buoyancy}: Type B rectangular distribution
 Value: 0.0010 unitless
 Halfwidth of Limits: 0.0002 unitless

The buoyancy factor is the part (around one thousandth under our conditions) of the mass that is added to the balance reading in order to get the physical mass of the weighed substance. The uncertainty estimate is deliberately very conservative.

m₁: Interim Result
m_{1_buoyancy}: Interim Result
m_{1_drift}: Type A summarized
 Mean: 0 mg
 Standard Uncertainty: 0.0097 mg
 Degrees of Freedom: 2
m_{1_electrost}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.10 mg

When weighing the standard substance, interference from electrostatics (instability of the reading) was quite serious and is thus taken into account as an uncertainty component. This uncertainty componen has been estimated as 0.5% of the mass of the substance.

m_{1_rep}: Type A summarized
 Mean: 20.42 mg
 Standard Uncertainty: 0.0196 mg
 Degrees of Freedom: 18
m_{1_round}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.005 mg

m₂: Interim Result
m_{2_buoyancy}: Interim Result
m_{2_drift}: Type A summarized
 Mean: 0 mg
 Standard Uncertainty: 0.0097 mg
 Degrees of Freedom: 2
m_{2_electrost}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.15 mg

When weighing the standard substance, interference from electrostatics (instability of the reading) was quite serious and is thus taken into account as an uncertainty component. This uncertainty componen has been estimated as 0.5% of the mass of the substance.

m_{2_rep}: Type A summarized
 Mean: 29.72 mg
 Standard Uncertainty: 0.0196 mg
 Degrees of Freedom: 18

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m_{2_round}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.005 mg

m₃: Interim Result

m_{3_buoyancy}: Interim Result

m_{3_drift}: Type A summarized
 Mean: 0 mg
 Standard Uncertainty: 0.0097 mg
 Degrees of Freedom: 2

m_{3_electrost}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.21 mg

When weighing the standard substance, interference from electrostatics (instability of the reading) was quite serious and is thus taken into account as an uncertainty component. This uncertainty componen has been estimated as 0.5% of the mass of the substance.

m_{3_rep}: Type A summarized
 Mean: 41.82 mg
 Standard Uncertainty: 0.0196 mg
 Degrees of Freedom: 18

m_{3_round}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.005 mg

m₄: Interim Result

m_{4_buoyancy}: Interim Result

m_{4_drift}: Type A summarized
 Mean: 0 mg
 Standard Uncertainty: 0.0097 mg
 Degrees of Freedom: 2

m_{4_electrost}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.25 mg

When weighing the standard substance, interference from electrostatics (instability of the reading) was quite serious and is thus taken into account as an uncertainty component. This uncertainty componen has been estimated as 0.5% of the mass of the substance.

m_{4_rep}: Type A summarized
 Mean: 49.83 mg
 Standard Uncertainty: 0.0196 mg
 Degrees of Freedom: 18

m_{4_round}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.005 mg

m₅: Interim Result

m_{5_buoyancy}: Interim Result

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m_{5_drift}: Type A summarized
 Mean: 0 mg
 Standard Uncertainty: 0.0097 mg
 Degrees of Freedom: 2

m_{5_electrost}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.31 mg

When weighing the standard substance, interference from electrostatics (instability of the reading) was quite serious and is thus taken into account as an uncertainty component. This uncertainty component has been estimated as 0.5% of the mass of the substance.

m_{5_rep}: Type A summarized
 Mean: 61.48 mg
 Standard Uncertainty: 0.0196 mg
 Degrees of Freedom: 18

m_{5_round}: Type B rectangular distribution
 Value: 0 mg
 Halfwidth of Limits: 0.005 mg

n: Constant
 Value: 5 unitless

n_{tab}: Constant
 Value: 8 tab

P_{std}: Type B rectangular distribution
 Value: 99.4 %
 Halfwidth of Limits: 0.6 %

R: Interim Result

R₀: Type A summarized
 Mean: 1.002068 unitless
 Standard Uncertainty: 0.002295 unitless
 Degrees of Freedom: 2

Recovery value and sample-to-sample variability uncertainty. The standard uncertainty is the standard deviation of the single mavlue, not the standard deviation of the mean

V₁₀₀: Interim Result

V_{100_cal}: Type B rectangular distribution
 Value: 100.00 ml
 Halfwidth of Limits: 0.1 ml

V_{100_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml

V_{100_temp}: Interim Result

V_{1_50}: Interim Result

V_{1_50_cal}: Type B rectangular distribution
 Value: 50.00 ml
 Halfwidth of Limits: 0.06 ml

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V_{1_50_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml
V_{1_50_temp}: Interim Result
V_{2_50}: Interim Result
V_{2_50_cal}: Type B rectangular distribution
 Value: 50.00 ml
 Halfwidth of Limits: 0.06 ml
V_{2_50_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml
V_{2_50_temp}: Interim Result
V_{3_50}: Interim Result
V_{3_50_cal}: Type B rectangular distribution
 Value: 50.00 ml
 Halfwidth of Limits: 0.06 ml
V_{3_50_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml
V_{3_50_temp}: Interim Result
V_{4_50}: Interim Result
V_{4_50_cal}: Type B rectangular distribution
 Value: 50.00 ml
 Halfwidth of Limits: 0.06 ml
V_{4_50_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml
V_{4_50_temp}: Interim Result
V_{5_50}: Interim Result
V_{5_50_cal}: Type B rectangular distribution
 Value: 50.00 ml
 Halfwidth of Limits: 0.06 ml
V_{5_50_fill}: Type B rectangular distribution
 Value: 0 ml
 Halfwidth of Limits: 0.09 ml
V_{5_50_temp}: Interim Result
Δt: Type B rectangular distribution
 Value: 0 °C
 Halfwidth of Limits: 4 °C
γ_w: Constant
 Value: 0.00021 1/°C
ΣAC: Interim Result
ΣCC: Interim Result

Correlation Coefficients:

	A _{1drift}	A _{2drift}	A _{3drift}	A _{4drift}	A _{5drift}
A _{1drift}	1	0.8	0.8	0.8	0.8
A _{2drift}	0.8	1	0.8	0.8	0.8
A _{3drift}	0.8	0.8	1	0.8	0.8
A _{4drift}	0.8	0.8	0.8	1	0.8
A _{5drift}	0.8	0.8	0.8	0.8	1

	m _{1_drift}	m _{2_drift}	m _{3_drift}	m _{4_drift}	m _{5_drift}
m _{1_drift}	1	0.8	0.8	0.8	0.8
m _{2_drift}	0.8	1	0.8	0.8	0.8
m _{3_drift}	0.8	0.8	1	0.8	0.8
m _{4_drift}	0.8	0.8	0.8	1	0.8
m _{5_drift}	0.8	0.8	0.8	0.8	1

	m _{1_electrost}	m _{2_electrost}	m _{3_electrost}	m _{4_electrost}	m _{5_electrost}
m _{1_electrost}	1	0.8	0.8	0.8	0.8
m _{2_electrost}	0.8	1	0.8	0.8	0.8
m _{3_electrost}	0.8	0.8	1	0.8	0.8
m _{4_electrost}	0.8	0.8	0.8	1	0.8
m _{5_electrost}	0.8	0.8	0.8	0.8	1

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Uncertainty Budget:

Quantity	Value	Standard Uncertainty	Degrees of Freedom	Distribution	Sensitivity Coefficient	Uncertainty Contribution	Index
A _{1drift}	0.0 AU	13900 AU	infinity	rectangular	-270·10 ⁻⁹	-0.0038 mg/tab	0.8 %
A _{1integr}	0.0 AU	10400 AU	infinity	rectangular	-270·10 ⁻⁹	-0.0029 mg/tab	0.0 %
A _{1rep}	4.4073·10 ⁶ AU	0.0120·10 ⁶ AU	12	normal	-270·10 ⁻⁹	-0.0033 mg/tab	0.0 %
A _{2drift}	0.0 AU	20800 AU	infinity	rectangular	-260·10 ⁻⁹	-0.0053 mg/tab	1.1 %
A _{2integr}	0.0 AU	16200 AU	infinity	rectangular	-260·10 ⁻⁹	-0.0041 mg/tab	0.1 %
A _{2rep}	6.4362·10 ⁶ AU	0.0120·10 ⁶ AU	12	normal	-260·10 ⁻⁹	-0.0031 mg/tab	0.0 %
A _{3drift}	0.0 AU	27700 AU	infinity	rectangular	-230·10 ⁻⁹	-0.0065 mg/tab	1.3 %
A _{3integr}	0.0 AU	22200 AU	infinity	rectangular	-230·10 ⁻⁹	-0.0052 mg/tab	0.2 %
A _{3rep}	8.9872·10 ⁶ AU	0.0120·10 ⁶ AU	12	normal	-230·10 ⁻⁹	-0.0028 mg/tab	0.0 %
A _{4drift}	0.0 AU	34600 AU	infinity	rectangular	-220·10 ⁻⁹	-0.0076 mg/tab	1.6 %
A _{4integr}	0.0 AU	27100 AU	infinity	rectangular	-220·10 ⁻⁹	-0.0059 mg/tab	0.3 %
A _{4rep}	10.6424·10 ⁶ AU	0.0120·10 ⁶ AU	12	normal	-220·10 ⁻⁹	-0.0026 mg/tab	0.0 %
A _{5drift}	0.0 AU	41600 AU	infinity	rectangular	-200·10 ⁻⁹	-0.0081 mg/tab	1.7 %
A _{5integr}	0.0 AU	33200 AU	infinity	rectangular	-200·10 ⁻⁹	-0.0065 mg/tab	0.3 %
A _{5rep}	13.0705·10 ⁶ AU	0.0120·10 ⁶ AU	12	normal	-200·10 ⁻⁹	-0.0023 mg/tab	0.0 %
A _{R_eff_integr}	3.00000·10 ⁶ AU	0.00727·10 ⁶ AU	infinity	rectangular	-3.2·10 ⁻⁶	-0.023 mg/tab	4.2 %
A _{R_eff_nonlin}	0.0 AU	23100 AU	infinity	rectangular	-3.2·10 ⁻⁶	-0.074 mg/tab	42.8 %
A _{sample_drift}	0.0 AU	34600 AU	infinity	rectangular	1.2·10 ⁻⁶	0.041 mg/tab	12.9 %
A _{sample_integr}	0.0 AU	20200 AU	infinity	rectangular	1.2·10 ⁻⁶	0.024 mg/tab	4.4 %
A _{sample_nonlin}	0.0 AU	23100 AU	infinity	rectangular	1.2·10 ⁻⁶	0.027 mg/tab	5.7 %
A _{sample_rep}	8.3491·10 ⁶ AU	0.0190·10 ⁶ AU	28	normal	1.2·10 ⁻⁶	0.022 mg/tab	3.9 %

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Quantity	Value	Standard Uncertainty	Degrees of Freedom	Distribution	Sensitivity Coefficient	Uncertainty Contribution	Index
f _{buoyancy}	0.001000 unitless	0.000115 unitless	infinity	rectangular	9.7	0.0011 mg/tab	0.0 %
m _{1_drift}	0.0 mg	0.00970 mg	2	normal	0.058	0.00056 mg/tab	0.0 %
m _{1_electrost}	0.0 mg	0.0577 mg	infinity	rectangular	0.058	0.0033 mg/tab	0.6 %
m _{1_rep}	20.4200 mg	0.0196 mg	18	normal	0.058	0.0011 mg/tab	0.0 %
m _{1_round}	0.0 mg	0.00289 mg	infinity	rectangular	0.058	0.00017 mg/tab	0.0 %
m _{2_drift}	0.0 mg	0.00970 mg	2	normal	0.054	0.00052 mg/tab	0.0 %
m _{2_electrost}	0.0 mg	0.0866 mg	infinity	rectangular	0.054	0.0047 mg/tab	0.8 %
m _{2_rep}	29.7200 mg	0.0196 mg	18	normal	0.054	0.0011 mg/tab	0.0 %
m _{2_round}	0.0 mg	0.00289 mg	infinity	rectangular	0.054	0.00016 mg/tab	0.0 %
m _{3_drift}	0.0 mg	0.00970 mg	2	normal	0.049	0.00048 mg/tab	0.0 %
m _{3_electrost}	0.0 mg	0.121 mg	infinity	rectangular	0.049	0.0060 mg/tab	1.1 %
m _{3_rep}	41.8200 mg	0.0196 mg	18	normal	0.049	0.00097 mg/tab	0.0 %
m _{3_round}	0.0 mg	0.00289 mg	infinity	rectangular	0.049	0.00014 mg/tab	0.0 %
m _{4_drift}	0.0 mg	0.00970 mg	2	normal	0.046	0.00045 mg/tab	0.0 %
m _{4_electrost}	0.0 mg	0.144 mg	infinity	rectangular	0.046	0.0066 mg/tab	1.2 %
m _{4_rep}	49.8300 mg	0.0196 mg	18	normal	0.046	0.00090 mg/tab	0.0 %
m _{4_round}	0.0 mg	0.00289 mg	infinity	rectangular	0.046	0.00013 mg/tab	0.0 %
m _{5_drift}	0.0 mg	0.00970 mg	2	normal	0.041	0.00040 mg/tab	0.0 %
m _{5_electrost}	0.0 mg	0.179 mg	infinity	rectangular	0.041	0.0074 mg/tab	1.4 %
m _{5_rep}	61.4800 mg	0.0196 mg	18	normal	0.041	0.00081 mg/tab	0.0 %
m _{5_round}	0.0 mg	0.00289 mg	infinity	rectangular	0.041	0.00012 mg/tab	0.0 %
n	5.0 unitless						

Assay of Simvastatin in Tablets by HPLC

Quantity	Value	Standard Uncertainty	Degrees of Freedom	Distribution	Sensitivity Coefficient	Uncertainty Contribution	Index
n_{tab}	8.0 tab						
P_{std}	99.400 %	0.346 %	infinity	rectangular	0.097	0.034 mg/tab	8.8 %
R_0	1.00207 unitless	0.00229 unitless	2	normal	-9.6	-0.022 mg/tab	3.8 %
V_{100_cal}	100.0000 ml	0.0577 ml	infinity	rectangular	0.097	0.0056 mg/tab	0.2 %
V_{100_fill}	0.0 ml	0.0520 ml	infinity	rectangular	0.097	0.0050 mg/tab	0.2 %
$V_{1_50_cal}$	50.0000 ml	0.0346 ml	infinity	rectangular	-0.024	-0.00082 mg/tab	0.0 %
$V_{1_50_fill}$	0.0 ml	0.0520 ml	infinity	rectangular	-0.024	-0.0012 mg/tab	0.0 %
$V_{2_50_cal}$	50.0000 ml	0.0346 ml	infinity	rectangular	-0.032	-0.0011 mg/tab	0.0 %
$V_{2_50_fill}$	0.0 ml	0.0520 ml	infinity	rectangular	-0.032	-0.0017 mg/tab	0.0 %
$V_{3_50_cal}$	50.0000 ml	0.0346 ml	infinity	rectangular	-0.041	-0.0014 mg/tab	0.0 %
$V_{3_50_fill}$	0.0 ml	0.0520 ml	infinity	rectangular	-0.041	-0.0021 mg/tab	0.0 %
$V_{4_50_cal}$	50.0000 ml	0.0346 ml	infinity	rectangular	-0.046	-0.0016 mg/tab	0.0 %
$V_{4_50_fill}$	0.0 ml	0.0520 ml	infinity	rectangular	-0.046	-0.0024 mg/tab	0.0 %
$V_{5_50_cal}$	50.0000 ml	0.0346 ml	infinity	rectangular	-0.051	-0.0018 mg/tab	0.0 %
$V_{5_50_fill}$	0.0 ml	0.0520 ml	infinity	rectangular	-0.051	-0.0026 mg/tab	0.0 %
Δt	0.0 °C	2.31 °C	infinity	rectangular	not valid!	$-430 \cdot 10^{-21}$ mg/tab	0.0 %
γ_w	0.00021 1/°C						
C_{SVT}	9.668 mg/tab	0.114 mg/tab	1300				

Result: Quantity: C_{SVT}
 Value: 9.67 mg/tab
 Expanded Uncertainty: ± 0.23 mg/tab
 Coverage Factor: 2.00
 Coverage: 95% (t-table 95.45%)