|  |  |  |  |
| --- | --- | --- | --- |
| **Primary Reviewer:** |  |  | **Date:** |
|  | ***[ Name, title, and aff*** | ***iliation]*** |  |
| **Secondary Reviewer:** |  |  | **Date:** |
|  | ***[Name, title, and affi*** | ***liation]*** |  |
| **[FOR JOINT REVIEWS ONLY- *otherwise delete*]** |
| **Approved by:** |  |  | **Date:** |
|  | ***[Name, title, and affi*** | ***liation]*** |  |

**DATA EVALUATION RECORD**

***[*NOTE TO REGISTRANT/APPLICANT: PLEASE DISREGARD *the header, footer, and reviewer information; reviewers’ comments in the conclusion section; and study classification statement. These sections are for EPA, PMRA, and OECD data entry only and will be populated upon Agency review.]***

**STUDY TYPE:** Acute Pulmonary Toxicity and Pathogenicity

#### U.S. EPA OPPTS Guideline: 885.3150

PMRA Data Code: M4.2.3–Acute Pulmonary Infectivity and Toxicity OECD Data Code: IIM 5.3.3

**TEST MATERIAL (PURITY):** *[use name of material tested as referred to in the study and include its*

potency, biological activity or concentration per unit weight or volume (% active ingredient name in parenthesis)] or [insert TGAI and EP names if a waiver request is made]

**SYNONYMS:** *[other names, code names and acronyms]*

**CITATION:** Author(s). *[Year]*. Study Title. Laboratory name and address. Laboratory report number, full study date. Unpublished *[OR if published, list Journal name, vol.:pages]*. MRID No. *[no hyphen],* PMRA *[number if applicable]*.

**SPONSOR:** [Name and address of Study Sponsor - indicate if different from Applicant]

**COMPLIANCE:** Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were *[not]* provided. The study was *[not]* conducted in compliance with GLP [40 CFR § 160]. *[Discuss deviations from regulatory requirements]* This DER does *[not]* contain FIFRA CBI.

**EXECUTIVE SUMMARY:** In an acute pulmonary infectivity and toxicity study (MRID *[number]*), groups of *[age] [strain] [species] [#/sex/group]* were exposed by the intratracheal route to *[formulation, note its potency, biological activity or concentration per unit weight or volume]* in *[name of vehicle, if applicable]* at a dose of *[in units of potency, biological activity or concentration per kg bw or animal]*. Animals were then observed for up to *[#]* days. *[Identify other control groups, if applicable]* The pulmonary LD50 of the test substance is ***[=, > or <] [#]*** *mg****/*** *kg bw****]* (95% C.I. if available)** *[note if limit test]* in *[male, female OR both sexes] [species]. [NOTE: include sex-specific LD50 values if different values].* Based on the results of this study, *[formulation, test material]*

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showed **[NO, LOW, SLIGHT, MODERATE, HIGH] Toxicity** on *[species]* after exposure to a single dose of *[dose level]* mg/kg by the intratracheal route *[include EPA Toxicity Category I, II, III or IV]* and *[insert formulation name] [is or is not]* pathogenic in the *[species].*

[Note if no mortality occurred. Include only major treatment related clinical signs, body weight or necropsy signs including onset and/or duration if any or the following statement: There were no treatment related clinical signs, necropsy findings or changes in body weight. Indicate if a pattern of clearance was achieved and when it was achieved. If applicable, note if there was a NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment.)]

This acute pulmonary infectivity and toxicity study is classified as *[acceptable, unacceptable (why)].* This study was *[not]* conducted in accordance with the guideline recommendations for an acute pulmonary infectivity and toxicity study (OPPTS 885.3150; PMRA: M4.2.; OECD Data Code: IIM 5.3.3) in the *[species]*. *[If it does not satisfy the requirement, concisely list only major deficiencies or refer to deficiency section.]*

## CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]

***Use the following template if a study report (i.e. toxicity test) was submitted. If a request for the use of alternative data is submitted in lieu of a new study, delete study template section and proceed to last section of DER template for alternative data requests)***

# (NOTE: Guidance on populating the DER are reflected as [red italics]- please replace this text with requested data. Guidance on study recommendations/ criteria are found in the respective OSCPP Guideline- Please refer to respective OSCPP Guideline and use both the DER template and guideline for best preparation of data submission. Guideline criteria should be deleted upon completion of the DER template, however, the overall structure of the templates should not be altered and data evaluation elements reflected in black text should not be deleted (i.e. headings, test parameters, tables, results section). Also- note for data elements of the template that are not applicable- insert “not applicable.” For unavailable information- insert “not available” with a brief explanation for the omission of data.)

## MATERIALS AND METHODS

1. **GUIDELINE FOLLOWED:** *[Indicate which guideline was followed most closely in testing.]*

**Deviations from guideline:** [Indicate if there were any deviations from the test procedures and reporting requirements stated in guideline(s).This information is usually stated in the Good Laboratory Practices

(GLP) and Quality Assurance (QA) statements in the introductory section of the study report. State the reasons for such deviations and its overall effect on the validity of the study.]

## MATERIALS:

* 1. **Test Material:** *As named in study*

**Description:** *[e.g. technical, nature, color, stability]*

**Lot/batch #:** [NOTE: Verify that test material is derived from same source (i.e. lot/batch #) of MPCA (TGAI, MP or EP) that was previously characterized and data were acceptable]

## Purity: CAS #:

**Storage conditions:** [Describe how the test sample was stored and comment on the stability of sample under these conditions.]

**Microbiology:** [Verification of concentration/homogeneity as necessary]

## Test Animals:

**Species:**

**Strain:**

**Number of animals/sex:**

**Age at test initiation**: *[Insert age of test organisms (mean and range).]* **Weight at test initiation:** *[Insert weight of test organisms (mean and range).]* **Source:** *[Insert source and/or supplier of test organisms.]*

**Rationale:** [Insert rationale for using this test organism, if different than recommended test species]

## STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

## Experimental Methods and Conditions:

**In life dates**: Start: End:

**Preliminary challenge assay:** *[if applicable, describe the preliminary study and summarize the results.]*

## Acclimation: Housing:

**Diet:** *[describe] ad libitum*

**Water:** *[describe] ad libitum*

**Animal assignment and treatment:** Animals were assigned to the test groups noted in Table 1. *[Briefly describe treatment.] [Following an overnight fast (if applicable)]*, *[species]* were given a single dose of *[test material name]* by the intratracheal route.

## TABLE 1. Doses, mortality/animals treated.

|  |  |  |  |
| --- | --- | --- | --- |
| **Test Group Number *[or Animal No.]*** | **Test Substance** | **Dose Level (mg/kg)** | **Mortality****(# dead/total # of animals tested)** |
| **Male** | **Female** | **Combined** |
| *#* | *[test material name (% active ingredient)* |  | *#/#* | *#/#* | *#/#* |
| *#* | Control*[if positive or negative controls were tested, differentiate as separate rows]* |  | *#/#* | *#/#* | *#/#* |

**Sample preparation:** *[Describe all sample preparation procedures.]*

**Controls:** [if applicable] [List all controls (e.g. heat-killed) and, if applicable, describe how the

|  |  |
| --- | --- |
| *samples were prepared.]* |  |
| **Environmental conditions:** | Temperature Humidity Air changes Photoperiod | *[#]* °C*[#]*%*[#]*/h*[#]*h dark/ *[#]* h light |

**Solvent/vehicle:** [if used] [Describe any solvent or carrier used in dose administration.]

**Microbial enumeration:** *[Describe how the tissues and organs were prepared and assayed for MPCA enumeration.]*

**Sensitivity of detection:** [Indicate if the sensitivity of the microbiological method(s) used to enumerate the MPCA in the various tissues was tested. If so, briefly describe how it was tested and summarize the results.]

## Duration of study:

**Other methods or conditions, if any:**

* 1. **Observations:**

**Clinical observations and body weights:** Cage-side observations for *[general condition, appearance, demeanor, mortality and moribundity]* were made *[frequency]*. Body weights were measured *[frequency]*.

**Feed consumption:** Feed consumption was measured *[frequency]*.

**Necropsy and organ weights:** Interim sacrifices *[#/sex/group]* were performed on days *[#]*. The test animals were *[or were not]* fasted overnight prior to sacrifice. On the day of scheduled sacrifice, animals were *[weighed and anaesthetized using (insert compound name) prior to blood collection/sacrifice by (method)]*. The necropsy included an examination of *[the external surface of the body, all orifices, cranial cavity, external surface of the brain, the thoracic, abdominal and pelvic cavities and the viscera]*.

**Microbial enumeration:** At interim sacrifices, the following tissues were collected from each test animal for organ weight determination and microbial enumeration: *brain, lungs, liver, kidneys, stomach and small intestine (duodenum, jejunum, ileum), caecum, mesenteric lymph nodes, and spleen*.

**Were raw data included?** *[Comment on the acceptability of the raw data provided.]*

## Other observations, if any:

1. **RESULTS**
2. **MORTALITY** is given in Table 1. The pulmonary LD50 of the test substance is ***[=, > or <*** *mg* ***/*** *kg bw*

(C.I. or standard deviation) *(if conducted*)*] [note if limit test]* in *[species].*

1. **CLINICAL OBSERVATIONS:** *[in one or two sentences, state only the prominent clinical signs stressing those believed to be specific for the sample being tested. State the duration of the major clinical signs and state the time when most animals recover. Avoid stressing single animals that persist but mention this phenomenon. Do not state reactions not believed to treatment related. Do not dwell on clinical signs that are most likely due to agonal death. If applicable, note if there was a NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment.)]*
2. **BODY WEIGHT:** *[Indicate if the animals gained or lost weight.]*
3. **FEED CONSUMPTION:** *[Indicate if there were any treatment related effects.]*
4. **NECROPSY:** *[single sentence or two as to whether there were any treatment related effects, do not stress effects due to agonal death.]*
5. **ORGAN WEIGHTS:** *[If applicable]*
6. **MICROBIAL ENUMERATION:** *[Summarize the enumeration data and note if a pattern of clearance was achieved.]*
7. **REPORTED STATISTICS:** *[If applicable]*

## CONCLUSION

1. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions]* Results of the acute pulmonary toxicity and pathogenicity study showed *[no]* mortality after a single dose of *[test substance name]* (containing % *a.i. name*) by the intratracheal route and *[is or is not]* pathogenic in *[species]*. Based on the results of this study, the pulmonary LD50 of *[Formulation]* is greater than # mg /kg in *[species].*
2. **REVIEWER’S COMMENTS:** The reviewer agrees *[does not agree]* with the study author’s conclusion. *[Formulation]* meets the requirements for EPA Toxicity Category *[I, II, III or IV]* for acute pulmonary toxicity. The study was *[not]* conducted in accordance with the guideline recommendations for an acute pulmonary infectivity and toxicity study (OPPTS 885.3150; PMRA: M4.2.; OECD Data Code: IIM 5.3.3) in the *[species].*
3. **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data can be provided to satisfy the deficiency.]*

## CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]

1. **REFERENCES** *[Provide full citations of references that were cited in the study report: methods, SOPs protocols, references to other relevant study reports in the submission or other studies conducted by the applicant.*

### [NOTE: If methods/protocols contain specific methodology that is not reported in detail in study report as requested in DER- include specific literature of method/SOP/protocol attached as an appendix and attached to the study report for the reviewer’s reference and verification of rationale. If no extra references were used, state “No references were cited.”].

***(This section of the DER represent the format for submitting alternative data for satisfying data requirement and supporting scientific rationale to justify the use of alternative data Alternative data include: waiver request(s), published study, and/or mini-literature review.***

***(Formatting instructions: Use cover page (first page of template) and include a brief executive summary of the waiver request/published study/OR mini- literature review (see example below) and its classification. Delete study template and proceed to the following sections)***

***(For a waiver request, otherwise delete)***

1. **WAIVER RATIONALE** *[Summarize the information and/or data presented by the author justifying why the required data element should be waived for the MPCA, TGAI or EP.]*

### [NOTE: All statements used as justification to support the scientific rationale for the waiver rationale should be individually supported by a reference (i.e. studies in the open literature, references to other study reports in the submission and/ or other studies conducted by the registrant/applicant). Include specific details and/or excerpts of relevant data/information from individual references. Supporting data include: background information of MPCA (e.g. previously reported characterization data related to its identity, mode of action, its nature, prevalence and/or interactions in the environment), supporting evidence/rationale for lack of adverse effects and lack (or minimal) environmental exposure to nontarget species, history of safe use, and/or significant similarities to other microbial strains.]

1. **CONCLUSION**
2. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions]*
3. **REVIEWER’S COMMENTS:** *[Note if in agreement with study authors.]*
4. **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data can be provided to satisfy the deficiency.]*

## CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]

1. **REFERENCES** *[List references that were cited in the study report]*

### [NOTE: Depending on the level of relevance- copies of published literature and any other supporting literature that support the use of alternative data/waiver rationale (including other studies reporting similar findings) should be provided as an appendix and attached to the study report for the reviewer’s reference and verification of rationale.]

***(For a published study, otherwise delete)***

1. **PURPOSE** *[Indicate the purpose of the study]*
2. **METHOD** *[Describe the experimental procedure]*
3. **RESULTS** *[Summarize the results using appropriate headers e.g.,* ***A. GENERAL OBSERVATIONS:***

### B. DETECTABLE LEVELS OF MPCA IN TISSUES, ORGANS:]

1. **CONCLUSION**
2. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions]*
3. **REVIEWER’S COMMENTS:** *[Note if in agreement with study authors.]*
4. **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data can be provided to satisfy the deficiency.]*

## CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]

1. **REFERENCES** *[Provide references that were cited in the study report: methods, studies in the open literature, references to other study reports in the submission or other studies conducted by the applicant.].*

### [NOTE: Include a copy of the published study and/or previously conducted unpublished study in the study report as an appendix attached to the study report for the reviewer’s reference and verification of study details. Any additional statements used as justification to support the use of alternative data should be individually cited- including the specific background information, details and/or excerpts of relevant data/information from individual references. Depending on the level of relevance- copies of published literature and any other supporting literature that support the use of a published study or previously conducted study as alternative data (including other studies reporting similar findings) should also be provided in the appendix.]

***(For a mini literature review, otherwise delete)***

**I. REVIEW OF PUBLISHED LITERATURE:** [Summarize the background information and published studies covered in this mini literature review. Grouping related papers for discussion under specific subheadings may be useful.

e.g.,MPCA-based products are widely used in forest management to control forest pests in Canada and the United States ... As noted by Fischer de Waldheim (1803), three approaches have been used to examine the effects of this MPCA on mammals. These include toxicity testing, infectivity testing, and irritation testing.

### ., A. TOXICITY TESTING:

* + 1. ***Article 1:*** *(summarize and report findings)*
		2. ***Article 2:*** *(summarize and report findings)*

### INFECTIVITY TESTING:

* + 1. ***Article 1:*** *(summarize and report findings)*
		2. ***Article 2:*** *(summarize and report findings)*

### IRRITATION TESTING:

|  |  |  |
| --- | --- | --- |
| ***1.*** | ***Article 1:*** | *(summarize and report findings)* |
| ***2*** | ***Article 2:*** | *(summarize and report findings)]* |
| **II.** | **CONCLUSION** |  |
| **A.** | **LITERATURE REVIEW CONCLUSION:***literature results/ findings]* | *[Summarize overall conclusion based on compilation of* |

1. **REVIEWER’S COMMENTS:** *[Note if in agreement with study authors.]*
2. **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data can be provided to satisfy the deficiency.]*

## CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]

**III. REFERENCES** [Provide references that were cited in the study report: methods, studies in the open literature, references to other study reports in the submission or other studies conducted by the applicant.].

### [NOTE: Depending on the level of relevance- copies of published literature, previously conducted unpublished study and any other background literature that support the use of a literature review as alternative data (including other studies reporting similar findings) should be provided as an appendix attached to the study report for the reviewer’s reference and verification of study details.]