

PharmaHemp d.o.o., Koprška ulica 106C, SI-1000 Ljubljana, Slovenija		PharmaHemp®
MEASUREMENT UNCERTAINTY		
Issue date:	Expiration date:	Code: SOP-LAB-005
		Revision No.: 05
		Appendixes: /
Author: Janja Ahej	Reviewer: Dr. Boštjan Jančar	Approver: Tine Lavrič

DEFINITIONS AND ABBREVIATIONS

SOP	Standard operation procedure
ISO	International Organization for Standardization
CRM	Certified reference material

TABLE OF CONTENTS

1	PURPOSE.....	2
2	DEFINITIONS	2
3	EVALUATION.....	3
3.1	Sampling (u_{sam})	4
3.2	Standard and sample solution preparation (u_{prep})	4
3.3	Calibration curve (u_{cal})	8
3.4	Method repeatability (u_{rep})	13
3.5	Intermediate precision – method MET-LAB-001/01 and MET-LAB-001/02	15
4	MEASUREMENT UNCERTAINTIES FOR ADDITIONAL CANNABINOIDS	15
4.1	Measurement uncertainties for cannabinoids CBL and 8-THC	15
4.2	Measurement uncertainties for cannabinoids CBE, CBNV, CBCA and CBT	15
5	CALCULATION OF COMBINED STANDARD MEASUREMENT UNCERTAINTY.....	15
5.1	Sampling is performed by the laboratory	16
5.2	Sampling is not performed.....	16
6	CALCULATION OF EXPANDED MEASUREMENT UNCERTAINTY.....	16
7	REFERENCES.....	18
8	APPENDIX	18
9	HISTORY OF THE DOCUMENT	19

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

1 PURPOSE

In every measurement procedure, it is important to define the correctness of the stated results - when reporting the results of a measurement it is obligatory that quantitative indication of the quality of the result of a measurement is given, that is, evaluating and expressing its uncertainty. Measurement uncertainty determination depends on the method and sample type and must be made according to good laboratory practice.

The SOP Measurement uncertainty describes the approach to define the measurement uncertainty when using the method Quantitative determination of cannabinoids by reverse phase chromatography. The determined uncertainty characterizes the dispersion of the values that could reasonably be attributed to the measurand. The expanded uncertainty represents an interval around the results where the unknown true value can be observed with a confidence level of 95%.

The measurement uncertainties were initially calculated for 10 cannabinoids using only one analytical method (MET-LAB-001). As new methods and cannabinoids were added, the measurement uncertainties were simplified for 4 different concentration levels, taking in consideration different HPLC system configurations and slightly different sample preparations (less dilutions of samples are needed on HPLC2 system).

The final calculation of expended measurement uncertainty for method (MET-LAB-001/01, MET-LAB-001/02 and MET-LAB-001/03) is based on the theoretical principle presented in the chapter 3 and then expended to the achieved measurement uncertainties, which were all proved through the validation of each method. The measurement uncertainties for method MET-LAB-001/01, MET-LAB-001/02 and MET-LAB-001/03 are presented in Chapter 5. The measurement uncertainties for additional 5 cannabinoids (8-THC, CBL, CBNV, CBCA and CBT) were evaluated through validation studies and added in Chapter 5. The measurement uncertainty for CBE is added in the Chapter 5, but was not evaluated in validation study, as the reporting of CBE is not part of accredited activities in LAB.

2 DEFINITIONS

Measurement uncertainty

The term measurement uncertainty means doubt about validity of the results of a measurement, uncertainty is parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand.

Standard uncertainty

Uncertainty of the result of a measurement expressed as a standard deviation.

Combined standard uncertainty

Standard uncertainty of the result of a measurement when that result is obtained from the values of a number of other quantities, weighted according to how the measurement result varies with changes in these quantities.

Expanded uncertainty

Quantity defining an interval about the results of a measurement that may be expected to encompass a large fraction of the distribution of values that could be attributed to the measurand.

Coverage factor

Numerical factor k used as a multiplier of the combined standard uncertainty in order to obtain expanded uncertainty.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

3 EVALUATION

Based on the validation results for the method MET-LAB-002 (see validation report RP-VP-007), The reporting uncertainties are updated to 4 different concentration ranges:

- from 0.03 to 0.10 %
- from 0.10 to 0.50 %
- from 0.50 to 1.0 %
- above 1.0 %

With the implementation of the method MET-LAB-001/02 the same acceptance criteria for intermediate precision were achieved (see validation report RP-VP-011 - Analytical method validation report for method MET-LAB-003). The results between the methods are comparable in the ranges of measurement uncertainties for MET-LAB-001/01 and MET-LAB-002 and the same measurement uncertainties can be adopted also for the method MET-LAB-001/02.

The approach presented below is based on identifying, quantifying, and combining all individual contributions to uncertainty. In this bottom-up approach, the overall uncertainty is derived from the uncertainties of the individual components and it is adopted by the International Organization for Standardization (ISO).

First, measurement uncertainty was evaluated using flow diagram, presented in Figure 1. Having identified the uncertainty sources, the next step was to identify influence parameters, that is, the measurement uncertainty components. To cover all parameters, we used Ishikawa (also known as fishbone) diagram, presented in Figure 2.

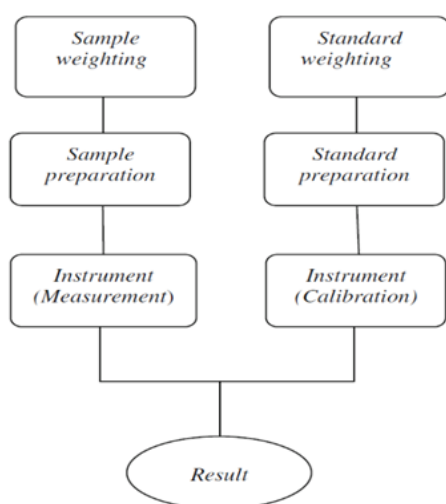


Figure 1: Flow diagram of the measurement procedure

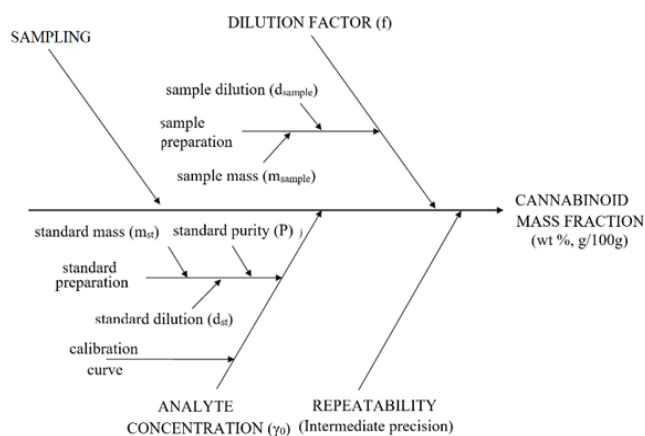


Figure 2: Ishikawa diagram for cannabinoid determination by RPC

In this SOP uncertainty sources are combined in following groups:

- 1) Uncertainty associated with **sampling**.
- 2) Uncertainty associated with **standard and sample solution preparation**.
- 3) Uncertainty associated with **calibration curve**.
- 4) Uncertainty associated with **method repeatability**
- 5) **Uncertainty associated with the intra-lab precision (MET-LAB-001/01, MET-LAB-002 and MET-LAB-001/2)**
- 6) **Measurement uncertainties for cannabinoids 8-THC, CBL, CBE, CBNV, CBCA and CBT (Chapter 4)**

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

Uncertainty of result may arise from each of those groups including examples such as sample representativeness, sample contamination, storage conditions, matrix effects and interferences, environmental conditions, reagent purity, uncertainty of masses and volumetric equipment, reference values, separation, identification, calibration, measurement precision and random variations. Not all of the components make a significant contribution to the combined uncertainty, thus a detailed estimation of the contribution of components to the uncertainty was made and was evaluated.

3.1 Sampling (u_{sam})

The sampling was evaluated initially, for 10 cannabinoids.

The contribution of the sampling must be taken into account only if the laboratory performs the sampling of the received material. This is the case only when:

- The sampling is requested by the client;
- A large quantity of the sample is received and a representative sample is difficult to obtained.

The detail instructions of the sampling are described in SOP-LAB-006 – Vzorčenje. When sampling is required the protocol for sampling must be followed and the report for each sampling issued in accordance to the instruction given within.

If the sampling is performed by the laboratory, the u_{sam} must be calculated. First the standard deviation between the results is calculated by the following equation:

$$s = \sqrt{\frac{\sum_{i=1}^N (x_i - \bar{x})^2}{n - 1}} \quad (1)$$

- number of samples taken (dependent on the sample quantity received)
- x_i - result of each of the sample
- $\bar{x}$ - average result of all samples

Then the u_{sam^*} is calculated by the following equation:

$$u_{\text{sam}^*} = \sqrt{\frac{s}{n}} \quad (2)$$

Finally, the uncertainty of sampling is calculated by the formula:

$$u_{\text{sam}} = \frac{u_{\text{sam}^*}}{\bar{x}} \quad (3)$$

3.2 Standard and sample solution preparation (u_{prep})

The standard and sample solution preparation was evaluated initially, for 10 cannabinoids.

For **standard solution preparation**, the main sources of uncertainty are contribution of certified reference material concentration and contribution of standard dilutions.

All reference standard solutions are obtained from the same vendor - the production of certified reference standards is certified under ISO guide 34 and registered testing laboratory according to the ISO 17025. The associated reference standard solution uncertainty for concentration was calculated by manufacturer in which the concentration reference standard solution was already corrected for chromatographic purity, residual solvents, and residual inorganics. Uncertainty was evaluated by statistical analysis of all aspects and is expressed as an expanded uncertainty in accordance with ISO 17025 at the approximate 95%

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

confidence interval using a coverage factor $k=2$. The formula for calculation of the certified reference material concentration contribution (CRM) is the following:

$$u_{CRM} = \frac{d}{\sqrt{3}} \quad (4)$$

Where **d** is the value of the confidence interval provided by the manufacturer. The factor $\sqrt{3}$ has been introduced because the assessment of the variability range is not based upon statistical evaluation but on an interval characterized by two extremes out of which no value is allowed and within which every value is equally probable (we are using so called “square” probability distribution).

The relative uncertainty value is then calculated as:

$$u_{STD} = \frac{u_{CRM}}{NV} \quad (5)$$

Where NV is the concentration of the CRM provided by the manufacturer.

The calculation of u_{STD8} for the standards with the d value of 0.6 % and NV value 100 % (CBDV, CBD, CBDA, CBG, CBGA, CBN, CBC and THCA):

$$u_{CRMSTD8} = \frac{0.6}{\sqrt{3}} = 0.3464 \quad (6)$$

$$u_{STD8} = \frac{0.3464}{100} = 3.46 \times 10^{-3} \quad (7)$$

The same can be used also for 8-THC and CBL as the CRM has same d value of 0.6 % and NV value of 100 %.

The calculation of u_{THCV} for the standard with the d value of 1.1 % and NV value 100 % (THCV):

$$u_{CRMTHCV} = \frac{1.1}{\sqrt{3}} = 0.6351 \quad (8)$$

$$u_{THCV} = \frac{0.6351}{100} = 6.35 \times 10^{-3} \quad (9)$$

The calculation of u_{9-THC} for the standard with the d value of 3.3 % and NV value 100 % (9-THC):

$$u_{CRMTHC} = \frac{3.3}{\sqrt{3}} = 1.905 \quad (10)$$

$$u_{THC} = \frac{1.9052}{100} = 1.91 \times 10^{-2} \quad (11)$$

Standard dilutions are made gravimetrically, thus uncertainty of weighting was evaluated for each standard. The CAL9N standard solution (containing CBDV, CBG, CBD, THCV, CBN, 9-THC, 8-THC, CBL, CBC) and CAL3A standard solution (containing CBGA, CBDA, THCA) are both prepared from the 60 µg/ml stock solution and then further diluted to 30, 15, 7.5, 3.8, 1.9, 0.9 and 0.3 µg/ml. All dilutions are prepared in triplicates.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

There are two types of uncertainties connected to the weighing process: the first is related to the weighing and is obtained by repeated weightings at the same order of magnitude of the load we are interested in. From these measurements we get their number (n), an average weight ($\bar{x}$) and a standard deviation (s). We can calculate the uncertainty of weighing using the formula:

$$u_{mass*} = \frac{s}{\sqrt{n}} = \frac{0.3059}{\sqrt{21}} = 0.06675 \quad (12)$$

The relative uncertainty is then calculated:

$$u_{mass} = 0.06675 / 76 = 8.78 \times 10^{-4} \quad (13)$$

The second is related to the balance calibration certificate provided by the balance calibration certificate. The certificate reports an extended uncertainty: the one that is of use in the sum of all the various contributions is therefore to be corrected for the coverage factor reported (factor 2). The extended uncertainty value of 0.5 mg is divided by 2 (coverage factor used):

$$u_{bal*} = 0.5 / 2 = 0.25 \quad (14)$$

The relative uncertainty is then calculated CAL7N and CAL3A standards:

$$u_{balCAL7N} = \frac{8 \cdot 0.25 \text{ mg}}{1290 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{460 \text{ mg}} \quad (15)$$

$$u_{balCAL7N} = 7.5 \times 10^{-3}$$

The same is used for the 8-THC and CBL.

$$u_{balCAL3A} = \frac{4 \cdot 0.25 \text{ mg}}{935 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{618 \text{ mg}} + \frac{2 \cdot 0.25 \text{ mg}}{460 \text{ mg}} \quad (16)$$

$$u_{balCAL3A} = 7.0 \times 10^{-3}$$

Finally, the uncertainty of weighting ($u_{weighting}$) can be calculated by combining the u_{mass} and u_{bal} :

$$u_{weighting} = \sqrt{u_{mass}^2 + u_{bal}^2} \quad (17)$$

$$\text{- for CAL9N: } \sqrt{0.000878^2 + 0.0075^2} = 7.6 \times 10^{-3}$$

$$\text{- for CAL3A: } \sqrt{0.000878^2 + 0.0070^2} = 7.1 \times 10^{-3}$$

For **sample solution preparation** the following two factors are significant:

- Sample mass ($u_{m\text{-sample}}$)
- Sample dilution ($u_{d\text{-sample}}$)

Uncertainty of weighting was evaluated based on manufacturer's tolerance for the analytical balance (same rules are applied as for equation 14).

$$u_{m\text{-sample}} = 0.25 \text{ mg} / 100.0 \text{ mg} = 2.5 \times 10^{-3} \quad (18)$$

Sample dilution is carried out in a volumetric flask to final volume of 100 ml and then each sample is further diluted in two steps. Sample dilution uncertainty is connected to a flask uncertainty and dilution uncertainty.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

Flask uncertainty consist of uncertainty from imperfect flask calibration ($u(V_C)$), and uncertainty from temperature difference between working temperature and temperature when flask was calibrated. ($u(V_T)$). Sample dilution uncertainty is done gravimetrically, thus consist of uncertainty from weighting. Uncertainty from imperfect flask calibration was calculated assuming a triangular distribution (the manufacturer's tolerance for the flask is ± 0.100 mL at 20°C):

$$u(V_C) = 0.1 \text{ mL} / 100 \text{ mL} = 1.0 \times 10^{-3} \quad (19)$$

Uncertainty of temperature effect is calculated using the following equation:

$$u(V_T) = ((\Delta T \cdot \alpha \cdot V) / \sqrt{3}) / 100 \text{ ml} \quad (20)$$

Where ΔT represents difference between temperature at which flask was calibrated (20°C) and expected laboratory temperature (23°C), α is coefficient of volume expansion for methanol ($1.5 \times 10^{-3} / ^\circ\text{C}$) and V is volume of a flask (100 mL). The calculated $u(V_T)$:

$$u(V_T) = (3 \cdot 0.0015 \cdot 100 / \sqrt{3}) / 100 \text{ ml} = 2.6 \times 10^{-3} \quad (21)$$

$u_{d\text{-sample}}$ was evaluated based on manufacturer's tolerance of the analytical balance and is presented in the following equation.

$$u_{d\text{-sample}} = 0.25 \text{ mg} / 75 \text{ mg} + 0.25 \text{ mg} / 400 \text{ mg} = 4.0 \times 10^{-3} \quad (22)$$

Single uncertainty components were combined by the error propagation rules in uncertainties associated with standard and sample preparation for each standard are as following:

$$u_{\text{prep}} = \sqrt{u_{\text{STD}}^2 + u_{\text{weighting}}^2 + u_{m\text{-sample}}^2 + u_{V_C}^2 + u_{V_T}^2 + u_{d\text{-sample}}^2} \quad (23)$$

For CBDV, CBD, CBG, CBN and CBC (u_{prep1}):

$$u_{\text{prep1}} = \sqrt{0.00346^2 + 0.0075^2 + 0.0025^2 + 0.001^2 + 0.0026^2 + 0.004^2} \quad (24)$$

$$u_{\text{prep1}} = 9.9 \times 10^{-3}$$

The same is used for the 8-THC and CBL.

For THCV (u_{prep2}):

$$u_{\text{prep2}} = \sqrt{0.00635^2 + 0.0075^2 + 0.0025^2 + 0.001^2 + 0.0026^2 + 0.004^2} \quad (25)$$

$$u_{\text{prep2}} = 1.1 \times 10^{-2}$$

For 9-THC (u_{prep3}):

$$u_{\text{prep3}} = \sqrt{0.0191^2 + 0.0075^2 + 0.0025^2 + 0.001^2 + 0.0026^2 + 0.004^2} \quad (26)$$

$$u_{\text{prep3}} = 2.1 \times 10^{-2}$$

For CBDA, CBGA and THCA (u_{prep4}):

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

$$u_{prep4} = \sqrt{0,006^2 + 0,0140^2 + 0,0005^2 + 0,001^2 + 0,0026^2 + 0,0006^2} \quad (27)$$

$$U_{prep4} = 9.6 \times 10^{-3}$$

3.3 Calibration curve (u_{cal})

The calibration curve was evaluated initially for the HPLC system HPLC1, for 10 cannabinoids.

Based on relative (comparative) nature of chromatographic methods, they involve a calibration step. Calibration curves were prepared by plotting the peak area versus the analyte concentration. The detail preparation of the calibration curves is described in VP-01 "Analytical method validation protocol for quantitative determination of cannabinoids by reverse phase chromatography". 3 independent preparations of calibration curve for each cannabinoid were prepared. Since the linear range for all 10 cannabinoids is from 0.3 to 30 µg/ml (proven within the method validation), only calibration points 0.3, 0.9, 1.8, 3.8, 7.5, 15 and 30 µg/ml were considered for uncertainty evaluation.

First the average areas and concentrations of calibration points were taken and the linear regression analyses was carried out. The calibration curves obtained during the validation of the method are presented in Table 1.

Table 1: Calibration curves of 10 cannabinoids

Analyte	Calibration curve	r2
Cannabidiol (CBD)	$y = 6131639.95x$	1.000
Cannabigerol (CBG)	$y = 5957523.94x$	1.000
Cannabidivarin (CBDV)	$y = 5842786.63x$	1.000
Cannabichromene (CBC)	$y = 6933511.76x$	1.000
Tetrahydrocannabivarin (THCV)	$y = 16440896.70x$	1.000
Cannabinol (CBN)	$y = 6392068.23x$	1.000
Delta-9-Tetrahydrocannabinol (9-THC)	$y = 16815125.97x$	1.000
Cannabidiolic acid (CBDA)	$y = 8624655.32x$	1.000
Cannabigerolic acid (CBGA)	$y = 8440742.65x$	1.000
Tetrahydrocannabinolic acid (THCA)	$y = 9078545.21x$	1.000

Y: peak area

X: analyte mass concentration (% w/w)

Then the following parameters were calculated, using the Add-in Data Analyses in Excel software:

- Slope of the calibration curve;
- y_{MEAN} (average response of the calibration curve);
- Variance X_s (estimates variance based on concentration values);
- SE_{REG} of the calibration curve (standard error of the predicted y-value for each x in the regression);
- Residuals and Residual plot (how far away the actual data points are from the predicted data points).

The standard uncertainty of calibration curve was calculated by the following equation:

$$u_x = \frac{SE_{REG}}{Slope} * \sqrt{\frac{1}{k} + \frac{1}{n} + \frac{(y_s - Y_{mean})^2}{Slope^2 * (n - 1) * Variance_{X_s}}} \quad (28)$$

Where:

k - number of replicates

n - number of calibration points

y_s - Area of the analyte (Area obtained from Concentration X_s)

MEASUREMENT UNCERTAINTY



Code: **SOP-LAB-005**

Revision No.: **05**

Note: The uncertainty of the calibration curve (u_{cal}) was calculated on three different concentration levels:
 - 2.0 µg/ml (0.2 % w/w) - covering the concentrations from 0.03 to less or equal to 0.2 % w/w ($X_S = 2.0$)
 - 10.0 µg/ml (1.0 % w/w) - covering the concentrations from 0.2 to less or equal to 1.0 % w/w ($X_S = 10.0$)
 - 50.0 µg/ml (5.0 % w/w) - covering the concentrations from 1.0 to 5.0 % w/w ($X_S = 50.0$)
 Concentrations above 50.0 µg/ml are further diluted to fit in the range of the analytical method.

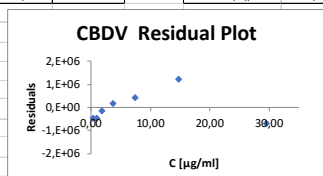
From the standard uncertainty (u_x) the relative uncertainty(u_{cal}) was calculated:

$$u_{cal} = \frac{u_x}{x_s} \quad (29)$$

Calculations for u_{cal} (for 3 different concentration levels) for all 10 cannabinoids are presented below (all calculations regarding the u_{cal} were done by Excel software).

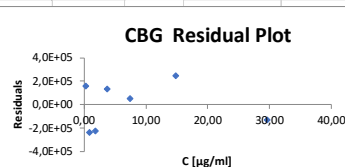
- CBDV:

CBDV						Calculations					
C [µg/ml]	Area [mA]	n =		Concentration of 2.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
0,31	2366649		6131639,95	$y_S = 12263300$	$k = 3$	-39521325	1561935163631050	37597008526775	2,53201E+16		0,06168754
0,93	6148593		Intercept, c =	$x_S = 2,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
1,86	12086142					9531775	90854726480532	37597008526774,80	√A	0,733401674	
3,71	23675421	Uncertainty, u_x	0,083	Uncertainty, $u_x =$	0,088		0,538				
7,39	46344545	Mean of Y	51784625	Relative uncertainty u_{cal}	0,044						
14,78	92080455	SE _{REG}	733461,6622	Concentration of 10.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
29,51	179790573	Variance, s_x^2	112,2434508	$y_S = 61316400$	$k = 3$				2,53201E+16		0,003588244
				$x_S = 10,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
		Uncertainty, $u_x =$	0,083				0,480		0,69266061		
		Relative uncertainty u_{cal}	0,0083	Concentration of 50.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
				$y_S = 306584288$	$k = 3$	254799663	64922868216380300	37597008526774,80	2,53201E+16		2,564083399
				$x_S = 50,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
		Uncertainty, $u_x =$	0,209				3,040		1,743638115		
		Relative uncertainty u_{cal}	0,0042								



- CBG:

CBG						Calculations					
C [µg/ml]	Area [mA]	n =		Concentration of 2.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
0,31	2547644		5957523,94	$y_S = 11915300$	$k = 3$	-38330697	1469242325204720	35492091513957,00	2,40496E+16		0,061092276
0,94	5848843		Intercept, c =	$x_S = 2,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
1,86	11368967					9330503	87058288010248	35492091513957,00	√A	0,732995738	
3,72	22728138	Uncertainty, u_x	0,025	Uncertainty, $u_x =$	0,026		0,537				
7,42	44571539	Mean of Y	50245997	Relative uncertainty u_{cal}	0,013						
14,82	88688808	SE _{REG}	214976,4436	Concentration of 10.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
29,60	175968040	Variance, s_x^2	112,9338888	$y_S = 59576500$	$k = 3$				2,40496E+16		0,003619954
				$x_S = 10,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
		Uncertainty, $u_x =$	0,025				0,480		0,692683499		
		Relative uncertainty u_{cal}	0,0025	Concentration of 50.0 ug/ml		y_S - Mean of Y	$(y_S - \text{Mean of Y})^2$	Slope ²	$\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2$	$(y_S - \text{Mean of Y})^2 / \text{SLOPE}^2$	$* (n-1) * \text{Variance, } s_x^2$
				$y_S = 297882500$	$k = 3$	247636503	61323837665237900	35492091513957,00	2,40496E+16		2,549894425
				$x_S = 50,00$		$=A=1/k+1/n+(y_S - \text{Mean of Y})^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_x^2)$					
		Uncertainty, $u_x =$	0,063				3,026		1,739564572		
		Relative uncertainty u_{cal}	0,0013								



MEASUREMENT UNCERTAINTY



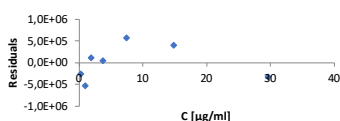
Code: SOP-LAB-005

Revision No.: 05

- CBD:

CBD		n = 7		Concentration of 2.0 ug/ml		Calculations		(yS - Mean of Y) ² / SLOPE ²	
C [µg/ml]	Area [mA]	Slope, m =	5842786,63	y _S = 11685000	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
0,311179	2422551	Intercept, c =	0	x _S = 2,00		-37813021	1429824539140240	34138155648875	2,31524E+16
0,935559	5774499					=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,061757167
1,864225	11791642,7								
3,72053	22489869	Uncertainty, u _x	0,051	Uncertainty, u _x	0,054		0,538		0,733449142
7,418619	44457656,3	Mean of Y	49498021	Relative uncertainty u _{rel}	0,027				
14,82903	87263095	SE _{REG}	433307,3281	Concentration of 10.0 ug/ml					
29,61654	172286832	Variance, s _x ²	113,0326928	y _S = 58425000	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 10,00		8926979	79690958317383	34138155648875	2,31524E+16
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,003442022
		Uncertainty, u _x	0,083	Uncertainty, u _x	0,083		0,480		0,692555051
		Relative uncertainty u _{rel}	0,0083	Concentration of 50.0 ug/ml					
				y _S = 292125000	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 50,00		242626979	58867851054203100	34138155648875	2,31524E+16
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	2,542627873
		Uncertainty, u _x	0,208	Uncertainty, u _x	0,208		3,019		1,737474705
		Relative uncertainty u _{rel}	0,0042						

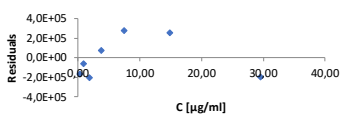
CBD Residual Plot



- THCv:

THCV		n = 7		Concentration of 2.0 ug/ml		Calculations		(yS - Mean of Y) ² / SLOPE ²	
C [µg/ml]	Area [mA]	Slope, m =	6933511,76	y _S = 12623300	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
0,31	2574269	Intercept, c =	0	x _S = 1,77		-46217042	2136014936016780	48073585393930	3,26038E+16
0,94	6994426					=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,065514358
1,86	13261306								
3,72	26351789	Uncertainty, u _x	0,023	Uncertainty, u _x	0,024		0,542		0,736006001
7,42	52086900	Mean of Y	58480342	Relative uncertainty u _{rel}	0,012				
14,83	103225731	SE _{REG}	227239,7785	Concentration of 10.0 ug/ml					
29,62	204867971	Variance, s _x ²	113,0342433	y _S = 61316400	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 10,00		2836058	8043227140170	48073585393930	3,26038E+16
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,000246696
		Uncertainty, u _x	0,023	Uncertainty, u _x	0,023		0,476		0,690244285
		Relative uncertainty u _{rel}	0,0023	Concentration of 50.0 ug/ml					
				y _S = 306584288	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 50,00		248103947	61555568375205200	48073585393930	3,26038E+16
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	1,887989394
		Uncertainty, u _x	0,050	Uncertainty, u _x	0,050		2,364		1,53758898
		Relative uncertainty u _{rel}	0,0010						

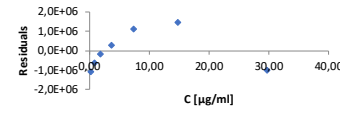
THCV Residual Plot



- CBN:

CBN		n = 7		Concentration of 2.0 ug/ml		Calculations		(yS - Mean of Y) ² / SLOPE ²	
C [µg/ml]	Area [mA]	Slope, m =	16440896,70	y _S = 32883300	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
0,31	4504583	Intercept, c =	0	x _S = 2,00		-105785279	11190525192659100	270303084251170	1,84769E+17
0,94	15253773					=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,060565024
1,87	31035961								
3,74	62083150	Uncertainty, u _x	0,046	Uncertainty, u _x	0,049		0,537		0,732635994
7,45	123852767	Mean of Y	138668579	Relative uncertainty u _{rel}	0,024				
14,89	246331958	SE _{REG}	1098817,663	Concentration of 10.0 ug/ml					
29,73	487617859	Variance, s _x ²	113,9269124	y _S = 164416500	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 10,00		25747921	662955450535339	270303084251170	1,84769E+17
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	0,003588028
		Uncertainty, u _x	0,046	Uncertainty, u _x	0,046		0,480		0,692660453
		Relative uncertainty u _{rel}	0,0046	Concentration of 50.0 ug/ml					
				y _S = 822082500	k = 3	y _S - Mean of Y	(yS - Mean of Y) ²	SLOPE ²	SLOPE ² * (n-1) * Variance, s _x ²
				x _S = 50,00		683413921	467054587807116000	270303084251170	1,84769E+17
						=A=1/k+1/n+(yS - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	2,527778778
		Uncertainty, u _x	0,116	Uncertainty, u _x	0,116		3,004		1,733196254
		Relative uncertainty u _{rel}	0,0023						

CBN Residual Plot



MEASUREMENT UNCERTAINTY



Code: SOP-LAB-005

Revision No.: 05

- 9-THC:

THC		n =		Concentration of 2.0 ug/ml		Calculations			
C [µg/ml]	Area [mA]	Slope, m =	6392068,23	y _S = 12763300	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
0,31	1624173	Intercept, c =	0	x _S = 2,00		-40676606	1654586248561500	40858536315844	2,76376E+16
0,93	5689406					=A=1/k+1/n+(y _S - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	(n-1) * Variance, s _x ²
1,86	11681750	Uncertainty, u _k =	0,026	Uncertainty, u _k =	0,027	0,536		0,732159556	
3,72	23721340	Relative uncertainty u _{rel}	0,014	Relative uncertainty u _{rel}	0,014				
7,41	47513123	Mean of Y	53439906	Concentration of 10.0 ug/ml					
14,81	94928322	SE _{REG}	237452,5327	y _S = 63920000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
29,58	188921226	Variance, s _x ²	112,737098	x _S = 10,00		10480094	109832377235565	40858536315844	2,76376E+16
		Uncertainty, u _k =	0,026	Uncertainty, u _k =	0,026	0,480		0,692939024	
		Relative uncertainty u _{rel}	0,0026	Relative uncertainty u _{rel}	0,0026				
		Concentration of 50.0 ug/ml		y _S = 319605000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	141341355	x _S = 50,00		266165094	70843857444172200	40858536315844	2,76376E+16
		SE _{REG}	1244657,015	Uncertainty, u _k =	0,065	3,040		1,743416598	
		Variance, s _x ²	113,0326928	Relative uncertainty u _{rel}	0,0013				
		Concentration of 2.0 ug/ml		y _S = 33630000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 2,00		-107711355	11601736006194200	282748461353080	1,91759E+17
		Uncertainty, u _k =	0,051	Uncertainty, u _k =	0,054	0,537		0,73259276	
		Relative uncertainty u _{rel}	0,0051	Relative uncertainty u _{rel}	0,027				
		Concentration of 10.0 ug/ml		y _S = 168150000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	141341355	x _S = 10,00		26808645	718703444182821	282748461353080	1,91759E+17
		SE _{REG}	1244657,015	Uncertainty, u _k =	0,051	0,480		0,692775887	
		Variance, s _x ²	113,0326928	Relative uncertainty u _{rel}	0,0051				
		Concentration of 50.0 ug/ml		y _S = 840750000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 50,00		699408645	489172452634126000	282748461353080	1,91759E+17
		Uncertainty, u _k =	0,129	Uncertainty, u _k =	0,129	3,027		1,739875495	
		Relative uncertainty u _{rel}	0,0026	Relative uncertainty u _{rel}	0,0026				
		Concentration of 2.0 ug/ml		y _S = 17263300	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 2,00		-54863093	3009558957851480	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,097	Uncertainty, u _k =	0,103	0,537		0,733017982	
		Relative uncertainty u _{rel}	0,0097	Relative uncertainty u _{rel}	0,051				
		Concentration of 10.0 ug/ml		y _S = 86239500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	72126393	x _S = 10,00		14113107	199179793225765	74384679401167	4,92428E+16
		SE _{REG}	1208330,58	Uncertainty, u _k =	0,097	0,480		0,692990137	
		Variance, s _x ²	110,3335935	Relative uncertainty u _{rel}	0,010				
		Concentration of 50.0 ug/ml		y _S = 431197500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 50,00		359071107	128932059984797000	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,246	Uncertainty, u _k =	0,246	3,094		1,759114689	
		Relative uncertainty u _{rel}	0,0049	Relative uncertainty u _{rel}	0,0049				
		Concentration of 2.0 ug/ml		y _S = 17263300	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 2,00		-54863093	3009558957851480	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,097	Uncertainty, u _k =	0,103	0,537		0,733017982	
		Relative uncertainty u _{rel}	0,0097	Relative uncertainty u _{rel}	0,051				
		Concentration of 10.0 ug/ml		y _S = 86239500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	72126393	x _S = 10,00		14113107	199179793225765	74384679401167	4,92428E+16
		SE _{REG}	1208330,58	Uncertainty, u _k =	0,097	0,480		0,692990137	
		Variance, s _x ²	110,3335935	Relative uncertainty u _{rel}	0,010				
		Concentration of 50.0 ug/ml		y _S = 431197500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 50,00		359071107	128932059984797000	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,246	Uncertainty, u _k =	0,246	3,094		1,759114689	
		Relative uncertainty u _{rel}	0,0049	Relative uncertainty u _{rel}	0,0049				

- CBC:

CBC		n =		Concentration of 2.0 ug/ml		Calculations			
C [µg/ml]	Area [mA]	Slope, m =	16815125,97	y _S = 33630000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
0,31	5059892	Intercept, c =	0	x _S = 2,00		-107711355	11601736006194200	282748461353080	1,91759E+17
0,94	15738707					=A=1/k+1/n+(y _S - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)		√A	(n-1) * Variance, s _x ²
1,86	31421230	Uncertainty, u _k =	0,051	Uncertainty, u _k =	0,054	0,537		0,73259276	
3,72	63231424	Relative uncertainty u _{rel}	0,0051	Relative uncertainty u _{rel}	0,027				
7,42	125762784	Mean of Y	141341355	Concentration of 10.0 ug/ml					
14,83	251674956	SE _{REG}	1244657,015	y _S = 168150000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
29,62	496500493	Variance, s _x ²	113,0326928	x _S = 10,00		26808645	718703444182821	282748461353080	1,91759E+17
		Uncertainty, u _k =	0,051	Uncertainty, u _k =	0,051	0,480		0,692775887	
		Relative uncertainty u _{rel}	0,0051	Relative uncertainty u _{rel}	0,0051				
		Concentration of 50.0 ug/ml		y _S = 840750000	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	141341355	x _S = 50,00		699408645	489172452634126000	282748461353080	1,91759E+17
		SE _{REG}	1244657,015	Uncertainty, u _k =	0,129	3,027		1,739875495	
		Variance, s _x ²	113,0326928	Relative uncertainty u _{rel}	0,0026				
		Concentration of 2.0 ug/ml		y _S = 17263300	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 2,00		-54863093	3009558957851480	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,097	Uncertainty, u _k =	0,103	0,537		0,733017982	
		Relative uncertainty u _{rel}	0,0097	Relative uncertainty u _{rel}	0,051				
		Concentration of 10.0 ug/ml		y _S = 86239500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Mean of Y	72126393	x _S = 10,00		14113107	199179793225765	74384679401167	4,92428E+16
		SE _{REG}	1208330,58	Uncertainty, u _k =	0,097	0,480		0,692990137	
		Variance, s _x ²	110,3335935	Relative uncertainty u _{rel}	0,010				
		Concentration of 50.0 ug/ml		y _S = 431197500	k = 3	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²
		Intercept, c =	0	x _S = 50,00		359071107	128932059984797000	74384679401167	4,92428E+16
		Uncertainty, u _k =	0,246	Uncertainty, u _k =	0,246	3,094		1,759114689	
		Relative uncertainty u _{rel}	0,0049	Relative uncertainty u _{rel}	0,0049				

- CBDA:

CBDA		Calculations										
C [µg/ml]	Area [mA]	n =	7	Concentration of 2.0 ug/ml						(y _S - Mean of Y) ² / SLOPE ² *		
0,30	2889158	Slope, m =	8624655,32	y _S =	17263300	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²	(n-1) * Variance, s _x ²		
0,92	8785562	Intercept, c =	0	k =	3	-54863093	3009958957851480	74384679401167	4,92428E+16	0,061124886		
1,84	16822849			x _S =	2,00	=A=1/k+1/n+(y _S - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)	√A	0,733017982				
3,65	32438099	Uncertainty, u _k	0,097	Uncertainty, u _k =	0,103	0,537						
7,30	65213350	Mean of Y	72126393	Relative uncertainty u _{rel}	0,051							
14,63	128186170	SE _{REG}	1208330,58	Concentration of 10.0 ug/ml								(y _S - Mean of Y) ² / SLOPE ² *
29,26	250549561	Variance, s _x ²	110,3335935	y _S =	86239500	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²	(n-1) * Variance, s _x ²		
				k =	3	141131307	199179793225765	74384679401167	4,92428E+16	0,004044853		
				x _S =	10,00	=A=1/k+1/n+(y _S - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)	√A	0,692990137				
		Uncertainty, u _k	0,097	Uncertainty, u _k =	0,101	0,480						
		Relative uncertainty u _{rel}	0,010	Concentration of 50.0 ug/ml								(y _S - Mean of Y) ² / SLOPE ² *
				y _S =	431197500	y _S - Mean of Y	(y _S - Mean of Y) ²	Slope ²	SLOPE ² * (n-1) * Variance, s _x ²	(n-1) * Variance, s _x ²		
				k =	3	359071107	128932059984797000	74384679401167	4,92428E+16	2,618294012		
				x _S =	50,00	=A=1/k+1/n+(y _S - Mean of Y) ² / (SLOPE ² * (n-1) * Variance, s _x ²)	√A	1,759114689				
		Uncertainty, u _k	0,246	Uncertainty, u _k =	0,246	3,094						
		Relative uncertainty u _{rel}	0,0049	Relative uncertainty u _{rel}	0,0049							

CBDA Residual Plot

C [µg/ml]	Residuals
0,30	-1,2E+06
0,92	1,2E+06
1,84	1,5E+06
3,65	1,8E+06
7,30	-1,2E+06
14,63	-1,2E+06

MEASUREMENT UNCERTAINTY



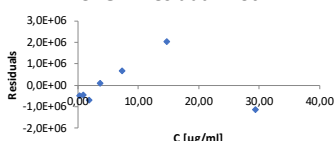
Code: **SOP-LAB-005**

Revision No.: **05**

- CBGA:

CBGA		n = 7		Concentration of 2.0 ug/ml		Calculations			
C [µg/ml]	Area [mA]	Slope, m =	8440742,65	$y_S = 16880000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
0,30	3025575	Intercept, c =	0	k = 3	-53799382	2894373467715670	71246136519417	4,75675E+16	0,060847762
0,92	8250411			$x_S = 2,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
1,84	15762172				0,537			0,732828928	
3,67	31847971	Uncertainty, u_k	0,096	Uncertainty, $u_k =$	0,102				
7,33	63178958	Mean of Y	70679382	Relative uncertainty u_{rel}	0,051				
14,69	126306638	SE _{REG}	1171408,967	Concentration of 10.0 ug/ml					
29,38	246383947	Variance, s_y^2	111,2749452	$y_S = 84400000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
				k = 3	13720618	188255367449003	71246136519417	4,75675E+16	0,00395765
				$x_S = 10,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
					0,480			0,692927216	
		Uncertainty, $u_k =$	0,096	Uncertainty, $u_k =$	0,096				
		Relative uncertainty u_{rel}	0,010	Concentration of 50.0 ug/ml					
				$y_S = 422000000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
				k = 3	351320618	12342617686016000	71246136519417	4,75675E+16	2,594760743
				$x_S = 50,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
					3,071			1,752412971	
		Uncertainty, $u_k =$	0,243	Uncertainty, $u_k =$	0,243				
		Relative uncertainty u_{rel}	0,0049						

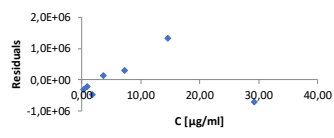
CBGA Residual Plot



- THCA:

THCA		n = 7		Concentration of 2.0 ug/ml		Calculations			
C [µg/ml]	Area [mA]	Slope, m =	9078545,21	$y_S = 18160000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
0,30	3148444	Intercept, c =	0	k = 3	-57439370	3299281280701060	82419983216019	5,46923E+16	0,060324431
0,92	8813620			$x_S = 2,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
1,84	16852171				0,537			0,732471779	
3,66	33912762	Uncertainty, u_k	0,056	Uncertainty, $u_k =$	0,060				
7,31	67134660	Mean of Y	75599370	Relative uncertainty u_{rel}	0,030				
14,65	134473312	SE _{REG}	738789,1422	Concentration of 10.0 ug/ml					
29,29	264860624	Variance, s_y^2	110,5967434	$y_S = 90800000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
				k = 3	15200630	231059137920110	82419983216019	5,46923E+16	0,004224711
				$x_S = 10,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
					0,480			0,693119894	
		Uncertainty, $u_k =$	0,056	Uncertainty, $u_k =$	0,056				
		Relative uncertainty u_{rel}	0,0056	Concentration of 50.0 ug/ml					
				$y_S = 453900000$	$y_S - \text{Mean of } Y$	$(y_S - \text{Mean of } Y)^2$	Slope ²	SLOPE ² * (n-1) * Variance, s_y^2	$(y_S - \text{Mean of } Y)^2 / \text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2$
				k = 3	378300630	143111366298111000	82419983216019	5,46923E+16	2,616664345
				$x_S = 50,00$	$= A = 1/k + 1/n + (y_S - \text{Mean of } Y)^2 / (\text{SLOPE}^2 * (n-1) * \text{Variance, } s_y^2)$		√A		
					3,093			1,758651421	
		Uncertainty, $u_k =$	0,143	Uncertainty, $u_k =$	0,143				
		Relative uncertainty u_{rel}	0,0029						

THCA Residual Plot



The relative uncertainties of calibration curves for all 10 cannabinoids as shown in the calculation above, are presented in the following table:

Table 2: Relative calibration curve uncertainties at different concentrations

Cannabinoid	Ux (standard calibration uncertainty)	ucal from 0.03 to 0.20 % w/w	ucal from 0.20 to 1.0 % w/w	ucal from 1.0 to 5.0 % w/w
CBDV	8.3×10^{-2}	4.4×10^{-2}	8.3×10^{-3}	4.2×10^{-3}
CBG	2.5×10^{-2}	1.3×10^{-2}	2.5×10^{-3}	1.3×10^{-3}
CBD	5.1×10^{-2}	2.7×10^{-2}	2.3×10^{-3}	1.0×10^{-3}
THCV	2.3×10^{-2}	1.2×10^{-2}	2.3×10^{-3}	1.1×10^{-3}
CBN	4.6×10^{-2}	2.4×10^{-2}	4.6×10^{-3}	2.3×10^{-3}
9-THC	2.6×10^{-2}	1.4×10^{-2}	2.6×10^{-3}	1.3×10^{-3}
CBC	5.1×10^{-2}	2.7×10^{-2}	5.1×10^{-3}	2.6×10^{-3}
CBDA	9.7×10^{-2}	5.1×10^{-2}	1.0×10^{-2}	4.9×10^{-3}
CBGA	9.6×10^{-2}	5.1×10^{-2}	1.0×10^{-2}	4.9×10^{-3}
THCA	5.6×10^{-2}	3.0×10^{-2}	5.6×10^{-3}	2.9×10^{-3}

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

3.4 Method repeatability (u_{rep})

The method repeatability was evaluated initially, for 10 cannabinoids.

One of the main factors influencing measurement uncertainty is uncertainty associated with repeatability of the measurements. We accomplish several measurements over the same sample in repeatability condition (the method validation experiment - repeatability was used).

The uncertainty related to the method repeatability was calculated using the following equations:

First the standard deviation was calculated by the formula:

$$s_{rep} = \sqrt{\frac{\sum_{i=1}^n (x_i - \bar{x})^2}{n - 1}} \quad (30)$$

x_i - result of each of the measurements

n - number of measurements

$\bar{x}$ - average concentration

Then the standard uncertainty u_{rep*} was calculated by the formula:

$$u_{rep*} = \sqrt{\frac{s}{n}} \quad (31)$$

In the end relative uncertainty u_{rep} was calculated by the formula:

$$u_{rep} = \frac{u_{rep*}}{\bar{x}} \quad (32)$$

Table 3: Calculated standard deviations and standard and relative uncertainties from data observed from validation experiment Precision - Repeatability (PHL_RPC_10C_2019_003)

#	CBDV	CBDA	CBG	CBD	THCV	CBN	9-THC
1 [% w/w]	7.68617	0.10228	3.26950	53.96367	5.56757	0.03182	0.19188
2 [% w/w]	7.71967	0.10128	3.12091	53.77260	5.67855	0.03166	0.18966
3 [% w/w]	7.54006	0.09887	3.15181	53.88920	5.48245	0.03244	0.18780
4 [% w/w]	7.73288	0.10004	3.24670	54.01950	5.60092	0.03236	0.18810
5 [% w/w]	7.68480	0.09988	3.16560	54.10170	5.67660	0.03263	0.18679
6 [% w/w]	7.70141	0.10209	3.21003	54.26220	5.59690	0.03139	0.18752
Average [% w/w]	7.67750	0.10074	3.19409	54.00148	5.60050	0.03205	0.18863
S_{rep}	0.0699	0.0014	0.0577	0.1702	0.0734	0.0005	0.0019
u_{rep*}	0.1079	0.0150	0.0981	0.1684	0.1106	0.0091	0.0176
u_{rep}	0.01	0.15	0.03	0.003	0.02	0.28	0.09

In addition, we analyzed and evaluate the results for QCS, which was prepared independently in every validation experiment. Total of 13 different independent preparations were carried out and the data processed for the inter-day variability of the measurements. The variability consists of the uncertainty of preparation and repeatability but not calibration, since the same calibration was used for all analysis. The results in % w/w are presented in the following table.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

Table 4: Results for QCS (13 analysis in total were obtained)

#	CBDV	CBDA	CBGA	CBG	CBD	THCV	CBN	9-THC	CBC	THCA
1 [% w/w]	3.39	12.98	0.26	0.69	26.02	0.88	0.04	0.40	0.28	0.31
2 [% w/w]	3.25	13.01	0.27	0.72	25.94	0.91	0.04	0.39	0.28	0.33
3 [% w/w]	3.39	13.17	0.26	0.69	26.27	0.89	0.04	0.39	0.29	0.31
4 [% w/w]	3.28	12.87	0.26	0.69	26.38	0.87	0.04	0.38	0.29	0.31
5 [% w/w]	3.37	13.11	0.26	0.70	26.36	0.90	0.04	0.39	0.29	0.33
6 [% w/w]	3.26	13.03	0.24	0.61	26.28	0.80	0.04	0.35	0.25	0.28
7 [% w/w]	3.27	12.88	0.27	0.61	25.77	0.86	0.04	0.39	0.29	0.30
8 [% w/w]	3.35	13.03	0.26	0.69	26.26	0.89	0.04	0.39	0.29	0.31
9 [% w/w]	3.32	13.22	0.25	0.68	26.56	0.86	0.04	0.37	0.27	0.30
10 [% w/w]	3.49	13.01	0.26	0.68	26.06	0.88	0.04	0.37	0.27	0.28
11 [% w/w]	3.39	13.08	0.26	0.70	26.28	0.89	0.04	0.38	0.29	0.30
12 [% w/w]	3.57	13.20	0.26	0.68	26.55	0.88	0.04	0.38	0.29	0.32
13 [% w/w]	3.54	13.21	0.26	0.67	26.34	0.86	0.04	0.37	0.27	0.30
Average [% w/w]	3.37	13.06	0.26	0.68	26.24	0.87	0.04	0.38	0.28	0.31
Srep	0.105	0.117	0.008	0.032	0.231	0.027	0.000	0.013	0.013	0.016
urep*	0.090	0.095	0.024	0.050	0.133	0.046	0.000	0.032	0.031	0.035
urep	0.03	0.01	0.09	0.07	0.01	0.05	0.00	0.08	0.11	0.11

As seen in tables 3 and 4, at higher concentrations the relative standard uncertainties are lower, which makes sense, since lower concentrations are more prone to error during the data integration. In addition, the inter-day variability cannot be considered, because it contains also the uncertainty of preparation, not only the uncertainty of repeatability. The u_{rep} presented in the Table 4 are only for orientation purposes.

Based on the presented results, both in Table 3 and Table 4, it is obvious that the u_{rep} is dependent on the chromatographic conditions or the analyte type as the similar concentrations observed in CBG, CBD, CBDV or THCV results in different u_{rep} .

Considering the presented results, we will consider the following u_{rep} :

Table 5: The u_{rep} at different concentrations

Cannabinoid	urep from 0.03 to 0.20 % w/w	urep from 0.20 to 1.0 % w/w	urep from 1.0 to 5.0 % w/w
CBDV	0.08	0.040	0.020
CBG	0.08	0.050	0.025
CBD	0.06	0.020	0.010
THCV	0.08	0.050	0.025
CBN	0.08	0.020	0.010
9-THC	0.08	0.020	0.010
CBC	0.08	0.020	0.010
CBDA	0.08	0.020	0.010
CBGA	0.08	0.020	0.010
THCA	0.08	0.020	0.010

As tested during validation of MET-LAB-001/2, the same u_{rep} can be used also for 8-THC and CBL.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

3.5 Intermediate precision – method MET-LAB-001/01 and MET-LAB-001/02

Based on the results for intermediate precision, tested during the method MET-LAB-002 validation (see validation report RP-VP-007, it is important to include the higher measurement uncertainties for very low concentrations (up to .10 %). Moreover, the uncertainties to 0.20 % should be changed to 0.50 % and uncertainties from 0.20 to 1.0 % should be changed to from 0.50 to 10.0.

To the calculation of each expended measurement uncertainty the intermediate precision uncertainty is added to form 4 different concentration ranges.

The same acceptance criteria were used also for validation of the method MET-LAB-001/02 and the same repeatability was achieved as for the method MET-LAB-002. The measurement uncertainties are the same for all methods.

4 MEASUREMENT UNCERTAINTIES FOR ADDITIONAL CANNABINOIDS

4.1 Measurement uncertainties for cannabinoids CBL and 8-THC

The cannabinoids 8-THC and CBL were evaluated through the validation of the method MET-LAB-001/02, where linearity, accuracy and repeatability were assessed. Based on the results obtain, the measurement uncertainties were added in the Chapter 5.

4.2 Measurement uncertainties for cannabinoids CBE, CBNV, CBCA and CBT

The cannabinoids CBNV, CBCA and CBT were evaluated through the validation study, where linearity, accuracy and repeatability were assessed for quantitative determination of CBNV, CBCA And CBT. Based on the results obtained, the measurement uncertainties were added in the Chapter 5.

Measurement uncertainty of CBE was not assessed through validation study, as the reporting of CBE is not under accredited activities. As there is no CRM standard available for calibration of CBE, the measurement uncertainty for CBE is set based on the experience with reporting other cannabinoids with the additional error – using only reference material for calibration. The measurement uncertainty for CBE is added in Chapter 5.

5 CALCULATION OF COMBINED STADNARD MEASUREMENT UNCERTAINTY

From quantified uncertainty components of each identified uncertainty source, combined standard measurement uncertainty of overall analytical method can be calculated. Laboratory follows a procedure for everyday control of quality control working material and by that bias of analytical procedure is not significant and can be neglected. The sampling is not performed for each sample; thus, the sampling was included in combined standard measurement uncertainty only when the sampling was performed by the laboratory. Based on the results presented in Chapter 3 the calculation of combined uncertainty was performed for each individual cannabinoid. Moreover, it was evaluated for 3 different concentration levels.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

5.1 Sampling is performed by the laboratory

In the case when sampling is performed by the laboratory, calculated standard deviation (s) between the taken samples is the contribution of sampling uncertainty. The combined standard measurement uncertainty is evaluated from the following expression:

$$u_c X = x * \sqrt{u_{\text{samp}}^2 + u_{\text{prep}}^2 + u_{\text{cal}}^2 + u_{\text{rep}}^2} \quad (33)$$

Sampling factor is added to the calculation of uncertainty, which is increased by the factor of repeatability between the 3 or 6 samples (from sampling).

5.2 Sampling is not performed

When sampling is not performed by the laboratory, sampling is neglected; therefore, expression for the determination of combined uncertainty is Eq. 33 reduced for factor u_{samp} .

6 CALCULATION OF EXPANDED MEASUREMENT UNCERTAINTY

The final step is to derive expanded uncertainty based on the combined uncertainty determined in previous step. Expanded measurement uncertainty (U) is dimension which represents the measurement result range inside which a result is with certain level of confidence and is provided by multiplying combined standard measurement uncertainty $u_c(x)$ with coverage factor k:

$$U = k * u_c(x) \quad (34)$$

Then the measurement result is expressed as:

$$X = x \pm U \quad (35)$$

The calculated final expanded measurement uncertainties for the three concentration ranges are presented below. In the calculation of the final expanded uncertainties also the data for intermediate precision are added and 4 different concentration ranges are formed.

The cannabinoids 8-THC and CBL were added to the tables below based on the linearity, accuracy and repeatability evaluation during the validation of the method MET-LAB-001/02.

Table 6: Calculated final expanded measurement uncertainty for the concentrations from 0.03 to below 0.2 w/w %

Analyte	u_{prep}^2	u_{cal}^2	u_{rep}^2	$\sqrt{\text{SUM}}$	$u_c(x)$ ($x=0.2$)	Expanded uncertainty y (k=2)	Relative expanded uncertainty [%]
CBDV	9.8×10^{-5}	1.9×10^{-3}	6.4×10^{-3}	0.0918	0.0184	0.037	18.4
CBG	9.8×10^{-5}	1.7×10^{-4}	6.4×10^{-3}	0.0817	0.0163	0.033	16.3
CBD	9.8×10^{-5}	7.3×10^{-4}	3.6×10^{-3}	0.0665	0.0133	0.027	13.3
THCV	1.2×10^{-4}	1.4×10^{-4}	6.4×10^{-3}	0.0816	0.0163	0.033	16.3
CBN	9.8×10^{-5}	5.8×10^{-4}	6.4×10^{-3}	0.0841	0.0168	0.034	16.8
9-THC	4.4×10^{-4}	2.0×10^{-4}	6.4×10^{-3}	0.0839	0.0168	0.034	16.8
8-THC	4.4×10^{-4}	2.0×10^{-4}	6.4×10^{-3}	0.0839	0.0168	0.034	16.8
CBL	4.4×10^{-4}	2.0×10^{-4}	6.4×10^{-3}	0.0839	0.0168	0.034	16.8
CBC	9.8×10^{-5}	7.3×10^{-4}	6.4×10^{-3}	0.0850	0.0170	0.034	17.0
CBDA	9.2×10^{-5}	2.6×10^{-3}	6.4×10^{-3}	0.0954	0.0191	0.038	19.1
CBGA	9.2×10^{-5}	2.6×10^{-3}	6.4×10^{-3}	0.0954	0.0191	0.038	19.1
THCA	9.2×10^{-5}	9.0×10^{-4}	6.4×10^{-3}	0.0860	0.0172	0.034	17.2

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

Table 7: Calculated final expanded measurement uncertainty for the concentrations from 0.2 to below 1.0 % w/w

Analyte	uprep2	ucal2	urep2	√SUM	uC (x) (x= 1.0)	Expanded uncertainty y	Relative expanded uncertainty [%]
CBDV	9.8 x 10 ⁻⁵	6.9 x 10 ⁻⁵	9.0 x 10 ⁻⁴	0.0327	0.0327	0.0653	6.5
CBG	9.8 x 10 ⁻⁵	6.3 x 10 ⁻⁶	9.0 x 10 ⁻⁴	0.0317	0.0317	0.0634	6.3
CBD	9.8 x 10 ⁻⁵	5.3 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.0224	0.0224	0.0449	4.5
THCV	1.2 x 10 ⁻⁴	5.3 x 10 ⁻⁶	9.4 x 10 ⁻⁴	0.0320	0.0320	0.0641	6.4
CBN	9.8 x 10 ⁻⁵	2.1 x 10 ⁻⁵	4.0 x 10 ⁻⁴	0.0228	0.0228	0.0456	4.6
9-THC	4.4 x 10 ⁻⁴	6.8 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.0291	0.0291	0.0582	5.8
8-THC	4.4 x 10 ⁻⁴	6.8 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.0291	0.0291	0.0582	5.8
CBL	4.4 x 10 ⁻⁴	6.8 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.0291	0.0291	0.0582	5.8
CBC	9.8 x 10 ⁻⁵	2.6 x 10 ⁻⁵	4.0 x 10 ⁻⁴	0.0229	0.0229	0.0458	4.6
CBDA	9.2 x 10 ⁻⁵	1.0 x 10 ⁻⁴	4.0 x 10 ⁻⁴	0.0243	0.0243	0.0487	4.9
CBGA	9.2 x 10 ⁻⁵	1.0 x 10 ⁻⁴	4.0 x 10 ⁻⁴	0.0243	0.0243	0.0487	4.9
THCA	9.2 x 10 ⁻⁵	3.1 x 10 ⁻⁵	4.0 x 10 ⁻⁴	0.0229	0.0229	0.0458	4.6

Table 8: Calculated final expanded measurement uncertainty for the concentrations 1.0 and above 1.0 % w/w

Analyte	uprep2	ucal2	urep2	√SUM	uC (x) (x= 50.0)	Expanded uncertainty y	Relative expanded uncertainty [%]
CBDV	9.8 x 10 ⁻⁵	1.8 x 10 ⁻⁵	6.3 x 10 ⁻⁴	0.027	1.36	2.72	5.4
CBG	9.8 x 10 ⁻⁵	1.7 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.022	1.12	2.24	4.5
CBD	9.8 x 10 ⁻⁵	1.0 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.014	0.71	1.41	2.8
THCV	1.2 x 10 ⁻⁴	1.2 x 10 ⁻⁶	4.0 x 10 ⁻⁴	0.023	1.14	2.29	4.6
CBN	9.8 x 10 ⁻⁵	5.3 x 10 ⁻⁵	1.0 x 10 ⁻⁴	0.014	0.71	1.43	2.9
9-THC	4.4 x 10 ⁻⁴	1.7 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.023	1.16	2.33	4.7
8-THC	4.4 x 10 ⁻⁴	1.7 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.023	1.16	2.33	4.7
CBL	4.4 x 10 ⁻⁴	1.7 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.023	1.16	2.33	4.7
CBC	9.8 x 10 ⁻⁵	6.8 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.014	0.72	1.43	2.9
CBDA	9.2 x 10 ⁻⁵	2.4 x 10 ⁻⁵	1.0 x 10 ⁻⁴	0.015	0.74	1.47	2.9
CBGA	9.2 x 10 ⁻⁵	2.4 x 10 ⁻⁵	1.0 x 10 ⁻⁴	0.015	0.74	1.47	2.9
THCA	9.2 x 10 ⁻⁵	8.1 x 10 ⁻⁶	1.0 x 10 ⁻⁴	0.014	0.71	1.42	2.8

Based on the relative expanded uncertainties above and the results for intermediate precision the following uncertainties are formed. Those are used for the method: MET-LAB-001/01, MET-LAB-001/02 and MET-LAB-001/03.

The cannabinoids CBNV, CBCA and CBT were added to the tables below based on the linearity, accuracy and repeatability evaluation during the validation of quantitative determination of CBNV, CBCA and CBT. Cannabinoid CBE was added based on the expected uncertainties, considering the use of reference standard instead of CRM.

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

Table 9: Calculated final relative expanded measurement uncertainties for all cannabinoids including the data from the intermediate precision for method MET-LAB-001/01, MET-LAB-001/02 and MET-LAB-001/03

Analyte	From 0.03 to 0.10 %	From 0.10 to 0.50 %	From 0.50 to 1.0 %	Above 1.0 %
CBDV	23	18	12	5
CBG	30	25	13	7
CBD	20	15	10	5
THCV	21	16	12	5
CBN	22	17	10	5
9-THC	22	17	11	5
8-THC	22	17	11	5
CBL	22	17	11	5
CBC	22	17	10	5
CBDA	23	17	10	5
CBGA	30	25	13	7
THCA	22	17	10	5
CBE	28	23	17	10
CBNV	22	17	10	5
CBCA	23	17	10	5
CBT	22	17	10	5

7 REFERENCES

- SOP-LAB-006 - Vzorčenje
- RP-VP-007 - Analytical method validation report for method MET-002
- RP-VP-011 - Analytical method validation report for method MET-003
- ISO 9001:2015 - Sistemi vodenja kakovosti - Zahteve
- ISO/IEC 17025:2017 - Splošne zahteve za usposobljenost preskuševalnih in kalibracijskih laboratorijev
- ISO 22000:2018 - Sistemi vodenja varnosti živil - Zahteve za vsako organizacijo v prehranski verigi
- ISO 22716:2007 - Kozmetika - Dobra proizvodna praksa (GMP) - Smernice za dobro proizvodno prakso
- Smernice z dne 19. marca 2015 o načelih dobre distribucijske prakse za zdravilne učinkovine za zdravila za uporabo v humani medicini (2015/C 95/01) (GDP)

8 APENDIX

/

MEASUREMENT UNCERTAINTY	Pharma  Hemp®
	Code: SOP-LAB-005
	Revision No.: 05

9 HISTORY OF THE DOCUMENT

Revision number	Amendments	Issue date	Change with new version (date, signature)
01	First issue	19. 08. 2019	18. 09. 2020
02	Measurement uncertainties for all cannabinoids were updated due to the implementation of the method MET-002. The same uncertainty is taken into account for both methods MET-001 and MET-002. The results of intermediate precision in the validation report RP-VP-007 are taken into account when calculating the total measurement uncertainty for all 10 cannabinoids. The chapter 3.5 was added to include the intermediate precision for the methods MET-001 and MET-002 in the total uncertainty calculation. The ranges for calculation were updated to total of 4 (0.03 to 0.10, 0.10 to 0.50, 0.50 to 1.0 and above 1.0). The table 9 was added to include the relative expended measurement uncertainties for all 10 cannabinoids for all 4 concentration ranges.	18. 09. 2020	05. 10. 2021
03	The measurement uncertainties for cannabinoids 8-THC and CBL were added. The measurement uncertainties for MET-003 were added. The same ranges and measurement uncertainties are used also for the method MET-003.	05. 10. 2021	24. 10. 2022
04	The measurement uncertainties for cannabinoids CBE, CBNV, CBCA and CBT were added. Chapter 4 was added to the document to explain the addition of 6 cannabinoids to the initial evaluation of the measurement uncertainty. The Chapter 5 was updated with the data of expended uncertainties for 16 cannabinoids.	24. 10. 2022	
05	Updated method references with new naming: MET-LAB-001 = MET-LAB-001/01 MET-LAB-003 = MET-LAB-001/02 Newly accredited THC method = MET-LAB-001/03 (Expanded measurement uncertainties for 9THC and THCA already determined as part of the validation of methods MET-LAB-001/01 and MET-LAB-001/02)		