|  |  |  |  |
| --- | --- | --- | --- |
| **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 Eye Irritation

#### U.S. EPA OCSPP Guideline: 870.2400 PMRA Data Code: M4.9

OECD Data Code/Guideline: IIIM 7.1.5/405

**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 Unpublished *[OR if published, list Journal name, vol.:pages]*.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 eye irritation study, *[volume or weight applied]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* in *[name of vehicle if appropriate]* was instilled into the conjunctival sac of *[which eye][young adult] [strain] [species - rabbits] [#/sex]* for *[#]* hours. *[Note if eyes were washed]* Animals then were observed for *[#]* days. *[Very briefly note type, severity and duration of irritation. Quantification is usually not needed].* Eye irritation score was calculated as *[#]*, according to the *[cite method]* scoring system. Based on the results of this study, *[formulation]* is *[is not]* an eye irritant *OR*

[formulation] is [minimally, mildly, moderately, severely, extremely irritating] to the eye 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 eye irritation study (OCSPP 870.2400; PMRA Data Code: M4.9; OECD IIIM 7.1.5/405) 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:** [Describe number of animals, which eye, procedure, volume of material instilled, washing of eye, observation frequency and duration of observation. Also give description and reference of irritation scoring method]

**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.]

## 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]*.

**Ocular 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. **OCULAR OBSERVATIONS:** *[Briefly describe irritation patterns if any, including the frequency, duration, type of irritation and scores.]* The eye 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 eye skin irritation scores used for the calculation of the highest mean eye irritation score (represented as the “Maximum Mean Total Score” (MMTS)) for all rabbits using the Kay and Calandra scoring system (Kay and Calandra 1962) is presented in Table 1.

## TABLE 1. Summary of Primary Eye Irritation Scores

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Time Post Instillation** | **Mean Irritation Scores**  **(# Incidences of positive effect/animal)** | | | **TOTAL Mean Score** |
| **Corneal Opacity** | **Iritis** | **Conjunctivitis** |
| 1 hour | *# (#/#)* | *# (#/#)* | *# (#/#)* | *#*\* |
| 24 hours |  |  |  |  |
| 48 hours |  |  |  |  |
| 72 hours |  |  |  |  |

**\*** Represents the MMTS (Maximum Mean Total Score) or the time interval with the highest mean eye irritation score

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.)]

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

## CONCLUSION

1. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions]* In an acute irritation study, a *[single OR #]* application of *[volume or weight applied]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing *[#]* % *a.i. name*) in *[name of vehicle if appropriate]* was instilled into the *[conjunctival sac OR (other type of application area of eye)]* of *[which eye]* in *[species]* for *[#]* hours. *[Very briefly note type, severity and duration of irritation.]* The eye irritation score was calculated as *[#]*, according to the *[cite method]* scoring system, which classifies *[formulation]* as *[minimally, slightly, mild, moderately, severely, extremely]* irritating in the eyes of *[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 eye irritation. The study was *[not]* conducted in accordance with the guideline recommendations for an acute eye irritation study (OCSPP 870.2400; PMRA Data Code: M4.9; OECD IIIM 7.1.5/405) in the *[species].*
3. **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency. If no data can be provided to satisfy the deficiency, indicate impact on the regulatory decision.]*
4. **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 Ocular Reactions**

#### Evaluation of Ocular Reactions Score

Cornea

1. Opacity - degree of density

No opacity 0

Scattered or diffuse area, details of iris clearly visible 1

Easily discernible translucent areas,

details of iris slightly obscured 2

Opalescent areas, no details of iris visible, size of pupil

barely discernable 3

Opaque, iris invisible 4

1. Area of cornea involved

One quarter (or less) but not zero 1

Greater than one quarter, but less than half 2

Greater than half, but less than three quarters 3

Greater than three quarters, up to whole area 4

Iris

Score = A × B × 5

1. Values

Normal 0

Folds above normal, congestion, swelling,

circumcorneal injection (any or all these or combination of any thereof), iris is still reacting to light (sluggish reaction is positive) 1

No reaction to light, hemorrhage, gross destruction

(any or all of these) 2

Score = A × 5 Conjunctivae

* 1. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris Vessels Normal 0

Vessels definitely injected above normal 1

More diffuse, deeper crimson red, individual vessels not easily discernable 2

Diffuse Beefy red 3

* 1. Chemosis
  2. Discharge

No swelling 0

Any swelling above normal 1

Obvious swelling with partial eversion of lids 2

Swelling with lids half closed 3

Swelling with lids about half closed to completely closed 4

No discharge 0

Any amount different from normal 1

Discharge with moistening of the lids and hairs just adjacent to

lids 2

Discharge with moistening of the lids and hairs, and considerable area around the eye 3

Score = (A + B + C) × 2

#### Note: Total irritation score is the sum of all scores obtained for the cornea, iris and conjunctivae.

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.]