B.7.8 Livestock Feeding Studies

 (Annex IIA 6.4; Annex IIIA 8.4)

B.7.8.1 [Livestock (cattle, poultry, swine, etc.)]

**Document ID:** MRID No.

PMRA No.

Report: Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1480 Meat/Milk/Poultry/Eggs (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 8 – Meat/Milk/Poultry/Eggs
OECD Guideline 505 Residues in Livestock (January 2007)

**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**

[Active ingredient] was administered [method of administration] to [number and breed] of [animal] for [duration] consecutive days. Dosing was made at [list dosing levels in mg/kg feed]. [Report details on depuration study, if applicable.]

Milk/egg samples were collected twice daily [provide details on sampling method]. Animals were sacrificed on Day xx within [xx] hours of last dose. Tissue samples of [liver, kidney, muscle, and fat] were taken from each sacrificed animal. All samples were maintained frozen at the testing facility, during shipping to the laboratory and were stored frozen until analysis. The maximum storage interval for samples between collection and analysis was [xx] days/months. Residues of [active ingredient] have been shown to be stable in [livestock matrices] for up to [xx] days under frozen conditions. Adequate storage stability data are therefore available to support the storage conditions and intervals for samples in the current study.

Samples in the current study were analyzed using Method [Method ID], a [describe method] to determine residues of [list analytes]. Acceptable [method validation and] concurrent recoveries were reported for [matrices] samples at fortification levels of [xx] ppm, thus validating the method. The limit of quantitation (LOQ) was [xx] ppm per analyte for [matrices].

Following a pre-slaughter interval of [xx] hours, individual sample residues ranged from xx ppm to yy ppm [list matrices and residue levels]. [Describe, qualitatively and quantitatively, the relationship between residue levels and dosing levels for the matrices addressed in the study.] Depuration results indicated that residues of [analytes(s)] will [describe depuration results, noting especially matrices where there appears to be little reduction of residues with time.]

[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**

**A. Materials**

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| --- |
| **Table B.7.8.1-1. Nomenclature for [Active Ingredient] and Metabolites of Interest.** |
| **Common name** | (active ingredient) |
| **Identity** | [CAS Chemical Name] |
| **CAS no.** |  |
| **Company experimental name** |  |
| **Other synonyms (if applicable)** |  |
|  |
| **Metabolite X** | (for each analyte) |
| **Identity** | [CAS Chemical Name] |
| **CAS no.** |  |
| **Company experimental name** |  |
| **Other synonyms (if applicable)** |  |

**B. Study Design**

**1. Test Procedure**

**Livestock**

|  |
| --- |
| **Table B.7.8.1-2. Description of Livestock Used in the Feeding Study.** |
| Species | Breed | Age | Weight at Study Initiation (kg) | Health Status | Description of Housing/Holding Area |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Diet**

|  |
| --- |
| **Table B.7.8.1-3. Test Animal Dietary Regime.** |
| Composition of Diet | Feed Consumption (kg/day) | Water | Acclimation Period | Predosing |
|  |  |  |  |  |
|  |  |  |  |  |

**Treatment**

|  |
| --- |
| **Table B.7.8.1-4. Dosing Regime.** |
| Treatment Group | Treatment Type | Level of Administered Dose (mg/day) | Residue Intake in Diet(ppm) | Vehicle | Timing/ Duration |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Sampling**

|  |
| --- |
| **Table B.7.8.1-5. Sample Collection.** |
| Treatment Group | Matrix | Interval From Last Dose to Sacrifice(hours or days) |
|  |  |  |
|  |  |  |

**Sample Handling and Preparation**

[Briefly describe how samples were handled after collection (shipment, storage, etc.) and any preparation that was done prior to extraction.]

**2. Description of Analytical Procedures**

Samples of [matrices] were analyzed for residues of [analyte(s)] using the Analytical Method [ID# and Title]. [Indicate if the method was previously reviewed and/or validated and for what commodities.]

[Reference study summary if method is described in the B.5.2 section of this review, or provide a description similar to that below if it is a different method.]

Briefly, samples were extracted with [solvent system]. Extracts were cleaned up using [SPE column, partitioning, etc.] and a portion of this extract was analyzed for residues of [list analytes] using [describe instrument/detector system]. The LOQ was [xx] ppm for each analyte. [State the LOD if available and how the LOQ and LOD were determined.]

**II. RESULTS AND DISCUSSION**

Method performance was evaluated [during method validation and] by use of concurrent recovery samples by fortifying [matrix] at [xx] and [yy] ppm. [n] samples of [livestock matrix] were fortified at [xx] ppm and individual recoveries ranged from [xx]% to [yy]% with a standard deviation of [xx]%. [n] samples of [livestock matrix] were fortified at [yy] ppm and individual recoveries ranged from [xx]% to [yy]% with a standard deviation of [xx]%. All recoveries were within the acceptable range of 70% to 120%; therefore, the method was considered valid for the analysis of [active ingredient and metabolites] residues in [livestock] matrices (Table B.7.8.1-6). [Note Table B.7.8.1.-6 should only be included if recoveries are consistently outside the acceptable range.] The fortification levels [did/did not] bracket the measured residues.

The detector response was linear (coefficient of determination, r2 > xx) within the range of [concentrations]. Representative chromatograms of control samples, fortified samples and treated samples were provided. The control chromatograms generally have no peaks of interest above the chromatographic background. [The fortified sample chromatograms contained only the analyte of interest, and peaks were symmetrical and well defined.] or [Residues in controls were ≤xx ppm. The reported residue values [were/were not] corrected for apparent residues in controls.] Metabolites were expressed in parent equivalents (if study did not, the reviewer may need to do so).

|  |
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| **Table B.7.8.1-6. Summary of Procedural/Concurrent Recoveries of [Active Ingredient] from [Matrix]1.** |
| Matrix | Fortification Level (ppm) | Recoveries(%) | Mean ± Std. Dev.(%) |
| [Analyte] |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

1 This table should be included only if recoveries are consistently outside the acceptable range.

The livestock commodity samples were stored frozen at [-xx]°C for a maximum of [xx days/months] from collection to analysis (Table B.7.8.1-7). [Table B.7.8.1-7 should only be included if storage stability data are not included in B.7.8.3, if it is included, then just cite location in monograph.]

The available freezer storage stability data indicate that residues of [active ingredient and metabolites (if applicable)] were stable when stored frozen at ≤-20°C in [livestock matrices] for up to [demonstrated period]. [Indicate if the freezer storage stability data were previously reviewed and report the demonstrated storage intervals for each matrix/analyte]; or

Freezer storage stability data were generated concurrently with the livestock feeding study. [Note: A summary table of these results should be inserted here.] Data showed that [active ingredient and metabolites (if applicable)] residues were stable in [matrices] under frozen storage for the duration of the storage period; or

No storage stability studies were conducted for milk matrices or any tissue matrices, as all samples were analyzed within 30 days of collection*.*

|  |
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| **Table B.7.8.1-7. Summary of Storage Conditions1.** |
| Matrix(RAC or Extract) | Storage Temperature(°C) | Actual Storage Duration(days/months) | Interval of Demonstrated Storage Stability[specify matrix if different](days/months) |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

1 Delete this table if storage stability addressed in B.7.8.3.

The results from the feeding study showed that when dosed at xx, yy, zz ppm, residues of [active ingredient and metabolites, if applicable] in [livestock matrices] ranged from [xx] ppm to [yy] ppm.

|  |
| --- |
| **Table B.7.8.1-8. [Whole Milk/Egg] Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].** |
| Animal Identification # | Matrix/Collection Time | Feeding Level (ppm) | Residues1 (ppm) |
| Analyte 1 | Analyte 2 | Analyte 3 | Total2,3(Mean) |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |

1 Expressed as parent equivalents.

2 Total = Parent + Metabolite X [which corresponds to the residue definition for enforcement purposes].

3 Do not include this column if the residue definition for enforcement purposes has not been determined.

|  |
| --- |
| **Table B.7.8.1-9. Tissue Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].** |
| Animal Identification # | Tissue/Collection Time | Feeding Level (ppm) | Residues1 (ppm) |
| Analyte 1 | Analyte 2 | Analyte 3 | Total2,3(Mean) |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |
|  |  |  | Rep 1 | Rep 1 | Rep 1 |  |
| Rep 2 | Rep 2 | Rep 2 |

1 Expressed as parent equivalents.

2 Total = Parent + Metabolite X [which corresponds to the residue definition for enforcement purposes].

3 Do not include this column if the residue definition for enforcement purposes has not been determined.

[Note: When the residue definition (RD) is different for tolerance/enforcement and risk assessment, the residues corresponding to the RD for risk assessment are reported in the dietary exposure assessment (risk assessment) template only.]

[DO NOT include the following table if the RDs are not determined at the time of the primary review. This table will be included only in the overview document (Level D Review) if the RDs are not determined. The statistics are compiled only for the RDs, not for each individual analyte.]

|  |
| --- |
| **Table B.7.8.1-10. Summary of Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].** |
| Matrix | Feeding Level (ppm) | [Specify which residues, e.g. Combined Residues of A and B]Residues1 (ppm) | Maximum Tissue Residue:Feeding Level Ratio2 |
| n | Min. | Max. | Median | Mean | Std. Dev. |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |

1 Expressed as parent equivalents.

2 Referred to as the transfer coefficient (TC) or transfer factor (Tf); to be used in the calculation of residues anticipated at the dietary burden.

**FIGURE B.7.8.1-1. [Active Ingredient] Residues in [Whole Milk/Eggs] as a Function of Time. Residues are Maximum Values for Each Treatment Group.**

[Provide Figure 7.8.1-1 if doing so will facilitate the description and interpretation of the residue profile across time.]

**FIGURE B.7.8.1-2. Linear Regression of Maximum Residues on Feeding Level.**

[Provide Figure B.7.8.1-2 if doing so will facilitate the description and interpretation of the residue profile across feeding level. ]

**Depuration Period**

|  |
| --- |
| **Table B.7.8.1-11. Summary of Residues of [Active ingredient] in [Whole Milk/Eggs] and Tissues of a [Species] From the Depuration Study.** |
| Matrix | Study Day | Animal # | Residues (ppm) |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**FIGURE B.7.8.1-3. Depuration Curve for Residues of [Active ingredient] in [Whole Milk/Eggs].**

[Provide Figure B.7.8.1-3 if doing so will facilitate the description and interpretation of the residue profile across depuration time.]

Feeding [active ingredient] at levels of at least [xx] ppm in the feed resulted in quantifiable residues of [analytes] in [matrices]. Analysis of [milk/eggs] indicates that residues reached a plateau by the [xx]th day of treatment. Ratios of residues in tissue to that in feed [were/were not] relatively consistent across feeding levels. [Discuss linearity of tissue:feed ratios as appropriate for the data]. Residues accumulated to the highest level in [matrix]. [Discuss similarity/difference in residue levels across the matrices.] Following removal of the test substance from the diet, residue levels in the tissue [remained relatively constant/decreased rapidly/decreased slowly] in [matrices].

**III. CONCLUSIONS**

The [livestock] feeding study is considered scientifically [acceptable or unacceptable]. The results of the study show that [describe the feeding level-residue relationship for the various matrices]. Depuration data indicate that the level of [active ingredient] residues in [matrices] [describe behavior] after [active ingredient] is removed from the diet. Adequate storage stability and method performance data are available to support the results of the feeding study.

**REFERENCES**

Cite references for analytical methods and freezer storage stability studies [include the EPA MRID# and PMRA# of both the study and the review (if available)].

B.7.8.2 [Livestock (poultry)]

**Document ID:** MRID No.

PMRA No.

Report: Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1480 Meat/Milk/Poultry/Eggs (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 8 – Meat/Milk/Poultry/Eggs
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**[Repeat previous sections, modify as appropriate.]**

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