Volume 3

Annex B

*Insert* Active Ingredient Name

**B.5 Methods of analysis**

**B.5.2 Analytical methods for the determination of residues**

**(all components included in the residue definition proposed)**

[Note 1: For a new use/second entry, the summary of the method that occurs in the residue evaluation (i.e., crop field trial, processing study, feeding study, etc.) will generally be sufficient for a method that has been reviewed, and completion of this template is not necessary.

Note 2: This template assumes that the analytical technique is LC-MS/MS. The contents will need to be changed, as appropriate, to accommodate other techniques. In addition to revisions to address changes in instrumentation and detectors, significant modifications will be necessary in the sections of the template dealing with method specificity. In particular, if the method does not employ a technique which in and of itself confers acceptable residue confirmation (e.g., GC-MS or LC-MS/MS), then a discussion of a separate confirmatory method and/or the results of an interference study will need to be included.]

[Note: In the table below, if a particular row is not applicable for the given regulatory action, do not complete the table for that row. Rather, indicate that the data are not required, that the row reflects a data gap, or indicate that the item was previously evaluated and provide the citation as appropriate.]

| **Table B.5.2-1. Overview of the Analytical Methods for the Determination of [Active Ingredient] Residues.** |
| --- |
| Data Requirement | Matrix | Analytes | Method Type | Limit of Quantitation (ppm) | Reference |
| Enforcement Method- Plant Commodities |  |  | [i.e., LC-MS/MS] | 0.xxOR0.xx all matrices except:0.xx ([matrix], all analytes) | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Data-Gathering Method- Plant Commodities |  |  | [i.e., LC-MS/MS] | 0.xxOR0.xx all matrices except:0.xx ([matrix], all analytes) | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| ILV of Enforcement Method- Plant Commodities |  |  |  |  | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Radiovalidation of Methods - Plant Commodities |  |  | N/A | N/A | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Enforcement Method- Livestock Commodities |  |  | [i.e., LC-MS/MS] | 0.xxOR0.xx all matrices except:0.xx ([matrix], all analytes) | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Data-Gathering Method- Livestock Commodities |  |  | [i.e., LC-MS/MS] | 0.xxOR0.xx all matrices except:0.xx ([matrix], all analytes) | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| ILV of Enforcement Method- Livestock Commodities |  |  |  |  | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Radiovalidation of Methods - Livestock Commodities |  |  | N/A | N/A | Study No. XXMRID xxxxxxxPMRA# xxxxxx |
| Multiresidue Method Testing |  |   | FDA-Pesticide Analytical Methods Multi-Residue testing program |  | Study No. XXMRID xxxxxxxPMRA# xxxxxx |

| **Table B.5.2-2. Chemical Structures of Analytes Addressed by Methods for the Analysis of [Active Ingredient].** |
| --- |
| Method ID | Chemical Name | Chemical Structure |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**B.5.2.1** **Analytical Methods for Plant Matrices (Annex IIA 4.3, Annex IIIA 5.3)**

**B.5.2.1.1** **Post-Registration Method (Enforcement)**

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citations (Probably multiple citations to cover the method, its ILV, and radiovalidation)

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1340 Residue Analytical Method (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 3 – Residue Analytical Method
EU SANCO 825/00/rev. 7 (17/3/04)

OECD Guidance Document on Pesticide Residue Analytical Methods

**GLP Compliance:** [No or Significant] deviations from regulatory requirements were reported which would have an impact on the validity of the study. [If “Significant,” then explain below the deficiencies and their impact on the acceptability of the study]

**Acceptability:** The study [is/is not] considered scientifically acceptable. [If not acceptable, then explain why below]

**Evaluator:** [Name of regulatory person who reviewed the study]

**EXECUTIVE SUMMARY**

Method [Method ID] is being proposed for analysis of [analytes] in/on [crop] commodities for purposes of regulatory enforcement. Residues are extracted from [matrices] using [solvent] and cleaned up by [clean-up method(s)]. Extracted residue levels are determined by LC-MS/MS [or other technique]. The method limit of quantitation (LOQ) is [xx] mg/kg (ppm) for each analyte [revise as necessary if there is more than one LOQ]. The method [is/is not] considered suitable for enforcement purposes.

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Principle of the Method: [Method ID]**

|  |
| --- |
| **Table B.5.2.1.1-1**. **Summary Parameters for the Post-Registration Analytical Method for the Analysis of [Active Ingredient] Residues in [Matrices].** |
| Method ID |  |
| Analyte(s) |  |
| Extraction solvent and technique |  |
| Clean-up strategies |  |
| Instrument and Detector |  |
| Standardization method |  |
| Stability of std solutions |  |
| Retention times |  |

[For methods that have multiple analytes, specify whether the analysis and quantitation is for individual compounds or via a common-moiety approach. Include a discussion of stoichiometric conversion factors, as appropriate, to obtain results in parent-equivalents.]

**II. Specificity**

The LC-MS/MS method is highly selective for both the quantitation and confirmation of [analytes]. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

Analyte 1 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M1+x ISTD) *m/z* xxx/yyy (quantitation)

Analyte 2 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M2+x ISTD) *m/z* xxx/yyy (quantitation)

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards and the confirmation ratios of the analytes in the samples were ±20% of the average confirmation ratios of the standards. The confirmation ratios for each analyte were determined by calculating the ratio of the confirmation transition peak area to the quantitation transition peak area. The confirmation ratios for each analyte in all sample matrices were within ±20% of the average confirmation ratios of the standards, indicating that the method is selective for the determination of [analytes] in [matrices].

[Note: If the method does not employ a technique which in and of itself confers acceptable residue confirmation (e.g., GC-MS or LC-MS/MS), then a discussion of a separate confirmatory method or the results of an interference study should be included here.]

**III. Linearity**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least-squares equation, which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of [xx] standards over the concentration range of [xx-yy] ng/mL demonstrated linearity with coefficients of determination (r2) of at least [0.zz].

**IV. Accuracy (Recovery) and Precision (Repeatability)**

The ability of Method [Method ID] to extract incurred residues was demonstrated by [provide information regarding radiovalidation, either via a radiovalidation study or by comparison with methods used in the metabolism studies].

| **Table B.5.2.1.1-2. Radiovalidation of the Post-Registration Analytical Method for Plant Matrices** |
| --- |
| Matrix | Analyte | Extraction Method | Radioactive Residues (ppm)  | Extraction Efficiency1 (%) |
|  | 1 | Metabolism study |  |  |
| Method ID |  |
| 2 | Metabolism study |  |  |
| Method ID |  |
| 3 | Metabolism study |  |  |
| Method ID |  |

1 Extraction efficiency = (residues determined by residue method ÷ residues determined in metabolism study)\*100.

For each analyte, the method was validated over the concentration range of [xx-yy] mg/kg (ppm) with a limit of quantitation of [xx] ppm. The individual recoveries were within the range of [xx-yy]%. [Discuss recoveries outside 70-120%; e.g., “While there were five recoveries from a total of 120 measurements that were between 65-69%, the mean recoveries were at least 70% with relative standard deviations ≤20%.”] At the [xx]-ppm level (LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%. At the [xx]-ppm level ([yy]X LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%.

Repeatability data were generated from at least [xx] samples fortified at the LOQ and at least [n] samples fortified at [xx]X LOQ for each matrix and analyte. The standard deviations (RSDs) obtained for each fortification level were less than [xx]%. Recovery and repeatability data are presented in Tables B.5.2.1.1-3, below.

| **Table B.5.2.1.1-3. Accuracy and Precision Data for the Validation of [Method ID].** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Validation Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

Analytical Method [Method ID] was [successfully/not successfully] validated by an independent a laboratory and/or personnel unfamiliar with the method. Samples of [matrices] were spiked with [analytes] at levels ranging from [xx] to [yy] ppm. Recovery of analytes from spiked samples ranged from [xx] to [yy]% with a maximum relative standard deviation of [xx]% (Table B.5.2.1.1-4). Contact with the sponsor [was/was not] required and acceptable recoveries were obtained after [x] trials. The validating laboratory recommends the following revisions to the method:

1. Revision 1
2. Revision 2
3. Etc.

| **Table B.5.2.1.1-4. Accuracy and Precision Data for the Independent Laboratory Validation of [Method ID] for Plant Matrices.** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Independent Laboratory Validation Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

**V. Limit of Quantitation**

|  |
| --- |
| **Table B.5.2.1.1-5. Summary of Detection and Quantitation Limits for [Method ID].** |
| Analyte | LOD (ppm)1 | LOQ (ppm)2 |
|  |  |  |
|  |  |  |
|  |  |  |

1 LOD = limit of detection, determined by [explain].

2 LOQ = limit of quantitation, defined as the lowest fortification level where acceptable precision and accuracy data were obtained.

**VI. Conclusions**

Pending revision recommended by the independent validation laboratory, the analytical procedure has [or has not] been successfully validated for [analytes] in terms of specificity, linearity, precision, accuracy, and LOQ. Furthermore, the method is considered acceptable for enforcement purposes in terms of materials, equipment, and analysis time.

**B.5.2.1.2** **Pre-Registration Method (Data-Gathering)**

Note: If the data-gathering method is the same as (or very similar to) the enforcement method, simply note that the enforcement method was used in the residue studies, reference Section B.5.2.1.1, noting any differences, and omit the remainder of Section B.5.2.1.2.

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1340 Residue Analytical Method (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 3 – Residue Analytical Method
EU SANCO 825/00/rev. 7 (17/3/04)

OECD Guidance Document on Pesticide Residue Analytical Methods

**GLP Compliance:** [No or Significant] deviations from regulatory requirements were reported which would have an impact on the validity of the study. [If “Significant,” then explain below the deficiencies and their impact on the acceptability of the study]

**Acceptability:** The study [is/is not] considered scientifically acceptable. [If not acceptable, then explain why below]

**Evaluator:** [Name of regulatory person who reviewed the study]

**EXECUTIVE SUMMARY**

Method [Method ID] was used for analysis of [analytes] in the MOR (magnitude of the residue) studies for [list MOR studies; [list crop(s)] field trials, freezer storage, processing or field accumulation]. Residues are extracted from [matrices] using [solvent] and cleaned up by [clean-up method(s)]. Extracted residue levels are determined by LC-MS/MS [or other technique]. The method limit of quantitation (LOQ) is [xx] mg/kg (ppm) for each analyte [revise as necessary if there is more than one LOQ]. The method [is/is not] considered suitable for pre-registration purposes.

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Principle of the Method: [Method ID]**

|  |
| --- |
| **Table B.5.2.1.2-1. Summary Parameters for the Pre-Registration Analytical Method Used for the Analysis of [Active Ingredient] Residues in [Matrices].** |
| Method ID |  |
| Analyte(s) |  |
| Extraction solvent and technique |  |
| Clean-up strategies |  |
| Instrument and Detector |  |
| Standardization method |  |
| Stability of std solutions |  |
| Retention times |  |

[For methods that have multiple analytes, specify whether the analysis and quantitation is for individual compounds or via a common-moiety approach. Include a discussion of stoichiometric conversion factors, as appropriate, to obtain results in parent equivalents.]

**II. Specificity**

The LC-MS/MS method is highly selective for both the quantitation and confirmation of [analytes]. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

Analyte 1 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M1+x ISTD) *m/z* xxx/yyy (quantitation)

Analyte 2 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M2+x ISTD) *m/z* xxx/yyy (quantitation)

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards and the confirmation ratios of the analytes in the samples were ±20% of the average confirmation ratios of the standards. The confirmation ratios for each analyte were determined by calculating the ratio of the confirmation transition peak area to the quantitation transition peak area. The confirmation ratios for each analyte in all sample matrices were within ±20% of the average confirmation ratios of the standards, indicating that the method is selective for the determination of [analytes] in [matrices].

**III. Linearity**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least-squares equation, which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of [xx] standards over the concentration range of [xx-yy] ng/mL demonstrated linearity with coefficients of determination (r2) of at least [0.zz].

**IV. Accuracy (Recovery) and Precision (Repeatability)**

For each analyte, the method was validated over the concentration range of [xx-yy] mg/kg (ppm) with a limit of quantitation of [xx] ppm. The individual recoveries were within the range of [xx-yy]%. [Discuss recoveries outside 70-120%; e.g., “While there were five recoveries from a total of 120 measurements that were between 65-69%, the mean recoveries were at least 70% with relative standard deviations ≤20%.”] At the [xx]-ppm level (LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%. At the [xx]-ppm level ([yy]X LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%.

Repeatability data were generated from at least [xx] samples fortified at the LOQ and at least [n] samples fortified at [xx]X LOQ for each matrix and analyte. The standard deviations (RSDs) obtained for each fortification level were less than [xx]%. Recovery and repeatability data are presented in Tables B.5.2.1.2-2, below.

| **Table B.5.2.1.2-2. Accuracy and Precision Data for Method [Method ID].** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Concurrent Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

**V. Limit of Quantitation**

|  |
| --- |
| **Table B.5.2.1.2-3. Summary of Detection and Quantitation Limits for [Method ID].** |
| Analyte | LOD (ppm)1 | LOQ (ppm)2 |
|  |  |  |
|  |  |  |
|  |  |  |

1 LOD = limit of detection, determined by [explain].

2 LOQ = limit of quantitation, defined as the lowest fortification level where acceptable precision and accuracy data were obtained.

**VI. Conclusions**

The analytical procedure used in the MOR studies (specify which MOR study) has [or has not] been successfully validated for [analytes] in terms of specificity, linearity, precision, accuracy, and LOQ.

**B.5.2.2** **Analytical Methods for Foodstuff of Animal Origin (Livestock Matrices; Annex IIA 4.3, Annex IIIA 5.3)**

**B.5.2.2.1** **Post-Registration Method (Enforcement)**

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citation (Probably multiple citations to cover the method, its ILV, and radiovalidation)

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1340 Residue Analytical Method (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 3 – Residue Analytical Method
EU SANCO 825/00/rev. 7 (17/3/04)

OECD Guidance Document on Pesticide Residue Analytical Methods

**GLP Compliance:** [No or Significant] deviations from regulatory requirements were reported which would have an impact on the validity of the study. [If “Significant,” then explain below the deficiencies and their impact on the acceptability of the study]

**Acceptability:** The study [is/is not] considered scientifically acceptable. [If not acceptable, then explain why below]

**Evaluator:** [Name of regulatory person who reviewed the study]

**EXECUTIVE SUMMARY**

Method [Method ID] is being proposed for analysis of [analytes] in/on [livestock] commodities for purposes of regulatory enforcement. Residues are extracted from [matrices] using [solvent] and cleaned up by [clean-up method(s)]. Extracted residue levels are determined by LC-MS/MS [or other technique]. The method limit of quantitation (LOQ) is [xx] mg/kg (ppm) for each analyte [revise as necessary if there is more than one LOQ]. The method [is/is not] considered suitable for enforcement purposes.

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Principle of the Method: [Method ID]**

|  |
| --- |
| **Table B.5.2.2.1-1**. **Summary Parameters for the Post-Registration Analytical Method for the Analysis of [Active Ingredient] Residues in [Matrices].** |
| Method ID |  |
| Analyte(s) |  |
| Extraction solvent and technique |  |
| Clean-up strategies |  |
| Instrument and Detector |  |
| Standardization method |  |
| Stability of std solutions |  |
| Retention times |  |

[For methods that have multiple analytes, specify whether the analysis and quantitation is for individual compounds or via a common-moiety approach. Include a discussion of stoichiometric conversion factors, as appropriate, to obtain results in parent equivalents.]

**II. Specificity**

The LC-MS/MS method is highly selective for both the quantitation and confirmation of [analytes]. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

Analyte 1 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M1+x ISTD) *m/z* xxx/yyy (quantitation)

Analyte 2 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M2+x ISTD) *m/z* xxx/yyy (quantitation)

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards and the confirmation ratios of the analytes in the samples were ±20% of the average confirmation ratios of the standards. The confirmation ratios for each analyte were determined by calculating the ratio of the confirmation transition peak area to the quantitation transition peak area. The confirmation ratios for each analyte in all sample matrices were within ±20% of the average confirmation ratios of the standards, indicating that the method is selective for the determination of [analytes] in [matrices].

[Note: If the method does not employ a technique which in and of itself confers acceptable residue confirmation (e.g., GC-MS or LC-MS/MS), then a discussion of a separate confirmatory method or the results of an interference study should be included here.]

**III. Linearity**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least-squares equation, which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of [xx] standards over the concentration range of [xx-yy] ng/mL demonstrated linearity with coefficients of determination (r2) of at least [0.zz].

**IV. Accuracy (Recovery) and Precision (Repeatability)**

The ability of Method [Method ID] to extract incurred residues was demonstrated by [provide information regarding radiovalidation, either via a radiovalidation study or by comparison with methods used in the metabolism studies].

| **Table B.5.2.2.1-2. Radiovalidation of the Post-Registration Analytical Method for Livestock Matrices.** |
| --- |
| Matrix | Analyte | Extraction Method | Radioactive Residues (ppm)  | Extraction Efficiency1 (%) |
|  | 1 | Metabolism study |  |  |
| Method ID |  |
| 2 | Metabolism study |  |  |
| Method ID |  |
| 3 | Metabolism study |  |  |
| Method ID |  |

1 Extraction efficiency = (residues determined by residue method ÷ residues determined in metabolism study)\*100.

For each analyte, the method was validated over the concentration range of [xx-yy] mg/kg (ppm) with a limit of quantitation of [xx] ppm. The individual recoveries were within the range of [xx-yy]%. [Discuss recoveries outside 70-120%; e.g., “While there were five recoveries from a total of 120 measurements that were between 65-69%, the mean recoveries were at least 70% with relative standard deviations ≤20%.”] At the [xx]-ppm level (LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%. At the [xx]-ppm level ([yy]X LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%.

Repeatability data were generated from at least [xx] samples fortified at the LOQ and at least [n] samples fortified at [xx]X LOQ for each matrix and analyte. The standard deviations (RSDs) obtained for each fortification level were less than [xx]%. Recovery and repeatability data are presented in Tables B.5.2.2.1-3, below.

| **Table B.5.2.2.1-3. Accuracy and Precision Data for the Validation of [Method ID].** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Validation Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

Analytical Method [Method ID] was [successfully/not successfully] validated by an independent a laboratory and/or personnel unfamiliar with the method. Samples of [matrices] were spiked with [analytes] at levels ranging from [xx] to [yy] ppm. Recovery of analytes from spiked samples ranged from [xx] to [yy]% with a maximum relative standard deviation of [xx]% (Table B.5.2.2.1-4). Contact with the sponsor [was/was not] required and acceptable recoveries were obtained after [x] trials. The validating laboratory recommends the following revisions to the method:

1. Revision 1
2. Revision 2
3. Etc.

| **Table B.5.2.2.1-4. Accuracy and Precision Data for the Independent Laboratory Validation of [Method ID] for Livestock Matrices.** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Independent Laboratory Validation Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

**V. Limit of Quantitation**

|  |
| --- |
| **Table B.5.2.2.1-05. Summary of Detection and Quantitation Limits for [Method ID].** |
| Analyte | LOD (ppm)1 | LOQ (ppm)2 |
|  |  |  |
|  |  |  |
|  |  |  |

1 LOD = limit of detection, determined by [explain].

2 LOQ = limit of quantitation, defined as the lowest fortification level where acceptable precision and accuracy data were obtained.

**VI. Conclusions**

Pending revision recommended by the independent validation laboratory, the analytical procedure has [or has not] been successfully validated for [analytes] in terms of specificity, linearity, precision, accuracy, and LOQ. Furthermore, the method [is/is not] considered acceptable for enforcement purposes in terms of materials, equipment, and analysis time.

**B.5.2.2.2** **Pre-Registration Method (Data Gathering)**

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1340 Residue Analytical Method (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 3 – Residue Analytical Method
EU SANCO 825/00/rev. 7 (17/3/04)

OECD Guidance Document on Pesticide Residue Analytical Methods

**GLP Compliance:** [No or Significant] deviations from regulatory requirements were reported which would have an impact on the validity of the study. [If “Significant,” then explain below the deficiencies and their impact on the acceptability of the study]

**Acceptability:** The study [is/is not] considered scientifically acceptable. [If not acceptable, then explain why below]

**Evaluator:** [Name of regulatory person who reviewed the study]

**EXECUTIVE SUMMARY**

Note: If the data-gathering method is the same as (or very similar to) the enforcement method, then simply note that the enforcement method was used in the residue studies, reference Section B.5.2.2.1, noting any differences, and omit the remainder of Section B.5.2.2.2.

Method [Method ID] was used for analysis of [analytes] in the MOR (magnitude of the residue) studies for [list MOR studies; [list crop(s)] field trials, freezer storage, processing or field accumulation]. Residues are extracted from [matrices] using [solvent] and cleaned up by [clean-up method(s)]. Extracted residue levels are determined by LC-MS/MS [or other technique]. The method limit of quantitation (LOQ) is [xx] mg/kg (ppm) for each analyte [revise as necessary if there is more than one LOQ]. The method [is/is not] considered suitable for pre-registration purposes.

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Principle of the Method: [Method ID]**

|  |
| --- |
| **Table B.5.2.2.2-1**. **Summary Parameters for the Pre-Registration Analytical Method Used for the Analysis of [Active Ingredient] Residues in [Matrices].** |
| Method ID |  |
| Analyte(s) |  |
| Extraction solvent and technique |  |
| Clean-up strategies |  |
| Instrument and Detector |  |
| Standardization method |  |
| Stability of std solutions |  |
| Retention times |  |

[For methods that have multiple analytes, specify whether the analysis and quantitation is for individual compounds or via a common-moiety approach. Include a discussion of stoichiometric conversion factors, as appropriate, to obtain results in parent equivalents.]

**II. Specificity**

The LC-MS/MS method is highly selective for both the quantitation and confirmation of [analytes]. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

Analyte 1 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M1+x ISTD) *m/z* xxx/yyy (quantitation)

Analyte 2 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M2+x ISTD) *m/z* xxx/yyy (quantitation)

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards and the confirmation ratios of the analytes in the samples were ±20% of the average confirmation ratios of the standards. The confirmation ratios for each analyte were determined by calculating the ratio of the confirmation transition peak area to the quantitation transition peak area. The confirmation ratios for each analyte in all sample matrices were within ±20% of the average confirmation ratios of the standards, indicating that the method is selective for the determination of [analytes] in [matrices].

**III. Linearity**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least-squares equation, which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of [xx] standards over the concentration range of [xx-yy] ng/mL demonstrated linearity with coefficients of determination (r2) of at least [0.zz].

**IV. Accuracy (Recovery) and Precision (Repeatability)**

For each analyte, the method was validated over the concentration range of [xx-yy] mg/kg (ppm) with a limit of quantitation of [xx] ppm. The individual recoveries were within the range of [xx-yy]%. [Discuss recoveries outside 70-120%; e.g., “While there were five recoveries from a total of 120 measurements that were between 65-69%, the mean recoveries were at least 70% with relative standard deviations ≤20%.”] At the [xx]-ppm level (LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%. At the [xx]-ppm level ([yy]X LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%.

Repeatability data were generated from at least [xx] samples fortified at the LOQ and at least [n] samples fortified at [xx]X LOQ for each matrix and analyte. The standard deviations (RSDs) obtained for each fortification level were less than [xx]%. Recovery and repeatability data are presented in Table B.5.2.2.2-2, below.

| **Table B.5.2.2.2-2. Accuracy and Precision Data for Method [Method ID].** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Concurrent Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

**V. Limit of Quantitation**

|  |
| --- |
| **Table B.5.2.2.2-3. Summary of Detection and Quantitation Limits for [Method ID].** |
| Analyte | LOD (ppm)1 | LOQ (ppm)2 |
|  |  |  |
|  |  |  |
|  |  |  |

1 LOD = limit of detection, determined by [explain].

2 LOQ = limit of quantitation, defined as the lowest fortification level where acceptable precision and accuracy data were obtained.

**VI. Conclusions**

The analytical procedure used in the MOR studies (specify which MOR study) has [or has not] been successfully validated for [analytes] in terms of specificity, linearity, precision, accuracy, and LOQ.

**B.5.2.3. Multiresidue Methods**

Note: If the post-registration method (i.e., enforcement method) is a multiresidue method, omit this section.

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1360 Multiresidue Method (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 4 – Multiresidue Method
EU SANCO 825/00/rev. 7 (17/3/04)

OECD Guidance Document on Pesticide Residue Analytical Methods

**GLP Compliance:** [No or Significant] deviations from regulatory requirements were reported which would have an impact on the validity of the study. [If “Significant,” then explain below the deficiencies and their impact on the acceptability of the study]

**Acceptability:** The study [is/is not] considered scientifically acceptable. [If not acceptable, then explain why below]

**Evaluator:** [Name of regulatory person who reviewed the study]

Note: For an LC-MS/MS-type multiresidue method (e.g., QuEChERS, DFG S-19), use the template immediately below. For FDA multiresidue methods, use the template beginning on Page 24.

**EXECUTIVE SUMMARY**

The performance of the [QuEChERS/DFG S-19/other] multiresidue method was evaluated for the analysis of [analytes]. [Describe rationale for the testing paradigm as well as any modifications to established method protocols.] Following fortification of control samples of [livestock matrix] with [analyte] at concentrations ranging from [xx] to [yy] mg/kg (ppm), samples were aged for [time] under [conditions]. Analysis using the [QuEChERS/DFG S-19/ other] multiresidue method resulted in recoveries ranging from [xx] to [yy]% (mean ± standard deviation = [xx]% ± [yy]%). Based on these recovery values, the [QuEChERS/DFG S-19/ other] multiresidue method [is/is not] considered suitable for the analysis of [analytes].

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Principle of the Method: [Method ID]**

|  |
| --- |
| **Table B.5.2.3-1**. **Summary Parameters for the Multiresidue Analytical Method for the Analysis of [Active Ingredient] Residues in [Matrices].** |
| Method ID |  |
| Analyte(s) |  |
| Extraction solvent and technique |  |
| Clean-up strategies |  |
| Instrument and Detector |  |
| Standardization method |  |
| Stability of std solutions |  |
| Retention times |  |

**II. Specificity**

The LC-MS/MS method is highly selective for both the quantitation and confirmation of [analytes]. Analysis of control samples resulted in no significant signals at the expected retention times of the analytes. Unambiguous identification is ensured by monitoring two MS/MS transitions characteristic of each analyte and one MS/MS transition characteristic of each internal standard as follows:

Analyte 1 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M1+x ISTD) *m/z* xxx/yyy (quantitation)

Analyte 2 *m/z* xxx/yyy (quantitation)
 *m/z* xxx/yyy (confirmation)
(M2+x ISTD) *m/z* xxx/yyy (quantitation)

Confirmation of the presence of the analytes in the recovery samples was indicated when the retention times of the analytes in the samples matched the retention times of the analytes in the calibration standards and the confirmation ratios of the analytes in the samples were ±20% of the average confirmation ratios of the standards. The confirmation ratios for each analyte were determined by calculating the ratio of the confirmation transition peak area to the quantitation transition peak area. The confirmation ratios for each analyte in all sample matrices were within ±20% of the average confirmation ratios of the standards, indicating that the method is selective for the determination of [analytes] in [matrices].

[Note: If the method does not employ a technique which in and of itself confers acceptable residue confirmation (e.g., GC-MS or LC-MS/MS), then a separate confirmatory method (i.e., the post-registration method) should be referenced here.]

**III. Linearity**

For each analyte, the linearity of detector response was evaluated using solvent standard solutions. Calibration curves were calculated by linear regression analysis with 1/x weighting. For the least-squares equation, which describes the detector response as a function of the standard concentration, calibration curves resulting from the injection of a minimum of [xx] standards over the concentration range of [xx-yy] ng/mL demonstrated linearity with coefficients of determination (r2) of at least [0.zz].

**IV. Accuracy (Recovery) and Precision (Repeatability)**

For each analyte, the method was validated over the concentration range of [xx-yy] mg/kg (ppm) with a limit of quantitation of [xx] ppm. The individual recoveries were within the range of [xx-yy]%. [Discuss recoveries outside 70-120%; e.g., “While there were five recoveries from a total of 120 measurements that were between 65-69%, the mean recoveries were at least 70% with relative standard deviations ≤20%.”] At the [xx]-ppm level (LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%. At the [xx]-ppm level ([yy]X LOQ), the mean recoveries were within the range of [xx-yy]%, with relative standard deviations within the range of [xx-yy]%.

Repeatability data were generated from at least [xx] samples fortified at the LOQ and at least [n] samples fortified at [xx]X LOQ for each matrix and analyte. The standard deviations (RSDs) obtained for each fortification level were less than [xx]%. Recovery and repeatability data are presented in Tables B.5.2.3-2, below.

| **Table B.5.2.3-2. Accuracy and Precision Data From the [Method ID] Multiresidue Method.** |
| --- |
| Analyte | Matrix | FortificationLevel (ppm) | Validation Recovery (%) | RSD(%) |
| Individual | Mean | Range |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(quantitation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 1*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 1 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 2 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |
| Analyte 2*m/z* xxx→yyy(confirmation) | Matrix 3 | xx |  |  |  |  |
| yy |  |  |  |  |
| zz |  |  |  |  |

**V. Limit of Quantitation**

|  |
| --- |
| **Table B.5.2.3-3. Summary of Detection and Quantitation Limits for the [Method ID] Multiresidue Method.** |
| Analyte | LOD (ppm)1 | LOQ (ppm)2 |
|  |  |  |
|  |  |  |
|  |  |  |

1 LOD = limit of detection, determined by [explain].

2 LOQ = limit of quantitation, defined as the lowest fortification level where acceptable precision and accuracy data were obtained.

**VI. Conclusions**

The [QuEChERS/DFG S-19/other] multiresidue method [is/is not] considered suitable for the analysis of [analytes]. [If modifications to the method are necessary, reiterate those modifications here.]

For FDA multiresidue methods, delete the template above (Executive Summary and Sections I through VI) and use the template below:

**EXECUTIVE SUMMARY**

The performance of the FDA multiresidue methods was evaluated for the analysis of [analytes]. Analysis of [analyte(s)] was not attempted through FDA Multiresidue Method Protocols [list protocol letters] because [provide rationale (e.g., chem-X does not fluoresce and is not amenable to GC analysis)]. FDA Multiresidue Method Protocols [list protocol letters] were evaluated. Following fortification of control samples of [matrix] with [analyte] at concentrations ranging from [xx] to [yy] mg/kg (ppm), samples were aged for [time] under [conditions]. Analysis using the FDA Multiresidue Method Protocols [list protocols and any modifications (e.g., with florisil)] resulted in recoveries ranging from [xx] to [yy]% (mean ± standard deviation = [xx]% ± [yy]%). Based on these recovery values, the FDA multiresidue method [is/is not] considered suitable for the analysis of [analytes].

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

**COMPLIANCE**

The following deviations from GLP requirements were reported: [list].

[Include this section only if the "Acceptability" prompt above is answered "The study is not considered scientifically acceptable."]

**STUDY DEFICIENCIES**

Under the conditions and parameters used in the study, the data are classified as scientifically unacceptable. [Explain the deficiencies and their impact on the acceptability of the study.] The study [can or cannot] be upgraded by submission of additional information; if “can be,” then list the additional data required.

**I. Materials and Methods**

Analysis of [analyte] by Protocol [Give protocol designation and describe technique and column (e.g., gas chromatography with a DB-25 megabore column)] resulted in [qualitative description] response on the [detector] detector. To determine recovery, control samples of [matrix] were spiked with [analyte] dissolved in [solvent]. The spiked samples were allowed to equilibrate for [time] under [describe conditions] conditions. Residues of [analyte] were extracted by method [Give extraction method designation (e.g., Sec. 302, E4) using (Provide a brief description of the FDA multiresidue extraction methods that were tested, including any clean-up procedures.].

**II. Results and Discussion**

|  |
| --- |
| **TABLE B.5.2.3-1. Results of Multiresidue Methods Testing with [Chemical].** |
| PAM I Protocol | Results | Comments |
| A |  |  |
| B |  |  |
| C |  |  |
| D |  |  |
| E |  |  |
| F |  |  |
| G |  |  |
| H |  |  |

**III. Conclusions**

[State whether or not the multiresidue methods are suitable for the analysis of the analyte(s). Include a statement that the data will be forwarded to the U.S. FDA for further evaluation.]

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