## B.7.9 Residues in Succeeding Crops

## (Annex IIA 6.6; Annex IIIA 8.6)

B.7.9.1 Metabolism and Distribution Studies on Representative Crops (Confined Accumulation in Rotational Crops)

**Document ID:** MRID No.

PMRA No.

**Report:** Report Citation

**Guidelines:** U.S. EPA Residue Chemistry Test Guideline OCSPP 860.1850 Confined Accumulation in Rotational Crops (August 1996)  
PMRA Regulatory Directive Dir98-02 – Residue Chemistry Guidelines, Section 13 - Confined Accumulation in Rotational Crops  
OECD Guideline 502 Metabolism in Rotational Crops (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**

The metabolism of [active ingredient] was investigated in rotational crops following application with [14C specify radiolabel]-[active ingredient] formulated as [specify formulation] to soil (indicate soil type) at an application rate of lb ai/A (kg ai/ha). Include details of testing environment (i.e., outdoor test plots, greenhouse, etc.). [Rotational crops] were planted at various plant-back intervals (PBIs): [specify intervals].

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

[Crop] samples were stored frozen for a maximum of [xx] days/months between collection and analysis. Storage stability of [active ingredient] was demonstrated in [crop] for up to [xx] days/months in the study. [or Given that samples were stored frozen for less than 6 months, storage stability data are not required.]

[Briefly summarize radioactivity in plant parts (absorption/distribution/disposition), extractability, and recoveries/accountabilities.]

[Describe the predominant residue(s) in soil (if reported). Indicate whether the parent or metabolite(s) was (were) found to be the predominant residue(s) (include ppm equivalents and corresponding % TRR/crop matrix). Indicate whether any other metabolites were identified and if any were present at concentrations >0.1 ppm and/or >10% TRR. Indicate at which PBI the maximum residues occurred.]

[Summarize the metabolic pathway.]

The metabolic pathway of [active ingredient] in [rotational crops] 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.7.9.1-1. [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 the formulated test substance** | a-label: xx mCi/mmol (xx mCi/mg) |
| b-label: xx mCi/mmol (xx mCi/mg) |
| **Position of radiolabels**  [Insert structures] | |

**2. Test Crops**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table B.7.9.1-2. Crop Information.** | | | | |
| Crop/Crop Group | Variety | PBIs  (days) | Growth Stage at Harvest | Harvested  Commodities |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

**3. Soil Type**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-3. Soil Physicochemical Properties.** | | | | | | | |
| Soil Type | pH | OM % | Sand % | Silt % | Clay % | Moisture Holding Capacity (at 1/3 bar) | CEC  (meg/100 g) |
|  |  |  |  |  |  |  |  |

OM = organic matter, CEC = cation-exchange capacity.

**B. STUDY DESIGN**

**Experimental Conditions**

[Briefly describe how the plants were grown (i.e., outdoor, greenhouse, etc.]

|  |  |
| --- | --- |
| **Table B.7.9.1-4. Use Pattern Information.** | |
| Chemical name |  |
| Application method |  |
| Application rate |  |
| Number of applications |  |
| Timing of applications |  |
| PBI (DAT1) |  |

1 DAT = days after treatment.

**Sampling**

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

**Extraction and Analysis**

[If available, 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, very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues as in lignin, cellulose, protein solubilization methodologies.]

**II. RESULTS AND DISCUSSION**

**A. Total Radioactive Residues**

**Quantitation**

[Briefly describe methods for determining TRR values.]

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-5. TRRs in [Matrices].** | | | | | |
| Matrix | PBI  (days) | A-label | | B-label | |
| % TRR | ppm | % TRR | ppm |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

PBI = plant-back interval.

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

**Extraction and Characterization of Residues in [Rotational Crop]**

**A label:**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-6. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Following Application of [A label] Radiolabeled [Active Ingredient] at [Rate].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.9.1-x as needed for each PBI and crop to accommodate additional radiolabel positions.] | | | | | | |
| Metabolite Fraction | Matrix 1 | | Matrix 2 | | Matrix 3 | |
| (TRR = xx ppm) | | (TRR = xx ppm) | | (TRR = xx 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) |  |  |  |  |  |  |

PES = post-extraction solids.

**B label:**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-7. Distribution of the Parent and the Metabolites in Rotational Crop Matrices Following Application of [B label] Radiolabeled [Active Ingredient] at [Rate].** [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.9.1-x as needed for each PBI and crop to accommodate additional radiolabel positions.] | | | | | | |
| Metabolite Fraction | Matrix 1 | | Matrix 2 | | Matrix 3 | |
| (TRR = xx ppm) | | (TRR = xx ppm) | | (TRR = xx 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) |  |  |  |  |  |  |

PES = post-extraction solids.

**C. Storage Stability of Residues**

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table B.7.9.1-8. Summary of Storage Conditions** | | | | |
| Matrix  (RAC or Extract) | PBI (days) | Storage Temperature  (°C) | Actual Storage Duration  (days or months) | Limit of Demonstrated Storage Stability  [specify crop/matrix if different] (days/months) |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

**D. Identity of Residues in [Rotational Crop]**

**A label:**

[Describe the residues in terms of levels, location in the plant (i.e., partitioning into leaves/stems/roots; i.e., is the chemical systemic), and adequacy for elucidating the nature of the residue in rotational crops. Point out the predominant residues.]

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-9. Summary of Characterization and Identification of Radioactive Residues in Rotational Crop Matrices Following Application of [A Label] Radiolabeled [Active Ingredient] at [Rate].** [Note: Create additional Tables B.7.9.1-x for each PBI and crop as needed to accommodate additional radiolabel positions.] | | | | | | | |
| Compound | Matrix 1 | | Matrix 2 | | Matrix 3 | | |
| % 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) |  |  |  |  | |  |  |
| % Accountability  Total (ppm)/TRR (ppm) \* 100 |  |  |  |  | |  |  |

PES = post-extraction solids.

**B label:**

[Describe the residues in terms of levels, location in the plant (i.e., partitioning into leaves/stems/roots; i.e., is the chemical systemic), and adequacy for elucidating the nature of the residue in rotational crops. Point out the predominant residues. Are there any major differences between labels?]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table B.7.9.1-10. Summary of Characterization and Identification of Radioactive Residues in Rotational Crop Matrices Following Application of [B Label] Radiolabeled [Active Ingredient] at [Rate].** [Note: Create additional Tables B.7.9.1-x for each PBI and crop as needed to accommodate additional radiolabel positions.] | | | | | | |
| Compound | Matrix 1 | | Matrix 2 | | Matrix 3 | |
| % 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) |  |  |  |  |  |  |
| % Accountability  Total (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.7.9.1. Proposed Metabolic Profile of [Active Ingredient] in Rotational Crops.**

[Insert metabolic profile]

|  |  |  |
| --- | --- | --- |
| **Table B.7.9.1-11. Identification of Compounds from Metabolism Study (both proposed and found).** | | |
| Common Name/Code  [Figure B.7.9.1 ID No.] | Chemical Name | Chemical Structure |
|  |  |  |
|  |  |  |
|  |  |  |

**III. CONCLUSIONS**

The confined rotational crop study is considered scientifically [acceptable or unacceptable]. [Briefly summarize the results of the submitted confined rotational crop studies such as: routes or pathways, mechanisms involved and extent/degree of metabolism observed, nature, amount, and distribution of the TRRs in the plant tissues and capability of the analytical method to determine the identity of all components. 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).]

Template Version – February 2016