Nuevas Guías Europeas de Control de Calidad

SANCO Document 12495/2011 on Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed

EU (D.G. SANCO) tools to assure the Quality of Pesticide Residues Analyses

http://www.europa.eu.int/comfood

http://www.crl-pesticides.eu

Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed

SANCO/12495/2011 (01/01/2012)

EU Proficiency Tests for Pesticide Residues in Foods (EU-PTs)
### Document SANCO/12495/2011

**METHOD VALIDATION AND QUALITY CONTROL**

**PROCEDURES FOR PESTICIDE RESIDUES**

**ANALYSIS IN FOOD AND FEED**

*Document No: SANCO/12495/2011*

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*Implementation by: 01/01/2012*

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**Revisions of the SANCO – AQC Document**

*The original document was elaborated by Alan Hill (UK)*

1. **Doc. 7826/VI/97**
   - (1st EU AQC, 1997, Portugal)
2. **Doc. SANCO/3103/2000**
   - (2nd EU AQC, 1999, Greece)
3. **Doc. SANCO/10476/2003**
   - (3rd EU AQC, 2003, UK)
4. **Doc. SANCO/10232/2006**
   - (4th EU AQC, 2005, Sweden)
5. **Doc. SANCO/2007/3131**
   - (5th EU AQC, 2007, Spain)
6. **Doc. SANCO/10684/2009**
   - (6th EU AQC, 2009, Denmark)
7. **Doc. SANCO/12495/2011**
   - (7th EU AQC, 2011, France)

[http://www.crl-pesticides.eu](http://www.crl-pesticides.eu)
Key objectives

- To harmonize a cost-effective quality assurance system in the EU
- To ensure the quality and comparability of analytical results
- To ensure that acceptable accuracy is achieved
- To ensure that false positives or false negatives are avoided
- To support compliance with, and specific implementation of, ISO/IEC 17025 (accreditation standard)

In EU Official Laboratories!

METHOD VALIDATION AND QUALITY CONTROL PROCEDURES
FOR
PESTICIDE RESIDUES ANALYSIS IN FOOD AND FEED

Document N° SANCO/12495/2011
1/January/2012

- Introduction (1-4)
- Accreditation and legal background (5)
- Sampling, transport, processing and storage of samples (6-14)
- Pesticide standards, calibration solutions, etc. (15-23)
- Extraction and concentration (24-27)
- Contamination and interference (28-34)
- Analytical calibration, representative analytes, matrix effects and chromatographic integration (35-53)
Analytical method validation and performance criteria (54-60)
Routine recovery determination (61-67)
Proficiency testing and analysis of reference materials (68-69)
Confirmation of results (70-81)
Reporting of results (82-93)

Annex 1 (Selection of matrices)
Appendix A (The validation procedure: outline and example approaches)
Appendix B (Examples of conversion factors)
Appendix C (Examples for estimation of measurement uncertainty)
Appendix D (Glossary)
Appendix E (Data elements of the Standard Sample Description)

Key for the interpretation of the document
SANCO/12495/2011
(Appendix D: Glossary)

may = option
should = recommendation
must = obligation
Validation

> Representative matrices may be used.

> As a minimum, one matrix from each Commodity Group.

> Complementary validation during the routine analyses.

Validation

10 Commodity Groups for Representative Matrices
(Annex 1)

VEGETABLES, FRUITS, and CEREALS (6 Groups)

- High water content
- High oil content
- High starch and/or protein content (low water & fat content)
- High acid content (and high water content)
- High sugar content (and low water content)
- Difficult or unique commodities
## Validation

10 Commodity Groups for Representative Matrices

(Annex 1)

**FOOD OF ANIMAL ORIGIN (4 Groups)**

- Meat and Seafood
- Milk and milk products
- Eggs
- Fat from food of animal origin

<table>
<thead>
<tr>
<th>Commodity groups</th>
<th>Commodity categories</th>
<th>Typical representative commodities included in the category</th>
</tr>
</thead>
<tbody>
<tr>
<td>High water content</td>
<td>Fruits</td>
<td>Apples, pears, apricots, cherries, peaches, bananas</td>
</tr>
<tr>
<td></td>
<td>Stone fruit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other fruit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bulb vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rooting vegetables/cucurbits</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Brassica vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leafy vegetables and fresh herbs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stem and stalk vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Forage fodder crops</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fresh legume vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leaves of root and tuber vegetables</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fresh fungi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Root and tuber vegetables or food</td>
<td></td>
</tr>
</tbody>
</table>
### Document N° SANCO/12495/2011: Annex 1

#### High oil content
- Few nuts: hazelnut, chestnut, walnuts, macadamia nuts, etc.
- Oil seeds and products thereof: sunflower, linseed, rapeseed, safflower, soybeans, sesame, etc.
- Oily fruits and products thereof: olives, avocados and oils and pastes thereof.

#### High starch and/or protein content and low water and fat content
- Dry legume vegetables/pulses: fava beans, lentils, peas, beans.
- Cereal grain and products thereof: wheat, rye, barley, oat grains, rye and wheat.

#### Commodity groups

<table>
<thead>
<tr>
<th>Commodity categories</th>
<th>Typical representative commodities included in the category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrus fruit</td>
<td>Oranges, lemons, tangerines, mandarins, citruses, oranges</td>
</tr>
<tr>
<td>Citrus fruit</td>
<td>Black currant, red currant, white currant, grapes, currants</td>
</tr>
<tr>
<td>Other</td>
<td>Kiwi fruit, pineapple, myrtles, loquats, rose hips</td>
</tr>
<tr>
<td>Honey, dried fruit</td>
<td>Honey, dates, dried apricots, dried plums, dates</td>
</tr>
<tr>
<td>Cocoa beans and products thereof</td>
<td>Coffee, cocoa beans</td>
</tr>
</tbody>
</table>

**Notes:**

1. If a buffer is used to stabilise the pH changes in the extraction step, then this commodity group can be merged into **one commodity group “High water content”**.
2. “Difficult commodities” should only be fully validated if they are frequently analysed. If they are only analysed occasionally, validation may be reduced to just checking the reporting limits using spiked blank extracts.
3. Laboratories using methods to determine non polar pesticides based on preliminary extracted fat can merge the commodities of this group into the corresponding commodity groups “Meat and Seafood” or “Milk and milk products”.

Validation Parameters and Criteria
(Quantitative Methods)
Appendix A: Outline and Example

Table 1. Validation parameters and criteria.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>What/how</th>
<th>Criterion</th>
<th>Cross reference to AOAC document</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unlinearity</td>
<td>Through calibration curve</td>
<td>Residuals &lt; ±20%</td>
<td>33-41</td>
</tr>
<tr>
<td>Matrix effect</td>
<td>Comparison of response from solvent standards and matrix-matched standards</td>
<td>-</td>
<td>44-45</td>
</tr>
<tr>
<td>LOQ</td>
<td>By definition, lowest level for which it has been demonstrated that criteria for trueness and precision have been met</td>
<td>≤ MRL</td>
<td>57</td>
</tr>
<tr>
<td>Specificity</td>
<td>Response in reagent blank and control samples</td>
<td>≤ 30% of LOQ</td>
<td>64</td>
</tr>
<tr>
<td>Precision (RSDs)</td>
<td>Determine reproducibility RSDs, determine for both spiked levels</td>
<td>≤ 20%</td>
<td>59</td>
</tr>
<tr>
<td>Precision* (RSDw)</td>
<td>Determine within-laboratory reproducibility*</td>
<td>≤ 20%</td>
<td>59</td>
</tr>
<tr>
<td>Robustness</td>
<td>Can be derived from on-going method validation/verification through establishing average recovery equal to LOQ</td>
<td>See above</td>
<td></td>
</tr>
<tr>
<td>Trueness (bias)</td>
<td>Determine the average recovery for spiked levels</td>
<td>70-120%</td>
<td>59</td>
</tr>
</tbody>
</table>

* Within-lab reproducibility is to be derived from on-going QC (see below)

2 Fortification Levels for each Representative Matrix:
- Reporting Limit (n = 5)
- Another higher level / MRL (n = 5)

For each Fortification Level/Representative Matrix*:
- Mean Recovery = 70-120 %
- RDS_w & RSD_wR ≤ 20 %

* In certain justified cases different values may be accepted
Ejemplo Estudio Validación Forchlorfenuron (QuEChERS/LC-TOF-MS)

Análisis de Forchlorfenuron en vegetales mediante LC-TOF-MS después de la extracción con el método QuEChERS.

**Matrices Representativas**
- Sandía
- Calabacín
- Tomate

<table>
<thead>
<tr>
<th>Matriz</th>
<th>Nivel de Inyección (μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sandía</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td>calabacín</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td>tomate</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>200</td>
</tr>
</tbody>
</table>

Figure 2. Espectro de masas obtenido a un voltaje de fragmentación de 150 V.
Patrón Forclorfenuron 0.01 mg/kg en extracto de calabacín

**LC-TOF-MS (XIC: 248.0 – 248.2 amu)**

![Graph showing the LC-TOF-MS analysis of Forclorfenuron](image1)

---

Patrón Forclorfenuron 0.01 mg/kg en extracto de calabacín

**TOF-MS a 20.89 min.**

![Graph showing the TOF-MS analysis of Forclorfenuron](image2)
### Estudio Validación Forchlorfenuron (QuEChERS/LC-TOF-MS)

#### Table 2: Forchlorfenuron Linear Calibration Curves Obtained along the Complete Validation

<table>
<thead>
<tr>
<th>chromatographic sequence/matrix</th>
<th>calibration points</th>
<th>slope x 10^3 (area units/µg kg⁻¹)</th>
<th>r²</th>
<th>RSD of response factors (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/solvent</td>
<td>5</td>
<td>1.14</td>
<td>0.9998</td>
<td>4</td>
</tr>
<tr>
<td>1/watermelon</td>
<td>5</td>
<td>1.08</td>
<td>0.9998</td>
<td>11</td>
</tr>
<tr>
<td>2/watermelon</td>
<td>6</td>
<td>1.07</td>
<td>0.9999</td>
<td>6</td>
</tr>
<tr>
<td>3/watermelon</td>
<td>6</td>
<td>1.09</td>
<td>0.9997</td>
<td>6</td>
</tr>
<tr>
<td>4/watermelon</td>
<td>6</td>
<td>1.10</td>
<td>0.9998</td>
<td>9</td>
</tr>
<tr>
<td>5/solvent</td>
<td>5</td>
<td>1.16</td>
<td>0.9992</td>
<td>5</td>
</tr>
<tr>
<td>5/zucchini</td>
<td>5</td>
<td>1.12</td>
<td>0.9998</td>
<td>10</td>
</tr>
<tr>
<td>6/zucchini</td>
<td>6</td>
<td>1.11</td>
<td>0.9998</td>
<td>10</td>
</tr>
<tr>
<td>7/zucchini</td>
<td>6</td>
<td>1.11</td>
<td>0.9999</td>
<td>11</td>
</tr>
<tr>
<td>8/zucchini</td>
<td>6</td>
<td>1.13</td>
<td>0.9996</td>
<td>8</td>
</tr>
<tr>
<td>9/solvent</td>
<td>5</td>
<td>1.14</td>
<td>0.9999</td>
<td>8</td>
</tr>
<tr>
<td>9/tomato</td>
<td>5</td>
<td>1.23</td>
<td>0.9997</td>
<td>14</td>
</tr>
<tr>
<td>10/tomato</td>
<td>6</td>
<td>1.18</td>
<td>0.9991</td>
<td>13</td>
</tr>
<tr>
<td>11/tomato</td>
<td>6</td>
<td>1.18</td>
<td>0.9998</td>
<td>11</td>
</tr>
<tr>
<td>12/tomato</td>
<td>6</td>
<td>1.16</td>
<td>0.9999</td>
<td>10</td>
</tr>
</tbody>
</table>

### Secuencia cromatográfica recuperaciones 10 ng/g

1) Matrix blank  
2) 10 ng/g STD  
3) Spike Sample #1  
4) Spike Sample #2  
5) Spike Sample #3  
6) Spike Sample #4  
7) Spike Sample #5  
8) 10 ng/g STD  
9) 50 ng/g STD  
10) 100 ng/g STD  
11) 200 ng/g STD  
12) 500 ng/g STD  
13) Solvent
Resultados Ensuyos de Recuperación

Tabla 3. Forchlorfenuron Recoveries from Spiked Blank Samples (n = 5)

<table>
<thead>
<tr>
<th>matrix</th>
<th>Spike level (μg/kg)</th>
<th>mean recovery (%)</th>
<th>RSD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>watermelon</td>
<td>10</td>
<td>87</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>82</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>84</td>
<td>3</td>
</tr>
<tr>
<td>zucchini</td>
<td>10</td>
<td>80</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>82</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>82</td>
<td>9</td>
</tr>
<tr>
<td>tomato</td>
<td>10</td>
<td>71</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>68</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>68</td>
<td>7</td>
</tr>
</tbody>
</table>

N° Total Recuperaciones = 45
Intervalo Recuperaciones Individuales = 60% - 95%
Recuperación Media = 72%; RSD = 12%
U (expandida) = 24%

Resumen Resultados Estándares (matriz) y Recuperaciones 10 ng/g

Relación S/N: Sandía = 350 – 600
               Calabacín = 110 – 130
               Tomate = 70 – 110

Recuperaciones Medias 10 ng/g > 71%
RSD Recuperaciones 10 ng/g < 10%
Error Masa Exacta < 0.5 ppm

LOQ Validado = 10 ng/g

LOD (cualitativo) diana a validar = 0.5 ng/g

Concentración estimada para dar una S/N 3-5 en la matriz menos favorable (tomate)
Validation
Qualitative Screening Methods (MS-based detection)

- Validation of qualitative MRMs is focused on detectability.
- The Screening Detection Limit (SDL) is the lowest concentration for which the analyte can be detected in at least 95% of the samples.
- A basic validation should involve analysis of at least 20 samples spiked at the anticipated SDL (for each commodity group).
- Negative results must be reported as < SDL mg/kg.
- Positive results can only be reported after quantitative analysis.

On-going performance Verification
Qualitative Screening Methods (MS-based detection)

At least 10 indicator analytes should be checked with each analytical batch.

<table>
<thead>
<tr>
<th>Table 2. Minimum requirements for routine method performance verification.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of analytes</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>At least 10 analytes</td>
</tr>
<tr>
<td>Frequency</td>
</tr>
<tr>
<td>Level</td>
</tr>
<tr>
<td>Criterion</td>
</tr>
</tbody>
</table>
Key Activities for Quality Control
SANCO/12495/2011

Analytical Calibration
Routine Recovery Determination
(On-going Performance Verification/Validation)
Confirmation of Results

Analytical Calibration

- Standards in matrix, if appropriate
- Alternative use of “analyte protectants” in GC
- Alternative (recommended) use of “standard addition”
- **Calibration in each batch of analysis**
- **Bracketing calibration (< 20% - 30% drift)**
- Residues below LCL* should be reported as < LCL
- LCL Signal/Noise ≥ 6:1

*LCL = Lowest Calibrated Level
**Analytical Calibration**

**Interpolation between 2 Calibration Levels**
- Difference between levels not greater than a factor of 4
- Higher RF/Lower RF < 120% *(110% if MRL is exceeded)*

**Multilevel Calibration Function**
- Individual residuals must not deviate more than ±20% *(10%)*

**Single-Level Calibration**
- May provide more accurate results
- Sample response should be within ±50% of the cal. *(20%)*

---

**Minimum frequencies for calibration**

A minimum number of Representative Analytes per detection system MUST BE used for calibration in each batch

**Representative Analytes ≥ 15 + 25% Tested Analytes**

<table>
<thead>
<tr>
<th>Table 1. Minimum frequencies for calibration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum frequency of calibration</td>
</tr>
<tr>
<td>In each batch of analyses.</td>
</tr>
<tr>
<td>At least one calibration point corresponding to the reporting limit.</td>
</tr>
</tbody>
</table>

*The minimum requirements are (i) at the beginning and end of a survey or programme and (ii) when potentially significant changes are made to the method.*
Example on the minimum number of Representative Analytes for Calibration

Analytical Scope with 140 pesticides
(40 by LC + 100 by GC)

Representative Analytes in LC = 15 + 10 → 25
Representative Analytes in GC = 15 + 25 → 40

Routine Recovery Determination
(On-going performance verification / validation)

- Ensure the validity of the results during routine analysis
- Determine within-laboratory reproducibility (RSD_{WR})
- Determine acceptable limits for individual recoveries
- Demonstrate applicability to other commodities / levels
- Demonstrate robustness
- Collect information for uncertainty estimation
Frequencies for Routine Recovery
(On-going performance verification)

Recoveries must be checked in each analytical batch for, at least, **10% of the Representative Analytes** with a **minimum of 5 analytes** per detection system.

**Table 3. Frequency for routine recovery (performance verification)**

<table>
<thead>
<tr>
<th>Minimum frequency of recovery</th>
<th>Representative analytes</th>
<th>All other analytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10% of representative analytes (at least 5 per detection system) in each batch of analytes</td>
<td>Within a rolling programme to include all other analytes at least every 12 months, but preferably every 6 months</td>
</tr>
<tr>
<td></td>
<td>Within a rolling programme covering all representative analytes as well as different types of commodities, at least at the level corresponding to the reporting limit</td>
<td>At least at the level corresponding to the reporting limit.</td>
</tr>
</tbody>
</table>

**Example on the minimum number Analytes for Routine Recovery**

Analytical Scope with 140 pesticides
(40 by LC + 100 by GC)

Representative Analytes in LC = 15 + 10 = 25
Representative Analytes in GC = 15 + 25 = 40

Routine Recovery Analytes in LC = 2.5 $\rightarrow$ 5
Routine Recovery Analytes in GC = 4 $\rightarrow$ 5
Acceptable Limits for Routine Recovery

Mean Recovery ± 2 x RSD
(calculated from results of different matrices for each commodity group)

but

a generalized range of **60-140 %** may be used

---

## Acceptable Limits for Routine Recovery

(mean recovery ± 2xRSD)

This Table was not included in the final version of the Document!

<table>
<thead>
<tr>
<th>RSD*</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
<th>110%</th>
<th>120%</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>63 - 77</td>
<td>72 - 88</td>
<td>81 - 99</td>
<td>90 - 110</td>
<td>99 - 121</td>
<td>108 - 132</td>
</tr>
<tr>
<td>10%</td>
<td>56 - 84</td>
<td>64 - 96</td>
<td>72 - 108</td>
<td>80 - 120</td>
<td>88 - 132</td>
<td>96 - 144</td>
</tr>
<tr>
<td>15%</td>
<td>49 - 91</td>
<td>56 - 104</td>
<td>63 - 117</td>
<td>70 - 130</td>
<td>77 - 143</td>
<td>84 - 156</td>
</tr>
<tr>
<td>20%</td>
<td>42 - 98</td>
<td>48 - 112</td>
<td>54 - 126</td>
<td>60 - 140</td>
<td>66 - 154</td>
<td>72 - 168</td>
</tr>
</tbody>
</table>

* From on-going validation of year before (if not available: from initial validation)
Confirmation of results
Requirements for Chromatography

75. ... the relative retention time of the analyte should correspond to that of the calibration solution with a tolerance of ±0.5% for GC and ±2.5% for LC.

Confirmation of results
Requirements for Mass Spectrometry (MS)

Table 4. Identification requirements for different types of mass spectrometers

<table>
<thead>
<tr>
<th>MS mode:</th>
<th>Single MS (standard mass resolution)</th>
<th>Single MS (high resolution/high mass accuracy)</th>
<th>MS/MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical systems (examples)</td>
<td>quadrupole, ion trap, time-of-flight (TOF)</td>
<td>TOF, Orbitrap, FTMS, magnetic sector</td>
<td>Triple quadrupole ion trap, hybrid MS (e.g., Q-TOF, Q-Trap)</td>
</tr>
<tr>
<td>Acquisition:</td>
<td>Full scan, limited m/z range, selected ion monitoring (SIM)</td>
<td>Full scan, limited m/z range, selected ion monitoring (SIM)</td>
<td>Selected/multiple reaction monitoring (SRM), full scan product ion spectra</td>
</tr>
<tr>
<td>Requirements for identification:</td>
<td>≥ 3 diagnostic ions, (preferably including quasi molecular ion)</td>
<td>≥ 2 diagnostic ions, (preferably including quasi molecular ion) \ Mass accuracy &lt; 5 ppm, At least one fragment ion</td>
<td>≥ 2 product ions</td>
</tr>
<tr>
<td>% Ion ratio(s):</td>
<td>according to Table 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Confirmation of results
Requirements for Mass Spectrometry (MS)

Table 5. Default recommended maximum permitted tolerances for relative ion intensities using a range of spectrometric techniques.

<table>
<thead>
<tr>
<th>Relative intensity (% of base peak)</th>
<th>Ei-GC-MS (relative)</th>
<th>CI-GC-MS, GC-MS*, LC-MS, LC-MS* (relative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 %</td>
<td>± 10 %</td>
<td>± 20 %</td>
</tr>
<tr>
<td>&gt; 20 % to 50 %</td>
<td>± 15 %</td>
<td>± 25 %</td>
</tr>
<tr>
<td>&gt; 10 % to 20 %</td>
<td>± 20 %</td>
<td>± 30 %</td>
</tr>
<tr>
<td>≤ 10 %</td>
<td>± 50 %</td>
<td>± 50 %</td>
</tr>
</tbody>
</table>

Using matrix-matched calibration standards at comparable concentrations

Reporting of results
Interpretation of results for enforcement purposes

91. Considering the results obtained to date from EU proficiency tests, a default expanded uncertainty figure of 50% (corresponding to a 95% confidence level and a coverage factor of 2), in general covers the inter-laboratory variability between the European laboratories and is recommended to be used by regulatory authorities in cases of enforcement decisions (MRL-exceedances).
If required, the result should be reported together with the expanded uncertainty (U), as follows: Result = x ± U (units), with x representing the measured value. In case of official food control by regulatory authorities, compliance with the MRL has to be checked by assuming that the MRL is exceeded if the measured value exceed the MRL by more than the expanded uncertainty (x – U > MRL).

With this decision rule, the value of the measurand is above the MRL with at least 97.5% confidence.
With this SANCO/12495/2011 “Decision Rule”, a result (X) will be violative when $X > 2 \text{MRL}$ (assuming an expanded uncertainty of 50%).

**Results without Uncertainty**

- MRL = 1.00 mg/kg
- No violative
- 2.01 mg/kg

**Results with Uncertainty (50%)**

- 1.00 mg/kg
- 1.65 mg/kg
- 1.80 mg/kg
- 2.01 mg/kg
- 2.20 mg/kg
- 2.40 mg/kg

Violative

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**EURACHEM / CITAC Guide**

*Use of uncertainty information in compliance assessment*

**First Edition 2007**
We need additional information to take a decision!

Confidence in a CORRECT DECISION!
"Quality" of ("Confidence" on) the Result

0.85 mg/kg (±10%?)
0.85 ± 0.10 mg/kg (±50%?)
0.85 ± 0.30 mg/kg (±95%?)

Value
with precision
with uncertainty K=2

Reported Result

Standard Uncertainty (U_u)

Confidence Level

Figure 1 Assessment of Compliance with an Upper Limit

"DESISSION RULES"

"PROBABILITY OF CORRECT DECISION"
SANCO/12495/2011 DECISION RULE for REJECTION

93. ... the MRL is exceeded if the measured value exceed the MRL by more than the expanded uncertainty \((x - U > MRL)\).

With this DECISION RULE, the Probability of correct REJECTION is: > 97.5%

DECISION FOR CORRECT REJECTION (97.5%)
If \(U = 50\%\) \(\rightarrow\) "Decision Limit" = 2 x MRL

A similar (95% confidence) DECISION RULE for correct ACCEPTANCE (by producers?)

Compliant with an upper limit if the measured value plus the expanded uncertainty \((k = 2, 95\%)\) is below the limit.

With this DECISION RULE, the Probability of correct ACCEPTANCE is > 97.5%

DECISION FOR CORRECT ACCEPTANCE (97.5%)
\(-\) Compliant if \(X + U < MRL\)
Figure 2: Acceptance and Rejection zones for an Upper Limit

**a)**
- High confidence of correct REJECTION (>97.5%)
- Upper limit (MRL)
- U (K = 2; 95%)
- Acceptance zone
- Rejection zone

**b)**
- High confidence of correct ACCEPTANCE (>97.5%)
- U (K = 2; 95%)
- Acceptance zone
- Rejection zone

Authorities and/or Producers must fix the confidence degree of their DECISION before establishing the “DECISION RULE”

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**Appendix C:**
Examples for the estimation of measurement uncertainty

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**Guidelines - Codex Alimentarius**

**CAC/GL 59-2006**
Guidelines on Estimation of Uncertainty of Results

CCPR 43rd Session (Beijing, P.R. China, 4-9 April 2011)

**Amendment 2011**
Introduction of an ANNEX with some examples on practical approaches for the estimation of uncertainty of results in pesticide residue tests (CX/PR.11/43/10)
1. Default-Fixed Value (50% / EU)

2. Concentration-Dependent Formula (HORWITZ)

3. Intra-Laboratory Validation/QC/PTs Data

\[ u' = (u'_{RW}^2 + u'_{bias}^2)^{1/2} \]

- **a**  \( u'_{bias\text{PT}} \)  
  - Root Mean Square of relative PTs bias & \( u'(C_{ref})_{PT} \)

- **b**  \( u'_{bias\text{QC}} \)  
  - Root Mean Square of relative QC bias & \( u'(C_{ref})_{QC} \)

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

Relative intra-laboratory reproducibility SD (QC)
Many thanks for your attention