B.7.2 Metabolism, Distribution, and Expression of Residues in Livestock

(Annex IIA 6.2; Annex IIIA, 8.2)

### B.7.2.1 Poultry

**Document ID:** MRID No.

 PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1300 Nature of the Residue – Plants, Livestock (August 1996)
PMRA Regulatory Directive Dir98-02 – Residue Chemistry Guidelines, Section 2 -Nature of the Residue - Plants, Livestock
OECD Guideline 503 Metabolism 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**

[14C specify radiolabel]-[active ingredient] (specific activity: xx Bq/mg) was administered to [number] laying hen at an average dose of [xx] mg/kg feed (corresponding to [xx] mg/kg bw/day). The radiolabeled compound was administered [specify route, e.g. orally] by [specify means, e.g. gelatin capsule] [once/twice] daily for [number] consecutive days. Eggs were collected twice a day and the excreta was collected once a day throughout the study period. The animals were sacrificed approximately [xx] hours following the last dose administration and the following tissues were collected for analysis: [list tissues, e.g. liver, fat, muscle, gastrointestinal (GI) tract and its contents].

[Discuss recoveries/accountabilities and routes of elimination of radioactivity; absorption and excretion of the compound; radioactivity in organs of concern (distribution/disposition), especially as it relates to bioaccumulation; extractability; major metabolites; other major factors.]

The majority of the administered dose (AD) was eliminated via excreta (xx% of the AD). An additional yy% of the AD was recovered from the GI tract and zz% of the AD from the cage wash. Throughout the study period, only xx% of the AD was transferred to eggs and less than yy% of the AD was transferred to edible tissues. The highest concentrations of residues were detected in [tissue] (xx ppm).

[Briefly summarize extraction procedures and analytical methods used to identify metabolites.]

Samples were analyzed within [xx] months of sacrifice. Freezer storage stability was investigated. Storage stability of [active ingredient] was demonstrated in [livestock matrices] for up to [xx] days/months in the study. [or [Tissue] samples were analyzed first at yy months of frozen storage, and then at zz months of frozen storage. The metabolite profiles in the chromatograms obtained from the first and second HPLC analysis were similar for [tissue] samples, thus demonstrating the stability of the analytes of interest in livestock commodities for up to zz months of frozen storage.] [Given that samples were stored frozen for less than 6 months, storage stability data are not required.]

[Indicate whether the parent or metabolite(s) was (were) found to be the predominant residue(s) in the various matrices (include ppm equivalents and corresponding %TRR/matrix). Indicate whether any other metabolites were identified and if any were present at concentrations >10% TRR.]

[Summarize the metabolic pathway in poultry.]

The metabolic pathway of [active ingredient] in poultry involves/proceeds via…

[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**

**1. Test Material**

|  |
| --- |
| **Table B.7.2.1-1. [Active Ingredient] Nomenclature.** |
| **Common name** |  |
| **Identity** | [CAS Chemical Name] |
| **CAS no.** |  |
| **Company experimental name** |  |
| **Other synonyms (if applicable)** |  |
| **Lot/Batch #** |  |
| **Radiochemical purity** | a-label: xx% |
| b-label: xx% |
| **Specific activity as received** | a-label: xx mCi/mmol (xx mCi/mg) |
| b-label: xx mCi/mmol (xx mCi/mg) |
| **Specific activity of dose** | a-label: xx mCi/mmol (xx mCi/mg) |
| b-label: xx mCi/mmol (xx mCi/mg) |
| **Position of radiolabels**[Insert structures] |

**2. Animals**

|  |
| --- |
| **Table B.7.2.1-2. General Test Animal Information.** |
| Species | Breed | Age | Weight at Study Initiation(kg) | Health Status | Description of Housing/Holding Area |
| Hen |  |  |  |  |  |
|  |  |  |  |  |  |

**B. STUDY DESIGN**

**Dose Regime**

|  |
| --- |
| **Table B.7.2.1-3. Test Animal Dietary Regime.** |
| Composition of Diet | Feed Consumption (kg/day) | Water | Acclimation Period | Predosing |
|  |  |  |  | Yes or No |
|  |  |  |  |  |

|  |
| --- |
| **Table B.7.2.1-4. Test Animal Dosing Regime.** |
| Treatment Type | Treatment Level(ppm in diet) | Vehicle | Dose(mg ai/kg bw/day) | Timing/Duration |
| Oral |  | capsule, feed, bolus, etc. |  |  |

**Sampling**

|  |
| --- |
| **Table B.7.2.1-5. Sample Collection Information.** |
| Eggs Collected | Excreta and Cage Wash Collected\* | Interval From Last Dose to Sacrifice | Tissues Harvested and Analyzed |
| XXX daily | XXX daily | XXX hours |  |
|  |  |  |  |

\*If available.

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

**Extraction and Analysis**

[If available, then include a flowchart of the extraction and fractionation schemes.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue including solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and other extraction techniques.]

[Briefly describe procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in the presence of heat, etc.)?]

**Identification and Characterization**

[Briefly describe the methods used for identification/characterization of the residues (LSC, TLC, GLC, HPLC, etc.). If applicable, then very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues.]

**II. RESULTS AND DISCUSSION**

**A. Total Radioactive Residues**

**Quantitation**

[Briefly describe methods for determining TRR values.]

|  |
| --- |
| **Table B.7.2.1-6. TRRs in Eggs, Tissue, and Excreta.** |
| Matrix | A-label | B-label |
| % TRR | ppm | % TRR | ppm |
| Excreta |  |  |  |  |
| Muscle |  |  |  |  |
| Fat |  |  |  |  |
| Liver |  |  |  |  |
| Eggs |  |  |  |  |
| GI tract |  |  |  |  |
| Other |  |  |  |  |

TRRs in eggs [did/did not] appear to have reached a plateau at the end of dosing (see Table B.7.2.1-7).

| **Table B.7.2.1-7. TRRs in Eggs as Function of Time.** |
| --- |
| Interval | A-Label | B-Label |
| ppm | % of dose | ppm | % of dose |
| Day 1 | AM |  |  |  |  |
| PM |  |  |  |  |
| Day 2 | AM |  |  |  |  |
| PM |  |  |  |  |
| Day 3 | AM |  |  |  |  |
| PM |  |  |  |  |
| [add rows as necessary] | AM |  |  |  |  |
| PM |  |  |  |  |
| Total |  |  |  |  |

[Note: A graphical plot of the data may be substituted for Table B.7.2.1-7.]

**B. Extraction, Characterization, and Distribution of Residues**

**Extraction and Characterization of Residues in Poultry**

**A label:**

|  |
| --- |
| **Table B.7.2.1-8. Distribution of the Parent and the Metabolites in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Excreta | Fat | Muscle | Liver | Eggs |
| (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Organosoluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Aqueous soluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Etc. (e.g. PES) |  |  |  |  |  |  |  |  |  |  |

**B label:**

|  |
| --- |
| **Table B.7.2.1-9. Distribution of the Parent and the Metabolites in Poultry Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Excreta | Fat | Muscle | Liver | Eggs |
| (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Organosoluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Aqueous soluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Etc. (e.g. PES) |  |  |  |  |  |  |  |  |  |  |

**C. Storage Stability of Residues**

[Discuss whether the petitioner demonstrated that residues are stable during storage.]

|  |
| --- |
| **Table B. 7.2.1-10. Summary of Storage Conditions.** |
| Matrix (RAC or Extract) | Storage Temperature(°C) | Actual Study Duration (days or months) | Interval of Demonstrated Storage Stability[specify crop/matrix if different](days/months) |
|  |  |  |  |
|  |  |  |  |

**D. Identity of Residues in Poultry**

**A label:**

[Briefly summarize the metabolites found in each matrix.]

|  |
| --- |
| **Table B.7.2.1-11. Summary of Characterization and Identification of Radioactive Residues in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.] |
| Compound | Muscle | Fat | Kidney | Liver | Eggs |
| % TRR | ppm | % TRR | ppm | % TRR | ppm | % TRR | ppm | %TRR | ppm |
| [Parent] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 1] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 2] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 3] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 4] |  |  |  |  |  |  |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |  |  |  |  |  |  |
| Total identified |  |  |  |  |  |  |  |  |  |  |
| Total unidentified |  |  |  |  |  |  |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |  |  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |  |  |  |  |  |  |

PES = post-extraction solids.

**B label:**

[Briefly summarize the metabolites found in each matrix. Are there any major differences between labels?]

|  |
| --- |
| **Table B.7.2.1-12. Summary of Characterization and Identification of Radioactive Residues in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.] |
| Compound | Muscle | Fat | Kidney | Liver | Eggs |
| % TRR | ppm | % TRR | ppm | % TRR | ppm | % TRR | ppm | %TRR | ppm |
| [Parent] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 1] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 2] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 3] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 4] |  |  |  |  |  |  |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |  |  |  |  |  |  |
| Total identified |  |  |  |  |  |  |  |  |  |  |
| Total unidentified |  |  |  |  |  |  |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |  |  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |  |  |  |  |  |  |

PES = post-extraction solids.

**E. Proposed Metabolic Pathway**

[Briefly describe the metabolic pathway and reactions (i.e., oxidation, hydrolysis, etc.)]

**Figure B.7.2.1. Proposed Metabolic Profile of [Active ingredient] in Poultry.**

 [Insert metabolic profile]

|  |
| --- |
| **Table B.7.2.1-13. Identification of Compounds from Metabolism Study (both proposed and found).** |
| Common Name/Code[Figure B.7.2.1 ID No.] | Chemical Name | Chemical Structure |
|  |  |  |
|  |  |  |
|  |  |  |

**III. CONCLUSIONS**

The poultry metabolism study is considered scientifically [acceptable or unacceptable]. [Briefly, summarize the results of the submitted poultry metabolism studies such as: routes or pathways, mechanisms involved and extent/degree of metabolism observed, nature, amount, and distribution of the TRRs in the poultry tissues. Conclusion should be very high level.]

**REFERENCES**

[Cite references for other metabolism studies (if applicable). Include the EPA MRID# and PMRA# of both the study and the review (if available).]

### B.7.2.2 Lactating Ruminants (Goat or Cow)

**Document ID:** MRID No.

 PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1300 Nature of the Residue – Plants, Livestock (August 1996)
PMRA Regulatory Directive Dir98-02 – Residue Chemistry Guidelines, Section 2 -Nature of the Residue - Plants, Livestock
OECD Guideline 503 Metabolism 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**

[14C specify radiolabel]-[active ingredient] (specific activity: xx Bq/mg) was administered to one lactating goat at an average dose of [xx] mg/kg feed (corresponding to [xx] mg/kg bw/day). The radiolabeled compound was [specify route, e.g. orally] by [specify means, e.g. gelatin capsule] [once/twice] daily for [number] consecutive days. Milk was collected twice a day and the excreta was collected once a day throughout the study period. The animal was sacrificed approximately [xx] hours following the last dose administration and the following tissues were collected for analysis: [list tissues, e.g. liver, kidney, fat, muscle, gastrointestinal (GI) tract and its contents, and bile].

[Discuss recoveries/accountabilities and routes of elimination of radioactivity; absorption and excretion of the compound; radioactivity in organs of concern (distribution/disposition), especially as it relates to bioaccumulation; extractability; major metabolites; other major factors.]

The majority of the administered dose (AD) was eliminated via urine (xx% of the AD) and feces (xx% of the AD). An additional yy% of the AD was recovered from the GI tract and zz% of the AD from the cage wash. Throughout the study period, only xx% of the AD was transferred to milk and less than yy% of the AD was transferred to edible tissues. The highest concentrations of residues were detected in [tissue] (xx ppm).

[Briefly summarize extraction procedures and analytical methods used to identify metabolites.]

Samples were analyzed within [xx] months of sacrifice. Freezer storage stability was investigated. Storage stability of [active ingredient] was demonstrated in [livestock matrices] for up to [xx] days/months in the study. [or [Tissue] samples were analyzed first at yy months of frozen storage, and then at zz months of frozen storage. The metabolite profiles in the chromatograms obtained from the first and second HPLC analysis were similar for [tissue] samples, thus demonstrating the stability of the analytes of interest in livestock commodities for up to zz months of frozen storage.] [Given that samples were stored frozen for less than 6 months, storage stability data are not required.]

[Indicate whether the parent or metabolite(s) was (were) found to be the predominant residue(s) in the various matrices (include ppm equivalents and corresponding %TRR/matrix). Indicate whether any other metabolites were identified and if any were present at concentrations >10% TRR.]

[Summarize the metabolic pathway in ruminant.]

The metabolic pathway of [active ingredient] in ruminant involves/proceeds via…

[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**

**1. Test Material**

|  |
| --- |
| **Table B.7.2.2-1. [Active Ingredient] Nomenclature.** |
| **Common name** |  |
| **Identity** | [CAS Chemical Name] |
| **CAS no.** |  |
| **Company experimental name** |  |
| **Other synonyms (if applicable)** |  |
| **Lot/Batch #** |  |
| **Radiochemical purity** | a-label: xx% |
| b-label: xx% |
| **Specific activity as received** | a-label: xx mCi/mmol (xx mCi/mg) |
| b-label: xx mCi/mmol (xx mCi/mg) |
| **Specific activity of dose** | a-label: xx mCi/mmol (xx mCi/mg) |
| b-label: xx mCi/mmol (xx mCi/mg) |
| **Position of radiolabels**[Insert structures] |

**2. Animals**

|  |
| --- |
| **Table B.7.2.2-2. General Test Animal Information.** |
| Species | Breed | Age | Weight at Study Initiation(kg) | Health Status | Description of Housing/Holding Area |
| Goat |  |  |  |  |  |
|  |  |  |  |  |  |

**B. STUDY DESIGN**

**Dose Regime**

|  |
| --- |
| **Table B.7.2.2-3. Test Animal Dietary Regime.** |
| Composition of Diet | Feed consumption (kg/day) | Water | Acclimation period | Predosing |
|  |  |  |  | Yes or No |
|  |  |  |  |  |

|  |
| --- |
| **Table B.7.2.2-4. Test Animal Dosing Regime.** |
| Treatment Type | Treatment Level(ppm in diet)1 | Vehicle | Dose(mg ai/kg bw/day) | Timing/Duration |
| Oral |  | capsule, feed, bolus, etc. |  |  |
| Dermal |  |  |  |  |

1 Dietary burden on a dry-weight basis.

**Sampling**

|  |
| --- |
| **Table B.7.2.2-5. Sample Collection Information.** |
| Milk Collected | Urine, Feces, and Cage Wash Collected\* | Interval From Last Dose to Sacrifice | Tissues Harvested and Analyzed |
| XXX daily | XXX daily | XXX hours |  |
|  |  |  |  |

\*If available.

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

**Extraction and Analysis**

[If available, then include a flowchart of the extraction and fractionation schemes.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue including solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and other extraction techniques.]

[Briefly describe procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in the presence of heat, etc.)?]

**Identification and Characterization**

[Briefly describe the methods used for identification/characterization of the residues (LSC, TLC, GLC, HPLC, etc.). If applicable, then very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues.]

**II. RESULTS AND DISCUSSION**

**A. Total Radioactive Residues**

**Quantitation**

[Briefly describe methods for determining TRR values.]

|  |
| --- |
| **Table B.7.2.2-6. TRRs in Milk, Tissue, and Excreta.** |
| Matrix | A-label | B-label |
| % TRR | ppm | % TRR | ppm |
| Urine |  |  |  |  |
| Feces |  |  |  |  |
| Muscle |  |  |  |  |
| Fat |  |  |  |  |
| Kidney |  |  |  |  |
| Liver |  |  |  |  |
| Milk |  |  |  |  |
| GI tract |  |  |  |  |
| Other |  |  |  |  |

TRRs in milk [did/did not] appear to have reached a plateau at the end of dosing (see Table B.7.2.2-7).

| **Table B.7.2.2-7. TRRs in Milk as Function of Time.** |
| --- |
| Interval | A-Label | B-Label |
| ppm | % of dose | ppm | % of dose |
| Day 1 | AM |  |  |  |  |
| PM |  |  |  |  |
| Day 2 | AM |  |  |  |  |
| PM |  |  |  |  |
| Day 3 | AM |  |  |  |  |
| PM |  |  |  |  |
| [add rows as necessary] | AM |  |  |  |  |
| PM |  |  |  |  |
| Total |  |  |  |  |

[Note: A graphical plot of the data may be substituted for Table B.7.2.2-7.]

**B. Extraction, Characterization, and Distribution of Residues**

**Extraction and Characterization of Residues in Ruminant**

**A label:**

|  |
| --- |
| **Table B.7.2.2-8. Distribution of the Parent and the Metabolites in Ruminant Excreta Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Urine | Feces |
| (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Organosoluble |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Aqueous soluble |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |
| Total identified |  |  |  |  |
| Total unidentified |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |

PES = post-extraction solids.

|  |
| --- |
| **Table B.7.2.2-9. Distribution of the Parent and the Metabolites in Ruminant Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Muscle | Fat | Kidney | Liver | Milk |
| (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Organosoluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Aqueous soluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |

**B label:**

|  |
| --- |
| **Table B.7.2.2-10. Distribution of the Parent and the Metabolites in Ruminant Excreta Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Urine | Feces |
| (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Organosoluble |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Aqueous soluble |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |
| Total identified |  |  |  |  |
| Total unidentified |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |

PES = post-extraction solids.

|  |
| --- |
| **Table B.7.2.2-11. Distribution of the Parent and the Metabolites in Ruminant Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Metabolite Fraction | Muscle | Fat | Kidney | Liver | Milk |
| (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) | (TRR = xx ppm) |
| %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm | %TRR | ppm |
| Surface wash |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Organosoluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |
| Aqueous soluble |  |  |  |  |  |  |  |  |  |  |
|  [Add a row for each identified compound] |  |  |  |  |  |  |  |  |  |  |
|  [Unidentified compound] |  |  |  |  |  |  |  |  |  |  |

**C. Storage Stability of Residues**

[Discuss whether the petitioner demonstrated that residues are stable during storage.]

|  |
| --- |
| **Table B.7.2.2-12. Summary of Storage Conditions.** |
| Matrix(RAC or Extract) | Storage Temperature(°C) | Actual Study Duration (days or months) | Interval of Demonstrated Storage Stability [specify crop/matrix if different](days or months) |
|  |  |  |  |
|  |  |  |  |

**D. Identity of Residues in Ruminant**

**A label:**

[Briefly summarize the metabolites found in each matrix.]

|  |
| --- |
| **Table B.7.2.2-13. Summary of Characterization and Identification of Radioactive Residues in Ruminant Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Compound | Muscle | Fat | Kidney | Liver | Milk |
| % TRR | ppm | % TRR | ppm | % TRR | ppm | % TRR | ppm | %TRR | ppm |
| [Parent] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 1] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 2] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 3] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 4] |  |  |  |  |  |  |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |  |  |  |  |  |  |
| Total identified |  |  |  |  |  |  |  |  |  |  |
| Total unidentified |  |  |  |  |  |  |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |  |  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |  |  |  |  |  |  |

PES = post-extraction solids.

**B label:**

[Briefly summarize the metabolites found in each matrix. Are there any major differences between labels?]

|  |
| --- |
| **Table B.7.2.2-14. Summary of Characterization and Identification of Radioactive Residues in Ruminant Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose].** [Note: Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.] |
| Compound | Muscle | Fat | Kidney | Liver | Milk |
| % TRR | ppm | % TRR | ppm | % TRR | ppm | % TRR | ppm | %TRR | ppm |
| [Parent] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 1] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 2] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 3] |  |  |  |  |  |  |  |  |  |  |
| [Metabolite 4] |  |  |  |  |  |  |  |  |  |  |
| Total extractable(Aqueous + organic) |  |  |  |  |  |  |  |  |  |  |
| Total identified |  |  |  |  |  |  |  |  |  |  |
| Total unidentified |  |  |  |  |  |  |  |  |  |  |
| Total bound residues (PES)  |  |  |  |  |  |  |  |  |  |  |
| % AccountabilityTotal (ppm)/TRR (ppm) \* 100 |  |  |  |  |  |  |  |  |  |  |

PES = post-extraction solids.

**E. Proposed Metabolic Pathway**

[Briefly describe the metabolic pathway and reactions (i.e., oxidation, hydrolysis, etc.).]

**Figure B.7.2.2. Proposed Metabolic Profile of [Active ingredient] in Ruminant.**

 [Insert metabolic profile]

|  |
| --- |
| **Table B.7.2.2-15. Identification of Compounds from Metabolism Study (both proposed and found).** |
| Common Name/Code[Figure B.7.2.2 ID No.] | Chemical Name | Chemical Structure |
|  |  |  |
|  |  |  |
|  |  |  |

**III. CONCLUSIONS**

The ruminant metabolism study is considered scientifically [acceptable or unacceptable]. [Briefly, summarize the results of the submitted ruminant metabolism studies such as: routes or pathways, mechanisms involved and extent/degree of metabolism observed, nature, amount, and distribution of the TRRs in the ruminant tissues. Conclusion should be very high level.]

**REFERENCES**

[Cite references for other metabolism studies (if applicable). Include the EPA MRID# and PMRA# of both the study and the review (if available).]

### B.7.2.3 Other Species (e.g., Fish, Molluscs, Crayfish, Swine)

**Document ID:** MRID No.

 PMRA No.

**Report:** Report Citation

**Guidelines:** EPA OCSPP Harmonized Test Guideline 860.1300 Nature of the Residue – Plants, Livestock (August 1996)
PMRA Regulatory Directive Dir98-02 – Residue Chemistry Guidelines, Section 2 -Nature of the Residue - Plants, Livestock
OECD Guideline 503 Metabolism 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]

**[Repeat previous sections, modify as appropriate.]**

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