|  |  |  |  |
| --- | --- | --- | --- |
| **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 Dermal Irritation |  |
|  | U.S. EPA OCSPP Guideline: | 870.2500 |
|  | PMRA Data Code: | M4.5.2 |
|  | OECD Data Code/Guideline: | IIIM 7.1.4/404 |

**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 Unpublished *[OR if published, list Journal name, vol.:pages]*.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 a primary dermal irritation study, *[young adult] [strain] [species - rats or rabbits] [#/sex]* were dermally exposed to *[volume or weight applied]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* in *[name of vehicle if appropriate]* for *[#]* hours to *[% or amount of body surface area]*. Animals then were observed for *[#]* days. *[Very briefly note type, severity and duration of irritation. Quantification is usually not needed].* The dermal irritation score was calculated as *[#]*, according to the *[cite method]* scoring system. Based on the results of this study, *[formulation]* is *[not]* a dermal

**EPA DER Template Version 2.1 (October 2011)**

irritant *OR [formulation]* is *[minimally, slightly, mild, moderately, severely, extremely]* irritating to the skin based on *[males or females whichever is lower][species] [Include EPA Toxicity Category I, II, III or IV].*

This study is classified as *[acceptable, unacceptable (why)]*. This study was conducted in accordance with the guideline recommendations for an acute dermal irritation study (OCSPP 870.2500; PMRA Data Code: M4.5.2; OECD Data Code: 404) 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.]*

## MATERIALS:

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

**Description:** *[e.g. technical, nature, colour, 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/weight at dosing: Source:**

1. **STUDY DESIGN AND METHODS:**

[Briefly describe the experimental design.]

## Experimental Methods and Conditions:

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

## Acclimation: Housing:

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

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

**Animal assignment and treatment:** Animals *[#/sex]* were given a *[single OR #]* dose of *[formulation]* dermally using *[describe very briefly methods used - shaved, % coverage, duration of exposure, washing if done, type of wrap if used].*

**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 | °C  %  /h |

#### Photoperiod h dark/ h light

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

## 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]*.

**Dermal observations:** Test animals were observed *[frequency]* for *[#]* days following exposure. *[Also give description and reference of irritation scoring method, including formula used for calculations].*

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

## Other observations, if any:

1. **RESULTS**
2. **MORTALITY:** *[Indicate if mortality was observed.]*
3. **DERMAL OBSERVATIONS:** *[Briefly describe irritation patterns if any, including the frequency, duration, type of irritation and scores.]* The dermal irritation score was calculated as *[#]*, according to the *[cite method]* scoring system, which classifies *[formulation]* as *[minimally, slightly, mild, moderately, severely, extremely]* irritating in *[species]. [Include a table if appropriate]*

For example: A summary of the primary skin irritation scores used for the calculation of Primary Dermal Irritation Index (PDII) is presented in Table 1.

## TABLE 1. Summary of Primary Dermal Irritation Scores

|  |  |  |  |
| --- | --- | --- | --- |
| **Time After Patch Removal** | **Mean Irritation Scores**  **(# Incidences of positive effect/animal)** | | **TOTAL**  **PDI Score** |
| **Erythema** | **Edema** |
| 30-60 mins | *# (#/#)* | *# (#/#)* | *#* |
| 24 hrs |  |  |  |
| 48 hrs |  |  |  |
| 72 hrs |  |  |  |
| Day 7 |  |  |  |

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. **REPORTED STATISTICS:** *[if applicable]*

## CONCLUSION

1. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions]* In a acute dermal irritation study, *[species]* were dermally exposed to a *[single OR #]* application of *[dose amount]* of *[formulation, test substance name]* (containing *[#]* % *a.i. name*) on a *[# size of skin site, usually in cm2]* dose site on *[species]*. *[Very briefly note type, severity and duration of irritation.]* The dermal irritation score was calculated as *[#]*, according to the *[cite method]* scoring system, which classifies *[formulation]* as *[minimally, slightly, mild, moderately, severely, extremely]* irritating to the skin in *[males or females whichever is lower] [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 dermal irritation. The study was *[not]* conducted in accordance with the guideline recommendations for an acute dermal irritation study (OCSPP 870.2500; PMRA Data Code: M4.5.2; OECD Data Code: 404) 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.”].

|  |  |
| --- | --- |
| **Appendix I: Description of Skin Reactions** |  |
| Evaluation of Skin Reactions | Score |
| Erythema and eschar formation |  |
| No erythema | 0 |
| Very slight erythema (barely perceptible) | 1 |
| Well-defined erythema | 2 |
| Moderate to severe erythema | 3 |
| Severe erythema (beet redness) to slight | 4 |

#### eschar formation (injuries in depth)

Edema Formation

No edema 0

#### Very slight edema (barely perceptible) 1

#### Slight edema (edges of area well-defined 2

#### by definite raising)

#### Moderate edema (raised approximately 3

#### 1.0 mm)

#### Severe edema (raised more than 1.0 mm 4

beyond the area of exposure)

Note:

IRRITATION SCORE = Erythema Score + Edema Score

from: Draize, J.H., *Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics*, Assoc. Food and Drug Officials of the U.S., Austin, Texas, 1959.

# (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, MP, 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.]*
5. **CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]**
6. **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 Preshaw (1916), three approaches have been used to examine the effects of this MPCA on rabbits. 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.]