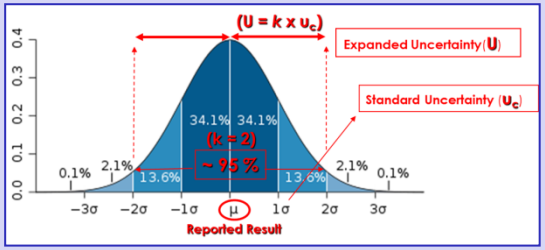
DG-SANTE Document «**AQC**»

***A**nalytical **Q**uality **C**ontrol and Method Validation Procedures for Pesticide Residues Analysis in Food and Feed*

Document Nº SANTE/12682/2019



Measurement Uncertainty (MU) in the DG-SANTE AQC Document

Part I

Estimation of Measurement Uncertainty of Results based on intra-laboratory validation/QC data

(SANTE/12682/2019: Appendix C – Approach 1)

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This tutorial has been prepared on behalf of the EURL-FV

Two important premises useful to understand the DG-SANTE AQC criteria on Measurement Uncertainty (MU)

The nature of the test methods used in pesticide residue analysis precludes a rigorous, and statistically valid, calculation of MU
(supported by the accreditation standard ISO/IEC 17025)

In multi-residue analysis of pesticides, it is not the goal to obtain very accurate MU estimates for one specific pesticide in a particular matrix. It is more important to obtain an overall and realistic estimate for a wide variety of materials and analyte levels covered by the validated scope
(supported by the EURACHEM / CITAC Guide CG 4)

«Uncertainty» in the Document SANTE/12682/2019

- A.- Introduction and legal background
- B.- Sampling, transport, traceability and storage of samples
- C.- Sample Analysis
- D.- Identification of analytes and confirmation of results
- **E.- Reporting results**
- F.- Pesticide standards, stock and calibration solutions
- G.- Analytical method validation and performance criteria
- H.- Additional recommendations

- Annex A *(Commodity groups and representative matrices)*
- Appendix A *(Method validation procedure: outline and example approaches)*
- Appendix B *(Examples of conversion factors)*
- **Appendix C *(Examples for the estimation of measurement uncertainty)***
- Appendix D *(Example of rounding, reporting and interpreting results)*
- Appendix E *(Glossary)*

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Correction for RECOVERY — **E4**

Qualifying results with UNCERTAINTY — **E7 – E11**

INTERPRETATION of results — **E12 – E15**

- Annex A *(Commodity groups and representative matrices)*
- Appendix A *(Method validation procedure: outline and example approaches)*
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Correction for RECOV

Qualifying NCERTAINTY — E7 – E11

ATION of results — E12 – E15

Will be discussed in Part II

- Annex A *(Commodity groups and representative matrices)*
- Appendix A *(Method validation procedure: outline and example approaches)*
- Appendix B *(Examples of conversion factors)*
- **Appendix C *(Examples for the estimation of measurement uncertainty)***
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New Example based on intra-laboratory validation/QC data

Appendix C in SANTE/12682/2019

Examples for the estimation of measurement uncertainty of results

Intra-Laboratory Validation/QC/PTs Data

CAC/GL 59-2006 – Amendment 2011 (Annex)

«These approaches do not include the uncertainty component associated to the heterogeneity of the laboratory sample»

Relative Standard Uncertainty

$$u' = (u'_{precision}{}^2 + u'_{bias}{}^2)^{1/2}$$

Appendix C in SANTE/12682/2019

Examples for the estimation of measurement uncertainty of results

Intra-Laboratory Validation/QC/PTs Data

CAC/GL 59-2006 – Amendment 2011 (Annex)

Relative Intra-Laboratory Reproducibility (RSD_{wR})

Validation/QC Data

Relative Standard Uncertainty

$$u' = (u'_{precision}{}^2 + u'_{bias}{}^2)^{1/2}$$

Proficiency Tests

Approach 2 in Appendix C

$(u'_{bias})_{PT}$

$(\sum(bias')^2/N)^{1/2}$

Root Mean Square of relative PTs bias

&

$u'(C_{ref})_{PT}$

Appendix C in SANTE/12682/2019

Examples for the estimation of measurement uncertainty of results

Intra-Laboratory Validation/QC/PTs Data

CAC/GL 59-2006 – Amendment 2011 (Annex)

Relative Intra-Laboratory Reproducibility (RSD_{wR})

Validation/QC Data

Relative Standard Uncertainty

$$u' = (u'_{precision}{}^2 + u'_{bias}{}^2)^{1/2}$$

$(\sum(bias')^2/N)^{1/2}$

Intra-Lab Validation/QC

Approach 1 in Appendix C

$(u'_{bias})_{QC}$ *No-correction* → Root Mean Square of relative QC bias & $u'(C_{ref})_{QC}$

New

$(u'_{bias})_{QC}$ *Mean Rec. Correction* → $u'(\text{Mean Rec.})_{QC}$ & $u'(C_{ref})_{QC}$

$RSD_{wR}/N^{1/2}$

Uncertainty – Analytical Measurement Guidelines

EURACHEM / CITAC Guide CG 4 (QUAM:2012.P1)
Quantifying Uncertainty in Analytical Measurement (3rd Edition, 2012)
Example A4: Pesticide Multiresidue Analysis

NORDTEST Technical Report TR537 (Ed. 3.1)
Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories (2012)

EUROLAB Technical Report No. 1/2006
Guide to the Evaluation of Measurement Uncertainty for Quantitative Test Results (2006)

EUROLAB Technical Report No. 1/2007
Measurement Uncertainty Revisited: Alternative Approaches to Uncertainty Evaluation (2007)

Codex Guidelines - Uncertainty - Pesticide Residues

CAC/GL 59-2006 *(Amendment 2011)*
Guidelines on Estimation of Uncertainty of Results

CONCLUSIONS from International Guidelines on the use of intra-laboratory Validation/QC data for estimation of MU

The most accepted approach (Eurachem/Nordtest/Codex) for estimation of the relative standard uncertainty (u´) by using just intra-laboratory Validation/QC data:

u´^2 = u´(bias)^2 + u´(precision)^2

In pesticide residue analysis, both the u´(precision) component and the u´(bias) component are estimated by using the same RECOVERY experiments.

Even if the bias is zero, the uncertainty bias component u´(bias) has to be estimated

$$u(bias) = \sqrt{RMS_{bias}{}^2 + u(Cref)^2} \text{ where } RMS_{bias} = \sqrt{\frac{\sum (bias_i)^2}{n_{CRM}}}$$

Root Mean Square of the Relative Bias

In pesticide residue analysis, when normal certified standards and calibrated/verified volumetric material/balances are used, it can be assumed that the uncertainty associated with the spiking level of the recovery tests is negligible *u´(Cref)* = 0

Appendix C (SANTE/12682/2019)

Approach 1: *Estimating MU based on intra-laboratory validation/QC data*

«This approach does not include the uncertainty component associated to the heterogeneity of the laboratory sample»

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Relative Standard Deviation of Recovery (RSD_{wR})

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%)
- Relative Standard Deviation of recovery (RSDwR) (%)

NO RECOVERY CORRECTION → (u'_{bias}) *No-correction* → Root Mean Square of relative bias: $(\sum(bias')^2/N)^{1/2}$ & ~~$u'(C_{ref})$~~

RECOVERY CORRECTION → (u'_{bias}) *Mean Rec. Correction* → u'(Mean Rec.) & ~~$u'(C_{ref})$~~

u'(Mean Rec.) → $RSD_{wR}/N^{1/2}$

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

NO RECOVERY CORRECTION

Relative Standard Deviation of Recovery (RSD_{wR})

(u'_{bias}) *No-correction* → Root Mean Square of relative bias → $(\sum(bias')^2/N)^{1/2}$

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%) → (Mean-recovery) – 100
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%) → 100*(SD-recovery)/(Mean-recovery)

$u'_{precision}$

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Relative Standard Deviation of Recovery (RSD_{wR})

NO RECOVERY CORRECTION

(u'_{bias}) *No-correction* → Root Mean Square of relative bias → $(\sum(bias')^2/N)^{1/2}$

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) → (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

Mean Square of relative bias → $(\sum(bias')^2/N) = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2$

$u'_{bias}{}^2$

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

NO RECOVERY CORRECTION

Relative Standard Deviation of Recovery (RSD_{wR})

(u'_{bias}) *No-correction* → Root Mean Square of relative bias → $(\sum(bias')^2/N)^{1/2}$

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) → (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

Mean Square of relative bias → $(\sum(bias')^2/N) = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2$

NO RECOVERY CORRECTION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$

Intra-Laboratory Validation/QC

RECOVERY CORRECTION

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Relative Standard Deviation of Recovery (RSD_{wR})

(u'_{bias}) *Mean Rec. Correction* → u'(Mean Recovery) → $RSD_{wR}/N^{1/2}$

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

100*(SD-recovery)/(Mean-recovery)

RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

(RSD_{wR})

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

$$(\sum(bias')^2/N) = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2$$

CONCLUSION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$ NO RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$ RECOVERY CORRECTION

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

(RSD_{wR})

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

$(\sum(bias')^2/N) = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2$

CONCLUSION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$ NO RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$ RECOVERY CORRECTION

Simplified formulas

N = 9

N > 9

$$u' = (RSD_{wR})$$ RECOVERY CORRECTION

Appendix C (SANTE/12682/2019) - Approach 1: *Estimating MU based on intra-laboratory validation/QC data*

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

$u'_{precision}$ (RSD_{wR})

(N) Recovery Tests

- Recovery (%) = (found level/spiking level)*100
- Relative bias (bias´)(%) = (recovery – 100)
- Mean-recovery (%)
- Mean relative bias (Mean-bias´) (%)
- Standard Deviation of recovery (SD-recovery) (%)
- Standard Deviation of relative bias (SD-bias´) (%) (stdev.p)
- Relative Standard Deviation of recovery (RSD_{wR}) (%)

$(\sum(bias')^2/N) = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2$

CONCLUSION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$ NO RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$ RECOVERY CORRECTION

Simplified formulas

N > 9 $u' = (RSD_{wR})$ RECOVERY CORRECTION

(SD-bias´) ~ (RSD_{wR}) $u'^2 = (Mean\text{-}bias')^2 + 2\,(RSD_{wR})^2$ NO RECOVERY CORRECTION

Procedural Calibration / IL-IS addition before extraction $u' = 2^{1/2}\,(RSD_{wR})$

Very low bias´

Table I. Example A, pesticide X (low bias, good within-lab reproducibility)

Date	QC samples spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%) [equation 3]
10/Jan	apple	0.051	2
26/Jan	Pear	0.045	-10
04/Feb	lettuce	0.050	0
08/Feb	cauliflower	0.056	12
22/Feb	cherries	0.052	4
28/Feb	onion	0.046	-8
05/Mar	French beans	0.048	-4
06/Mar	carrots	0.045	-10
22/Mar	Leek	0.037	-26
*	N	9	
*	mean	0.0478	-4.444
*	SD.Pbias (stdev.p) (%)		10.232
	standard dev. measured (mg/kg) (stdev.s)	0.00543	
*	RSDwR (%)	11.357	
	u'(bias) (%) [equation 5]		11.1555
	u'(precision) = RSDwR (%) [equation 8]	11.357	
	u' combined (%) [equation 2 and 9]	15.920	
	U' (expanded MU) (%) [equation 1]	31.839	

Mean bias´ = - 4.4%

Mean Recovery = 95.6%

RSD_{wR} = 11.4%

NO RECOVERY CORRECTION

Table I. Example A, pesticide X (low bias, good within-lab reproducibility)

Date	QC samples spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%) [equation 3]
10/Jan	apple	0.051	2
26/Jan	Pear	0.045	-10
04/Feb	lettuce	0.050	0
08/Feb	cauliflower	0.056	12
22/Feb	cherries	0.052	4
28/Feb	onion	0.046	-8
05/Mar	French beans	0.048	-4
06/Mar	carrots	0.045	-10
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	* N	9	
	* mean	0.0478	-4.444
	* SD.Pbias (stdev.p) (%)		10.232
	standard dev. measured (mg/kg) (stdev.s)	0.00543	
	* RSDwR (%)	11.357	
	u'(bias) (%) [equation 5]		11.1555
	u'(precision) = RSDwR (%) [equation 8]	11.357	
	u' combined (%) [equation 2 and 9]	15.920	
	U' (expanded MU) (%) [equation 1]	31.839	

Mean Recovery = 95.6%

RSD_{wR} = 11.4%

NO RECOVERY CORRECTION

NO RECOVERY CORRECTION

$$u'^2 = (\text{Mean-bias}')^2 + (\text{SD-bias}')^2 + (RSD_{wR})^2$$

$$u'^2 = (-4.444\ \%)^2 + (10.232\ \%)^2 + (11.357\ \%)^2$$

u´ = 15.92 %

U´= 31.84 %

(K = 2; 95%)

Table I. Example A, pesticide X (low bias, good within-lab reproducibility)

Date	QC samples spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%) [equation 3]
10/Jan	apple	0.051	2
26/Jan	Pear	0.045	-10
04/Feb	lettuce	0.050	0
08/Feb	cauliflower	0.056	12
22/Feb	cherries	0.052	4
28/Feb	onion	0.046	-8
05/Mar	French beans	0.048	-4
06/Mar	carrots	0.045	-10
22/Mar	Leek	0.037	-26
	* N	9	
	* mean	0.0478	-4.444
	* SD.Pbias (stdev.p) (%)		10.232
	standard dev. measured (mg/kg) (stdev.s)	0.00543	
	* RSDwR (%)	11.357	
	u'(bias) (%) [equation 5]		11.1555
	u'(precision) = RSDwR (%) [equation 8]	11.357	
	u' combined (%) [equation 2 and 9]	15.920	
	U' (expanded MU) (%) [equation 1]	31.839	

Mean Recovery = 95.6%

RSD_{wR} = 11.4%

NO RECOVERY CORRECTION

NO RECOVERY CORRECTION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$

$$u'^2 = (-4.444\ \%)^2 + (10.232\ \%)^2 + (11.357\ \%)^2$$

u´ = 15.92 %

U´= 31.84 %

(K = 2; 95%)

RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$

$$u'^2 = (11.357\ \%)^2/9 + (11.357\ \%)^2$$

u´ = 11.97 %

U´= 23.94 %

(K = 2; 95%)

Table I. Example A, pesticide X (low bias, good within-lab reproducibility)

Date	QC samples spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%) [equation 3]
10/Jan	apple	0.051	2
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04/Feb	lettuce	0.050	0
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22/Mar	Leek	0.037	-26
	* N	9	
	* mean	0.0478	-4.444
	* SD.Pbias (stdev.p) (%)		10.232
	standard dev. measured (mg/kg) (stdev.s)	0.00543	
	* RSDwR (%)	11.357	
	u'(bias) (%) [equation 5]		11.1555
	u'(precision) = RSDwR (%) [equation 8]	11.357	
	u' combined (%) [equation 2 and 9]	15.920	
	U' (expanded MU) (%) [equation 1]	31.839	

Mean Recovery = 95.6%

RSD_{wR} = 11.4%

NO RECOVERY CORRECTION

NO RECOVERY CORRECTION

$$u'^2 = (\text{Mean-bias}')^2 + (\text{SD-bias}')^2 + (RSD_{wR})^2$$

$$u'^2 = (-4.444\ \%)^2 + (10.232\ \%)^2 + (11.357\ \%)^2$$

u´ = 15.92 % → **U´= 31.84 %** (K = 2; 95%)

u´ = 16 %

Simplied Formulas

RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$

$$u'^2 = (11.357\ \%)^2/9 + (11.357\ \%)^2$$

u´ = 11.97 % → **U´= 23.94 %** (K = 2; 95%)

u´ = 11.5 %

Table II. Example B, pesticide Y (high bias, good within-lab reproducibility)

Date	QC sample spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%)
10/Jan	apple	0.038	-24
26/Jan	pear	0.034	-32
04/Feb	lettuce	0.037	-26
08/Feb	cauliflower	0.042	-16
22/Feb	cherries	0.039	-22
28/Feb	onion	0.034	-32
05/Mar	French beans	0.036	-28
06/Mar	carrots	0.034	-32
22/Mar	Leek	0.028	-44
	* N	9	
	* mean	0.0358	-28.444
	* SD.Pbias (stdev.p) (%)		7.470
	standard dev. measured (mg/kg) (stdev.s)	0.00396	
	* RSDwR (%)	11.073	
	u'(bias) (%) [equation 5]		29.4090
	u'(precision) = RSDwR (%) [equation 8]	11.073	
	u' combined (%) [equation 2 and 9]	31.424	
	U' (expanded MU) (%) [equation 1]	62.849	

Mean bias´ = - 28.4%

Mean Recovery = 71.6%

RSD_{wR} = 11.1%

NO RECOVERY CORRECTION

Table II. Example B, pesticide Y (high bias, good within-lab reproducibility)

Date	QC sample spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%)
10/Jan	apple	0.038	-24
26/Jan	pear	0.034	-32
04/Feb	lettuce	0.037	-26
08/Feb	cauliflower	0.042	-16
22/Feb	cherries	0.039	-22
28/Feb	onion	0.034	-32
05/Mar	French beans	0.036	-28
06/Mar	carrots	0.034	-32
22/Mar	Leek	0.028	-44
	* N	9	
	* mean	0.0358	-28.444
	* SD.Pbias (stdev.p) (%)		7.470
	standard dev. measured (mg/kg) (stdev.s)	0.00396	
	* RSDwR (%)	11.073	
	u'(bias) (%) [equation 5]		29.4090
	u'(precision) = RSDwR (%) [equation 8]	11.073	
	u' combined (%) [equation 2 and 9]	31.424	
	U' (expanded MU) (%) [equation 1]	62.849	

Mean Recovery = 71.6%

RSD_{wR} = 11.1%

NO RECOVERY CORRECTION

NO RECOVERY CORRECTION

$$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$$

$$u'^2 = (-28.444\ \%)^2 + (7.47\ \%)^2 + (11.073\ \%)^2$$

u´ = 31.42 %

U´= 62.85 %

(K = 2; 95%)

RECOVERY CORRECTION

$$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$$

$$u'^2 = (11.073\ \%)^2/9 + (11.073\ \%)^2$$

u´ = 11.67 %

U´= 23.34 %

(K = 2; 95%)

Table II. Example B, pesticide Y (high bias, good within-lab reproducibility)

Date	QC sample spiked @0.05 mg/kg	measured (mg/kg)	rel. bias (%)
10/Jan	apple	0.038	-24
26/Jan	pear	0.034	-32
04/Feb	lettuce	0.037	-26
08/Feb	cauliflower	0.042	-16
22/Feb	cherries	0.039	-22
28/Feb	onion	0.034	-32
05/Mar	French beans	0.036	-28
06/Mar	carrots	0.034	-32
22/Mar	Leek	0.028	-44
	* N	9	
	* mean	0.0358	-28.444
	* SD.Pbias (stdev.p) (%)		7.470
	standard dev. measured (mg/kg) (stdev.s)	0.00396	
	* RSDwR (%)	11.073	
	u'(bias) (%) [equation 5]		29.4090
	u'(precision) = RSDwR (%) [equation 8]	11.073	
	u' combined (%) [equation 2 and 9]	31.424	
	U' (expanded MU) (%) [equation 1]	62.849	

Mean Recovery = 71.6%

RSD_{wR} = 11.1%

NO RECOVERY CORRECTION

NO RECOVERY CORRECTION

$u'^2 = (Mean\text{-}bias')^2 + (SD\text{-}bias')^2 + (RSD_{wR})^2$

$u'^2 = (-28.444\ \%)^2 + (7.47\ \%)^2 + (11.073\ \%)^2$

$u' = 31.42\ \%$

$U' = 62.85\ \%$ (K = 2; 95%)

Simplied Formulas

$u' = 32.5\ \%$

RECOVERY CORRECTION

$u'^2 = (RSD_{wR})^2/N + (RSD_{wR})^2$

$u'^2 = (11.073\ \%)^2/9 + (11.073\ \%)^2$

$u' = 11.67\ \%$

$U' = 23.34\ \%$ (K = 2; 95%)

u´ = 11 %

EXAMPLE in CAC/GL 59-2006 – Amendment 2011 (Annex)

Spiking Level = 0,50 mg/kg	
N = 14	
Mean Recovery = 86%	
RSDwR = 15%	CAC/GL 59-2006 Example

QC-sample Concentration (mg/kg)	Recovery (%)	
0,45	90	
0,5	100	
0,43	86	
0,44	88	
0,45	90	
0,39	78	
0,38	76	
0,33	66	
0,4	80	
0,41	82	
0,57	114	
0,53	106	
0,38	76	
0,37	74	

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Intra-Laboratory Validation/QC

Spiking Level = 0,500 mg/kg	
N = 14	
Mean Recovery = 86%	
RSDwR = 15%	CAC/GL 59-2006 Example

Appendix C (SANTE/12682/2019) - Approach 1

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Intra-Laboratory Validation/QC

QC-sample Concentration (mg/kg)	Recovery (%)	
0,45	90	
0,5	100	
0,43	86	
0,44	88	
0,45	90	
0,39	78	
0,38	76	
0,33	66	
0,4	80	
0,41	82	
0,57	114	
0,53	106	
0,38	76	
0,37	74	

Mean Recovery (%) =	**86,14285714**	
SD (%) =	**13,23083312**	
SD-P (%) =	12,74954981	
RSDwR (%) =	**15,36%**	**u´(precision)**
RSDwR /(N)^1/2 =	**4,11%**	**u´(bias) RECOVERY CORRECTION**

QC-sample Concentration (mg/kg)	Recovery (%)		Relative Bias (%) bias´(%) = Recovery - 100		bias´^2
0,45	90		-10		100
0,5	100		0		0
0,43	86		-14		196
0,44	88		-12		144
0,45	90		-10		100
0,39	78		-22		484
0,38	76		-24		576
0,33	66		-34		1156
0,4	80		-20		400
0,41	82		-18		324
0,57	114		14		196
0,53	106		6		36
0,38	76		-24		576
0,37	74		-26		676
		Mean-bias´ (%) =	-13,85714286		
		SD-P (bias´)(%) =	12,74954981		
		(Mean-bias´)^2 + (SD-P bias´)^2 = 354,57 =		Mean Square of bias´ =	354,5714286
				Root Mean Square of bias´ =	18,83%

$(\sum(bias')^2/N)^{1/2}$

Appendix C (SANTE/12682/2019) - Approach 1

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

u´ (bias) NO RECOVERY CORRECTION

Intra-Laboratory Validation/QC

Spiking Level = 0,500 mg/kg
N = 14
Mean Recovery = 86%
RSDwR = 15%

CAC/GL 59-2006 Example

Appendix C (SANTE/12682/2019) - Approach 1

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Intra-Laboratory Validation/QC

QC-sample Concentration (mg/kg)	Recovery (%)		Relative Bias (%) bias´(%) = Recovery - 100
0,45	90		-10
0,5	100		0
0,43	86		-14
0,44	88		-12
0,45	90		-10
0,39	78		-22
0,38	76		-24
0,33	66		-34
0,4	80		-20
0,41	82		-18
0,57	114		14
0,53	106		6
0,38	76		-24
0,37	74		-26
		Mean-bias´ (%) =	-13,85714286
		SD-P (bias´)(%) =	12,74954981
		(Mean-bias´)^2 + (SD-P bias´)^2 = 354,57 =	
Mean Recovery (%) =	86,14285714	u´ (bias)^2 *NO RECOVERY CORRECTION*	
SD (%) =	13,23083312		
SD-P (%) =	12,74954981		
RSDwR (%) =	15,36%	u´(precision)	
RSDwR /(N)^1/2 =	4,11%	u´(bias) RECOVERY CORRECTION	
Root Mean Square of bias´ =	18,83%	u´ (bias) NO RECOVERY CORRECTION	

CAC/GL 59-2006 – Amendment 2011 (Annex)

Spiking Level = 0,500 mg/kg
N = 14
Mean Recovery = 86%
RSDwR = 15%

Appendix C (SANTE/12682/2019) - Approach 1

CAC/GL 59-2006 Example

QC-sample Concentration (mg/kg)	Recovery (%)		Relative Bias (%) bias´(%) = Recovery - 100
0,45	90		-10
0,5	100		0
0,43	86		-14
0,44	88		-12
0,45	90		-10
0,39	78		-22
0,38	76		-24
0,33	66		-34
0,4	80		-20
0,41	82		-18
0,57	114		14
0,53	106		6
0,38	76		-24
0,37	74		-26
		Mean-bias´ (%) =	-13,85714286
		SD-P (bias´)(%) =	12,74954981

(Mean-bias´)^2 + (SD-P bias´)^2 = 354,57 =
u´ (bias)^2 NO RECOVERY CORRECTION

Mean Recovery (%) =	86,14285714	
SD (%) =	13,23083312	
SD-P (%) =	12,74954981	
RSDwR (%) =	15,36%	u´(precision)
RSDwR /(N)^1/2 =	4,11%	u´(bias) RECOVERY CORRECTION
Root Mean Square of bias´ =	18,83%	u´ (bias) NO RECOVERY CORRECTION

Intra-Laboratory Validation/QC

$$u' = (u'_{bias}{}^2 + u'_{precision}{}^2)^{1/2}$$

Relative Standard Uncerainty

u´(NO RECOVERY CORRECTION) = 24,30 %
u´(RECOVERY CORRECTION) = 15,90 %

Simplied Formulas/Approximate values

u´(NO RECOVERY CORRECTION) = 25 %
u´(RECOVERY CORRECTION) = 15,5 %

U´ = 50 % No-correction
U´ = 31 % Rec. Correction

Expanded Uncertainty
K = 2 (95%)

Example in the CAC/GL 59-2006 – Amendment 2011 (Annex)

Intra-laboratory QC Recovery data (3 months)
N = 14; Mean Rec = 86%; RSD_{wR} = 15%; *(Mean-bias´ = 14 %)*

A measurement result of 0.34 mg/kg reported with correction and no correction for recovery

$u'_{precision} = RSD_{wR} = 15\ \%$

$(u'_{bias})_{QC}$ No-correction *19%*

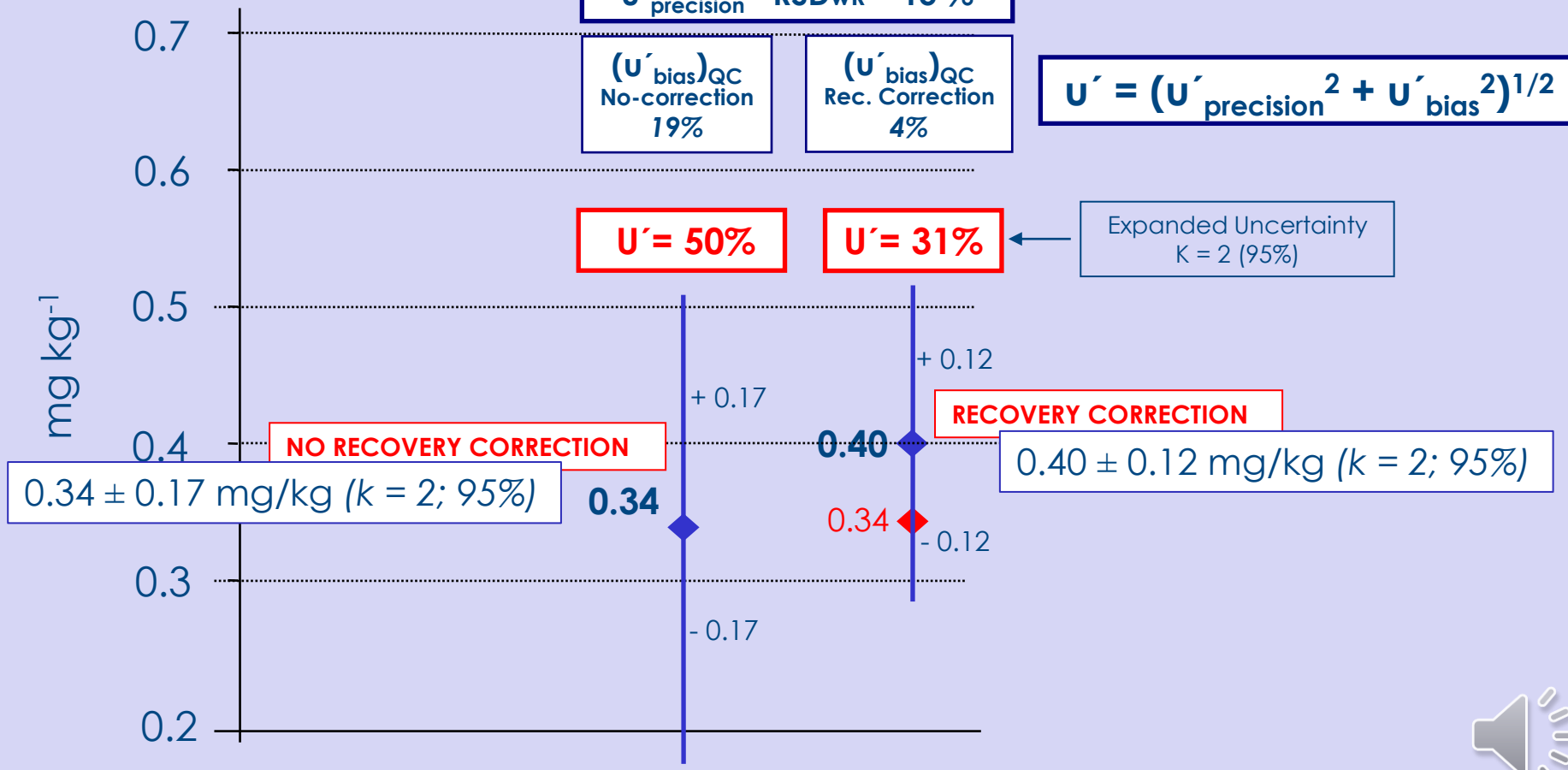
$(u'_{bias})_{QC}$ Rec. Correction *4%*

$u' = (u'_{precision}{}^2 + u'_{bias}{}^2)^{1/2}$

U´= 50%

U´= 31%

Expanded Uncertainty K = 2 (95%)



NO RECOVERY CORRECTION

0.34 ± 0.17 mg/kg *(k = 2; 95%)*

RECOVERY CORRECTION

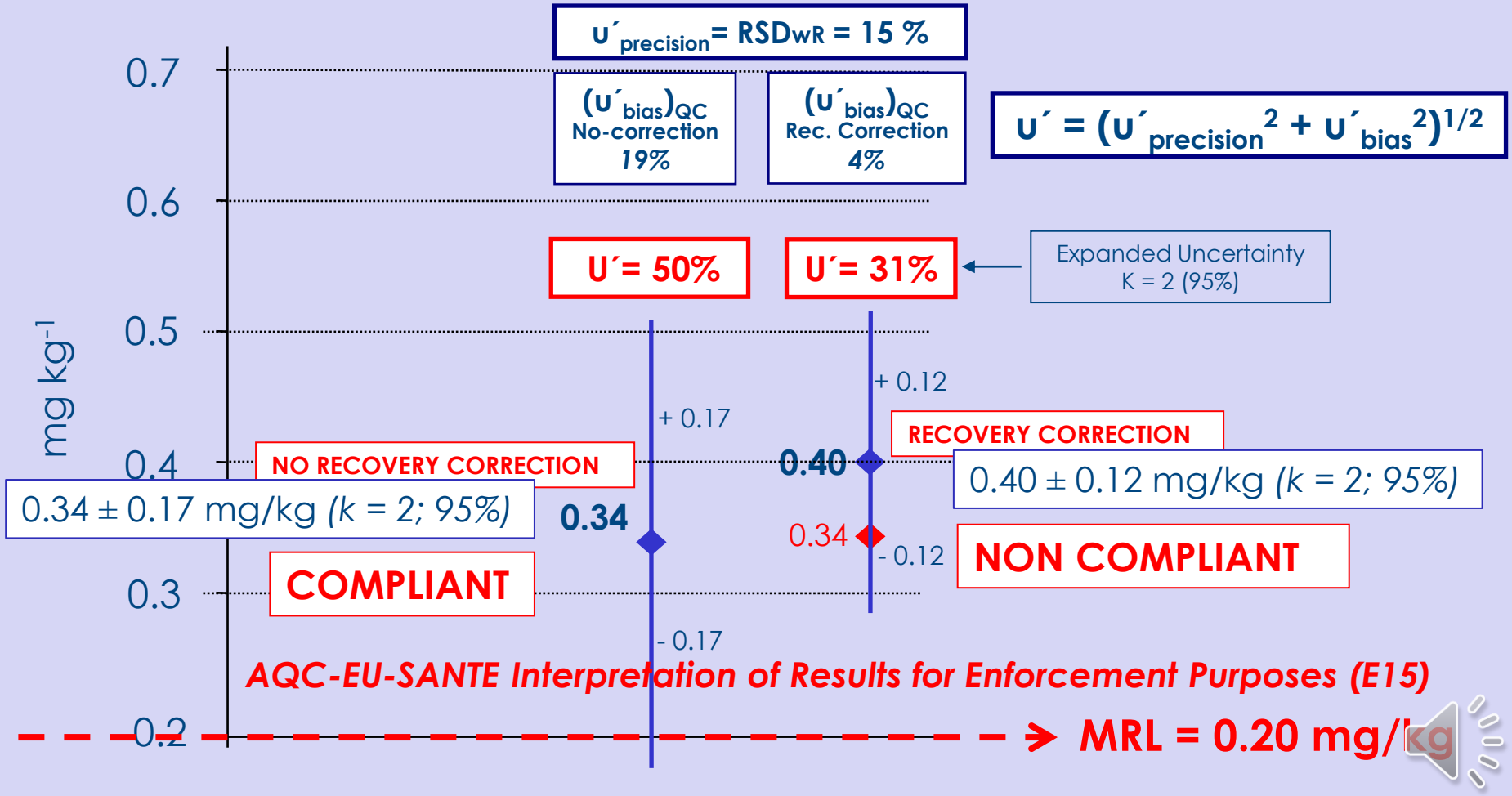
0.40 ± 0.12 mg/kg *(k = 2; 95%)*

Example in the CAC/GL 59-2006 – Amendment 2011 (Annex)

Intra-laboratory QC Recovery data (3 months)

N = 14; Mean Rec = 86%; RSD_{wR} = 15%; *(Mean-bias´ = 14 %)*

A measurement result of 0.34 mg/kg reported with correction and no correction for recovery



«Uncertainty» in the Document SANTE/12682/2019

- A.- Introduction and legal background
- B.- Sampling, transport, traceability and storage of samples
- C.- Sample Analysis
- D.- Identification of analyte[illegible]ults
- **E.- Reporting results**
- F.- Pesticide standards, sto[illegible]
- G.- Analytical method validation and performance criteria
- H.- Additional recommendations

Correction for RECOVERY

Qualifying results with UNCERTAINTY

INTERPRETATION of results

- Annex A *(Commodity groups and representative matrices)*
- Appendix A *(Method validation procedure: outline and example approaches)*
- Appendix B *(Examples of conversion factors)*
- **Appendix C *(Examples for the estimation of measurement uncertainty)***
- Appendix D *(Example of rounding, reporting and interpreting results)*
- Appendix E *(Glossary)*

«Uncertainty» in the Document SANTE/12682/2019

- A.- Introduction and legal background
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- F.- Pesticide standards, sto…
- G.- Analytical method validation and performance criteri…
- H.- Additional recommendations

Correction for RECOVERY

Qualifying results with UNCERTAINTY

INTERPRETATION of results

Will be discussed in Part II

- Annex A *(Commodity groups and representative…*
- Appendix A *(Method validation proced… …ample approaches)*
- Appendix B *(Examples of con…*
- **Appendix C** ***(Exam… …timation of measurement uncertainty)***
- Appendix D *(Exam… …ding, reporting and interpreting results)*
- Appendix E *(Glossary)*

DG-SANTE Document «**AQC**»

***A**nalytical **Q**uality **C**ontrol and Method Validation Procedures for Pesticide Residues Analysis in Food and Feed*

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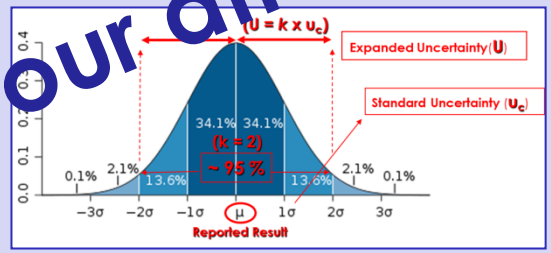

Many thanks for your attention!!!