|  |  |  |  |
| --- | --- | --- | --- |
| **Primary Reviewer:** |  |  | **Date:** |
|  | ***[Name, title, and affi*** | ***liation]*** |  |
| **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.]***

|  |  |  |
| --- | --- | --- |
| **REQUIREMENT:** | Wild Mammal Testing, Tier I |  |
|  | U.S. EPA OCSPP Guideline: | 885.4150 |
|  | PMRA Data Code: | M9.3–Wild Mammals |
|  | OECD Data Code: | IIM 8.10, IIIM 10.7 |

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

##### *potency, lot no., 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 Unpublished *[OR if published, list Journal name, vol.: pages]*.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:** *[Describe the study and its findings.]*

In a *[#]*-day *[pulmonary, inhalation, oral, dietary or injection]* toxicity and pathogenicity study, *[#]*-day-old *[common name (scientific name)]* were exposed to a *[single OR #] [indicate exposure method]* dose of *[dose amount]* of *[formulation, note its potency, biological activity and/or concentration per unit weight or volume]* (containing % *a.i. name*).*]*

DER Template Version 2.1 (October 2011)

The *[#]*-day LD50 *[or LC50]* of *[formulation, note its potency, biological activity and/or concentration per unit weight or volume]* was *[****=, > or <****] [insert LD50 or LC50 if applicable in mg a.i./kg bw and/or cfu/kg bw]*. The *[#]*- day NOEL of *[test material]* to the *[species]*, based on *[endpoint]* was *[****=, > or <****] [insert NOEL if applicable in mg a.i./kg bw and/or cfu/kg bw]*.

##### *[Describe toxicity or pathogenicity briefly including mortality, behavioral abnormalities, and other clinical signs.* If there was no toxicity, state that there was no test material-related toxicity effect. Describe microbial clearance, if assessed.]

This study is classified as *[acceptable, unacceptable, supplemental].* This study was *[not]* conducted in accordance with the guideline recommendations for a *[pulmonary, inhalation, oral, dietary or injection]* toxicity and pathogenicity study for wild mammal testing (OCSPP 885.4150; PMRA: M9.3and OECD: IIM 8.10, IIIM 10.7) 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. Excerpts of study recommendations/criteria are reflected as blue italicized text from the respective OSCPP Guideline and should be deleted upon completion of the DER template. For best preparation of data submission- refer to respective OSCPP Guideline and use both the DER template and guideline criteria. 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:

**A. GUIDELINE FOLLOWED:** *[Indicate which guideline was followed most closely in testing. Such as:*

##### *U.S. EPA OCSPP 885.4150–Wild Mammal Testing, Tier I1* PMRA 2001-02 Part 9.31

*Environment Canada EPS 1/RM/44 Section 14.21]*

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*1 Guideline designed to test acute oral infectivity and pathogenicity of microbial agents.*

**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.]*

1. **MATERIALS:**
   1. **Test Material:** *[Name of test material as cited in the study report.]*

##### **Description:** *[e.g., Physical-chemical state of the test material.]*

**Lot/Batch #:** *[Insert the test material’s lot or batch number.]*

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

##### **Purity:** *[Insert the test material’s nominal potency and/or concentration per unit weight or* volume.]

**Storage conditions:** *[Indicate how the test material was maintained, i.e., frozen, refrigerated, maintained in the dark, etc., and indicate if the MPCA is stable under these conditions.]*

* 1. **Test Organism:**

**Species (common and scientific names):** *[Insert test species name(s).]*

***U.S. EPA OCSPP 885.4150*** *Testing shall be performed on a mammalian species representative or indicative of those found in areas likely to be* affected by the proposed use pattern. Endangered or threatened animals should not be used.

***PMRA DIR 2001-02*** *Testing should be performed on representative species from the ecozone(s) of intended use that are most likely to be* affected by the use of the MPCA. Tests on rumen function in wild ruminant animals may be required in cases where such effects are considered likely or if effects are reported in domestic animals.

***Environment Canada EPS 1/RM/44*** *Testing should be performed on common laboratory strains of rats or mice (e.g., CD-1 or B6C3F-1 mice,* and Sprague Dawley Wirstar rats). Females should be nulliparous and nonpregnant.

**Age at study initiation:** *[Give age of test animals (mean and range).]*

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.*

***PMRA DIR 2001-02*** *The use of immature animals is recommended.*

***Environment Canada EPS 1/RM/44*** *Young adults. Test animals should be as similar in age as possible.*

## Number of animals/sex:

**Weight at study initiation:** *[Give weight of test animals (mean and range).]*

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.*

***PMRA DIR 2001-02*** *No specific recommendations.*

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***Environment Canada EPS 1/RM/44*** *Test animals should be as similar in weight as possible; weight should not exceed ±20% of the mean weight for each sex.*

## Sex:

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.* ***PMRA DIR 2001-02*** *No specific recommendations.* ***Environment Canada EPS 1/RM/44*** *5/sex.*

##### **Source:** *[Give the source or supplier of the test organisms.]*

***U.S. EPA OCSPP 885.4150*** *Test animals may be reared in pens or captured in the wild, and must be phenotypically indistinguishable from wild* mammals.

***PMRA DIR 2001-02*** *Test animals may be reared in pens or captured in the wild and must be phenotypically indistinguishable from wild* animals.

***Environment Canada EPS 1/RM/44*** *In a given test, all animals must come from one source and be of the same strain..*

##### **Rationale:** *[Insert rationale for using this test organism, if applicable.]*

1. **STUDY DESIGN AND METHODS:**

*[Briefly describe the experimental design.]*

***U.S. EPA OCSPP 885.4150*** *The test material should be administered by gavage or by intranasal instillation at the maximum hazard dose* followed by an observation period that is consistent with avian testing, i.e. 30 days. The method of dosing should reflect the expected exposure route and shall be determined after consultation with the Agency.

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *A single-concentration test is done in at least 10 rodents (5/sex) at the maximum hazard dose or a multi-* concentration test of at least 5 concentrations of the test substance is done in 10 rodents (5/sex) per concentration. The dose is administered once by oral gavage or by inhalation (via intranasal or intratracheal instillation). Rodents are observed for ≥21 days for mortality and clinical or behavioral signs of toxicity or pathogenicity.

## Experimental Methods and Conditions:

**Acclimation:**

#### Period: Conditions: Feeding: Water:

Health *(any mortality observed?)*:

##### *[Were they the same as those reported during the study?]*

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.*

***PMRA DIR 2001-02*** *No specific recommendations.*

***Environment Canada EPS 1/RM/44*** *Acclimation to test chambers and test conditions for ≥7 days before start of test.*

## Housing and construction materials:

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*[Insert details of cage size and construction.]*

***U.S. EPA OCSPP 885.4150*** *No specific size or construction material is recommended due to the wide range of possible test organisms.*

***PMRA 2001-02*** *No specific recommendations.*

***Environment Canada EPS 1/RM/44*** *All-metal cages with a floor area of ≥250 cm2 for singly caged rats, or ≥100 cm2 for singly caged mice.*

## Method of administration:

##### *[Describe the dosing regimen and method of dose administration.]*

***U.S. EPA OCSPP 885.4150*** *The test material should be administered by gavage (acute oral dose) or by intranasal instillation. The method of* dosing should reflect the expected route of exposure and shall be determined after consultation with the Agency.

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, dosing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *The test material should be administered orally (gavage) or by inhalation (via intranasal or intratracheal instillation).*

## Dose levels:

#### Nominal:

Measured: *(from confirmation of dose viability)*

##### *[List doses used, and insert calculation of maximum hazard dose, where applicable.]*

***U.S. EPA OCSPP 885.4150*** *The standards for maximum hazard dosage level, determination of an LD50 or ID50, are found in the avian oral* pathogenicity toxicity test and the avian inhalation pathogenicity test, i.e., for oral, [MPCA] in TGAI × 5 mL/kg bw × weight of animal (kg); for injection, 0.5 mL/kg bw for intravenous and 2 mL/lg bw for intraperitoneal; for inhalation, [MPCA] in TGAI × 0.2 mL/kg bw × weight of animal (kg).

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *Single-concentration test at the maximum hazard dose (MHD; i.e.,108 units, administered as a single* dose), or multi-concentration test using ≥5 doses, one being the maximum hazard dose.

## Dose preparation:

##### *[Briefly describe methods for dose preparation.]*

***U.S. EPA OCSPP 885.4150*** *The method of dosing and the expected exposure route should be determined in consultation with the Agency.* ***U.S. EPA OCSPP 885.4340*** *The actual form of the material to be regarded as the test substance is discussed in OCSPP Guideline: 885.0001- under section (g)(1)(i-vi).* ***From U.S. EPA OCSPP 885.4000 Background for Nontarget Organism Testing of Microbial Pesticide Control Agents*** *Testing the technical grade of the active ingredient (TGAI) applies in all tests except the simulated and actual field testing (OPPTS 885.4900), where the use of the formulated product applies in order to simulate or reproduce actual field use. In some cases the technical grade of the active ingredient and the formulated product may be identical.*

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *Oral doses should be prepared such that the dosing volume should not exceed 20 mL/kg bw. Intranasal* and intratracheal doses should be prepared such that the dosing volume does not exceed 3.0 mL/kg bw.

**Solvent/vehicle:** *[if used]*

##### *[Describe any solvent or carrier used in dose administration.]*

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***U.S. EPA OCSPP 885.4150*** *Test reports shall contain the same information required for the avian oral pathogenicity/toxicity test OCSPP* 885.4050 and the avian inhalation pathogenicity test OCSPP 885.4100, adapted appropriately for mammalian test procedures. Based on these guidelines, water or saline are recommended in avian testing. The vehicle must not alter the absorption, distribution, metabolism or retention of the test substance; does not alter, enhance, reduce the chemical or biological properties of the test substance; does not produce physiological effects and is nontoxic at the level used; and it should be identical to, or closely resemble the vehicle, if any, used in the EP.

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *For oral studies: If the test material is a liquid suspension, the dose may be administered directly by* gavage. If the test material is a solid, the desired quantity of the test material to achieve the test doses should be suspended in water or in gelatin capsules. A solvent other than deionized water should not be used, but in some cases corn oil and carboxymethylcellulose may be used for hydrophobic test materials. For inhalation studies: If the test material is a liquid suspension, the dose may be administered directly by intranasal or intratracheal instillation. If a solvent is required, the use of isotonic saline to dilute the test material is recommended. No other solvent should be used.

## Confirmation of MPCA viability:

##### *[Describe methods used to confirm the concentration and/or viability of the MPCA in the dosing* suspensions.]

***U.S. EPA OCSPP 885.4150*** *The actual form of the material to be regarded as the test substance is discussed in OCSPP 885.0001.* ***From U.S. EPA OCSPP 885.4000 Background for Nontarget Organism Testing of Microbial Pesticide Control Agents*** *The concentration of MPCA in the water or food must be monitored to ensure that the test organisms are exposed to a sufficient MPCA level throughout the test period.*

***PMRA DIR 2001-02*** *Viability or potency of the MPCA in the dosing suspension should be confirmed. No specific methods are recommended.* ***Environment Canada EPS 1/RM/44*** *Analytical techniques permitting, the concentration of the MPCA in the test suspension administered to* each treatment (including controls) should be determined.

## Was feed withheld prior to dosing?

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.* ***PMRA DIR 2001-02*** *No specific recommendations.* ***Environment Canada EPS 1/RM/44*** *None recommended.*

## Positive control / reference material: *[if used]*

##### *[Insert a description of the reference material, with the number of rodents treated and frequency of* testing (if not concurrent).]

***U.S. EPA OCSPP 885.4150*** *Not required.*

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *The inclusion of a positive microbial control is not required and is not recommended for most* applications. In instances where a suitable pathogen is available (i.e., genetically related with known toxic/pathogenic effects), a positive microbial control might be warranted. A positive chemical control is not required.

## Other controls:

##### *[Insert description of each control group included in the test.]*

***U.S. EPA OCSPP 885.4150*** *A negative control group should be performed. An infectivity control group should be treated with the MPCA inactivated in such a way as to retain the structural integrity of the cell.* ***From U.S. EPA OCSPP 885.0001 Overview for Microbial Pest Control Agents*** *All controls shall, to the extent possible, be from the same source, be of the same age, receive the same care, and receive the same*

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*nutrients as the animals or plants receiving the test substance. To prevent bias, a method to assign organisms to treatment and control groups* randomly is required and must be referenced in the report.

***PMRA DIR 2001-02*** *With respect to appropriate Tier I requirements, testing should be performed in accordance with Part M4 Human Health* and Safety Testing requirements. If higher tier testing is required, the testing approach should be similar to that for birds, adapted appropriately for mammalian test methods.

***Environment Canada EPS 1/RM/44*** *Each test must include a negative control. A non-infectious control is strongly recommended. A sterile* filtrate control is optional.

## Number of test organisms per group/treatment:

#### For negative control:

For solvent/vehicle control: For non-infective control: For sterile filtrate control: For treated test organisms:

***U.S. EPA OCSPP 885.4150*** *Test reports shall contain the same information required for the avian oral pathogenicity/toxicity test OCSPP* 885.4050 and the avian inhalation pathogenicity test OCSPP 885.4100, adapted appropriately for mammalian test procedures. Based on these guidelines, the number of animals should be reported.

***PMRA DIR 2001-02*** *A sufficient number of test organisms must be treated to allow for adequate controls, statistical analysis, interpretation of* data and for interim sacrifice, if applicable. The number in each test group will depend on the species to be tested, the expected duration of the study, whether single or multiple groups are to be treated.

***Environment Canada EPS 1/RM/44*** *For a single-concentration test, at least 10 rodents (5/sex) should be treated. For a multi-concentration* test, 10 rodents (5/sex) should be treated per dose level.

## Recovery of MPCA from tissues:

##### *[Describe methods used to recover the MPCA from collected tissues.]*

***U.S. EPA OCSPP 885.4150*** *Test reports shall contain the same information required for the avian oral pathogenicity/toxicity test OCSPP* 885.4050 and the avian inhalation pathogenicity test OCSPP 885.4100, adapted appropriately for mammalian test procedures. Based on these guidelines, attempts should be made using appropriate techniques to re-isolate the MPCA from examined tissues at necropsy.

***PMRA DIR 2001-02*** *Required for MPCAs that are pathogens. Various methods for detection may be employed to detect the MPCA but it* should be appropriate for both the organism (e.g., bacterium) and the mode of action of the MPCA.

***Environment Canada EPS 1/RM/44*** *Analytical techniques permitting, the recovery of the MPCA in selected organs (e.g., heart, brain, kidney,* liver), tissues, or body fluids (e.g., blood or urine) of rodents from each treatment is required at test end. The recovery of the MPCA is optional during the test.

## Feeding:

##### *[Describe the feeding regime used during the experiment.]*

***U.S. EPA OCSPP 885.4150*** *No specific recommendations.*

***PMRA DIR 2001-02*** *No specific recommendations.*

***Environment Canada EPS 1/RM/44*** *Commercial rodent food of a suitable size, fed ad libitum.*

## Test conditions:

#### Temperature:

Ventilation:

Relative humidity:

Lighting:

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#### Photoperiod:

***U.S. EPA OCSPP 885.4150*** *No specific test conditions are recommended due to the wide range of possible test organisms.*

***PMRA DIR 2001-02*** *No specific recommendations.*

***Environment Canada EPS 1/RM/44*** *Daily mean temperature 22 ± 2°C, relative humidity 40 to 70%, lighting may be incandescent or* fluorescent, 500 to 1000 lux, with a photoperiod of 12 ± 1 h light/12 ± 1 h dark (gradual transition from light to dark and dark to light.

## Duration of study:

##### *[Specify the test duration, and comment on any observations that necessitated the extension of the test* period.]

***U.S. EPA OCSPP 885.4150*** *The test duration should be consistent with avian oral and inhalation pathogenicity/toxicity tests, i.e., an* observation period of at least 30 days after dosing initiation. If symptomatology or toxic signs are manifested at the 30th day, observation should continue until recovery, mortality, or unequivocal moribundity is established.

***PMRA DIR 2001-02*** *The duration of the observation period depends on the mode of pesticidal action. In general, a duration of 30 days permits* time for incubation, infection and manifestation of adverse effects in the test organism. For infectivity testing, the study should continue until a pattern of microbial clearance from tissues is shown.

***Environment Canada EPS 1/RM/44*** *The test duration is ≥21 days.*

## Other methods or conditions, if any:

* 1. **Observations:**

**Parameters measured including sublethal effects/toxicity symptoms:**

##### *[List the parameters measured during the experiment, e.g., survival, abnormal behavior or appearance,* temperature, relative humidity, individual body weights, concentration of the MPCA in the dosing suspension. Provide references to data summary tables, if used.]

***U.S. EPA OCSPP 885.4150*** *No specific recommendations. However, test reports should be consistent with avian oral and inhalation* pathogenicity/toxicity tests, i.e., measurements of temperature and relative humidity in the test facility, individual body weights of birds, and concentration of the MPCA in each dosing suspension is required; and observations for signs of intoxication, abnormal behavior and regurgitation, pathogenic symptomatology or pathological changes.

***PMRA DIR 2001-02*** *Regular observations are required to record mortalities and note any behavioral, pathogenic or toxic adverse effects.* ***Environment Canada EPS 1/RM/44*** *Measurement of the temperature and relative humidity in the test facility; individual body weights of* rodents, and concentration of the MPCA in each dosing suspension are required. Daily observations for survival, abnormal behavior (e.g., lethargy, excessive aggression) and appearance (including external lesions) of rodents in each test cage.

## Observation/measurement intervals:

##### *[List time points at which observations or measurements were made.]*

***U.S. EPA OCSPP 885.4150*** *Observation intervals not specified.*

***PMRA DIR 2001-02*** *Regular observation intervals are required to record mortalities and note any behavioral, pathogenic or toxic adverse* effects.

***Environment Canada EPS 1/RM/44*** *Temperature measured daily (min/max) or continuously; relative humidity measured weekly, body weight* measured weekly. Rodents observed daily for survival, behavior and appearance. The concentration of the MPCA in the test suspension should be determined on the day of dosing.

## Testing for infectivity:

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*[Briefly describe how infectivity was tested, and list the organs, tissues or fluids tested, if applicable]*

***U.S. EPA OCSPP 885.4150*** *Test reports should contain the same information required for the avian oral pathogenicity/toxicity test OCSPP* 885.4050 and the avian inhalation pathogenicity test OCSPP 885.4100, adapted appropriately for mammalian test procedures. Based on these guidelines, attempts should be made using appropriate techniques to re-isolate the MPCA from examined tissues at necropsy.

***PMRA DIR 2001-02*** *For MPCAs that are pathogens, pathogenicity testing should be performed. The specific test method used should match the* infectivity requirements of the pathogen and host and should be capable of detecting both infection and disease symptoms. When the MPCA is not a pathogen, applicants can rely on standard toxicity test methods.

***Environment Canada EPS 1/RM/44*** *Infectivity testing is required at test end based on measured concentrations of new microbial substance in* selected organs, tissues and body fluids. Infectivity testing is optional during the test.

## Necropsy:

##### *[Indicate on which groups necropsies were performed, and list observations made at necropsy (gross* lesions, histological examination).]

***U.S. EPA OCSPP 885.4150*** *Test reports should contain the same information required for the avian oral pathogenicity/toxicity test OCSPP* 885.4050 and the avian inhalation pathogenicity test OCSPP 885.4100, adapted appropriately for mammalian test procedures. Based on these guidelines, the study report must provide results of gross necropsies and histopathological findings on all dying animals or enough animals to characterize any gross lesions using appropriate techniques.

***PMRA DIR 2001-02*** *Gross necropsy and histopathological examination should be performed on exposure site tissues and other organs or* tissues showing anatomical or physiological abnormalities in adversely affected test organisms. In cases where tissue preferences are known or suspected, the tissues should be examined whether or not gross anatomical or physiological changes are seen.

***Environment Canada EPS 1/RM/44*** *All rodents dying as well as those surviving at test termination must be necropsied; organs and tissues* must be examined for evidence of lesions and abnormalities. Selected tissues must be collected for future microscopic examination where necessary.

## Were raw data included?

##### *[Comment on the acceptability of the raw data provided.]*

**Other observations, if any:**

1. **RESULTS:**
2. **VIABILITY OF DOSING SUSPENSIONS:** *[Summarize the dose verification data and indicate if the tested sample was still viable.]*

**TABLE *[#]*.** Viability and potency of *[test substance]* in *[dosing suspension/diet]* administered to *[test organism]* over *[#]* days.

|  |  |  |  |
| --- | --- | --- | --- |
| **Dose Group** | **Dosing Day** | **Nominal Dose *[count or potency]***  **(*insert units*)** | **Measured Dose *[count or potency]***  **(*insert units*)** |
| Negative control | 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |

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|  |  |  |  |
| --- | --- | --- | --- |
| **Dose Group** | **Dosing Day** | **Nominal Dose *[count or potency]***  **(*insert units*)** | **Measured Dose *[count or potency]***  **(*insert units*)** |
| *Test dose 1* | 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |
| *Test dose 2* | 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |
| *Test dose n* | 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |

*[Table suitable for microbial infectivity/pathogenicity (maximum hazard dose) testing. Modify as appropriate to accommodate differences in experimental design.]*

1. **MORTALITY:** *[Briefly summarize mortality results (if any). If values for LD50, LC50, LT50, NOEL, NOEC are greater than the MHD level, use* ***<*** *symbol. Comment on dose response relationship; Slope of response, if provided. Compare the mortality with control treatment and/or the reference chemical. Data may be summarized in a table such as those presented below. Modify table to accommodate differences in experimental design.]*

***From U.S. EPA OCSPP 885.0001 Overview for Microbial Pest Control Agents*** *The Agency realizes that it would be very difficult to establish* specific LC50, ED50, or LD50 values (e.g. LD50 = 1,000 mg/kg) and 95 percent confidence limits for most MPCAs whose mechanism of action is pathogenicity, because test data are not likely to exhibit a log-Probit dose-response relationship that is typical of chemical pesticides. Therefore, data that establishes an LC50, ED50, or LD50 that is greater than the maximum hazard dosage level (e.g. LD50 >1,000 mg/kg) would often be adequate for the purposes of hazard assessment and reporting in this section.

**TABLE *[#]***. Effect of *[test substance]* on mortality of *[test organism]* exposed by *[dosing method]* over *[#]*

days.

|  |  |  |  |
| --- | --- | --- | --- |
| **Treatment** | **Cumulative Mortality/Total Number of *[test organism]*** | | |
| **Negative Control** | **Killed *[test substance]* Control** | ***[Test substance]*** |

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Treatment** | | **Cumulative Mortality/Total Number of *[test organism]*** | | |
| **Negative Control** | **Killed *[test substance]* Control** | ***[Test substance]*** |
| Cumulative mortality | *Day 0* |  |  |  |
| *Day x1* |  |  |  |
| *Day x2* |  |  |  |
| *Day n* |  |  |  |
| *LD50 (if applicable)* | |  | | |

*[Table suitable for maximum hazard dose testing. Modify as appropriate to accommodate differences in experimental design.]*

**TABLE *[#]***. Effect of *[test material]* on mortality of *[test organism]* exposed by *[dosing method]* over *[#]*

#### days.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Treatment (mg a.i./kg bw)** | **Total No. of Test Animals** | **Cumulative Mortality** | | | | |
| ***Day 0*** | ***Day x1*** | ***Day x2*** | ***Day x3*** | ***Day n*** |
| Negative control |  |  |  |  |  |  |
| *Test dose 1* |  |  |  |  |  |  |
| *Test dose 2* |  |  |  |  |  |  |
| *Test dose 3* |  |  |  |  |  |  |
| *Test dose n* |  |  |  |  |  |  |
| LD50 |  | | | | | |
| NOEL |  | | | | | |

###### *[Table suitable multiple-dose testing. Modify as appropriate to accommodate differences in experimental design.]*

1. **SUBLETHAL TOXICITY ENDPOINTS:** *[Include if any sublethal effects are observed- Briefly summarize behavioral abnormalities or other signs of toxicity (body weight loss, decreased food consumption, organ effects, etc.). Indicate effects that were related to the test-material. Compare sub- lethal effects with control treatment and/or the reference chemical (if used). Data may be summarized in a table such as those presented below. Modify tables to accommodate differences in experimental design. For acute oral and dietary, provide information about palatability of the treated diet, rate of consumption of diet in treated and untreated groups.]*

**TABLE *[#]*.** Sublethal effect of [test material] on *[test organism]*exposed by *[dosing method]* over *[#]* days.

|  |  |  |  |
| --- | --- | --- | --- |
| **Treatment** | **Observation** | | |
| **Body Weight (g)** | **Food Consumption (g/test animal/day)** | **Other Endpoint** |

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|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | ***Day 0*** | ***Day x1*** | ***Day n*** | ***Day 0*** | ***Day x1*** | ***Day n*** | **(% Affected)** |
| Negative control |  |  |  |  |  |  |  |
| *Test dose 1* |  |  |  |  |  |  |  |
| *Test dose 2* |  |  |  |  |  |  |  |
| *Test dose 3* |  |  |  |  |  |  |  |
| *Test dose n* |  |  |  |  |  |  |  |
| LD50 |  | | | | | | |
| NOEL |  | | | | | | |

###### *[Table suitable multiple-dose testing. Modify as appropriate to accommodate differences in experimental design.]*

**TABLE *[#]*.** Mean body weight and weight gain for control and *[test material]*-treated *[test organism]*

measured *[frequency of weighing]*.

|  |  |  |  |
| --- | --- | --- | --- |
| **Day** | **Body Weight (g)** | | |
| **Negative Control** | **Killed *[test substance]***  **Control** | ***[test substance]*** |
| *Initiation* |  |  |  |
| *Day 7* |  |  |  |
| *Day 14* |  |  |  |
| *Day 21* |  |  |  |
| *Day 28* |  |  |  |
| *Termination* |  |  |  |

###### *[Table suitable for maximum hazard dose testing. Modify as appropriate to accommodate differences in experimental design]*

**TABLE *[#]*.** Mean daily food consumption of control and *[test material]*-treated *[test organism]* measured

*[frequency of measurement]*.

|  |  |  |  |
| --- | --- | --- | --- |
| **Day** | **Food Consumption (g/test animal/day)** | | |
| **Negative Control** | **Killed *[test substance]***  **Control** | ***[test substance]*** |
| *Initiation* |  |  |  |
| *Day 7* |  |  |  |
| *Day 14* |  |  |  |

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|  |  |  |  |
| --- | --- | --- | --- |
| **Day** | **Food Consumption (g/test animal/day)** | | |
| **Negative Control** | **Killed *[test substance]***  **Control** | ***[test substance]*** |
| *Day 21* |  |  |  |
| *Day 28* |  |  |  |
| *Termination* |  |  |  |

*[Table suitable for microbial infectivity/pathogenicity (maximum hazard dose) testing. Modify as appropriate to accommodate differences in experimental design.]*

**TABLE *[#]*.** Body weights and weight gain in control and *[test material]*-treated *[test organism]*.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Body Weight (g)** | | | | | |
| ***Day 0*** | ***Day 7*** | ***Day 14*** | ***Day 21*** | ***Day 30*** | **Total Change** |
| Negative control |  |  |  |  |  |  |
|  |  |  |  |  |  |
| Killed *[test material]* control |  |  |  |  |  |  |
|  |  |  |  |  |  |
| *[Test dose 1]* |  |  |  |  |  |  |
|  |  |  |  |  |  |
| *[Test dose 2]* |  |  |  |  |  |  |
|  |  |  |  |  |  |
| *[Test dose 3]* |  |  |  |  |  |  |
|  |  |  |  |  |  |
| *[Test dose n]* |  |  |  |  |  |  |
|  |  |  |  |  |  |

*[Table suitable for microbial infectivity/pathogenicity (multiple dose) testing. Modify as appropriate to accommodate differences in experimental design or delete if acute toxicity test is used.]*

**TABLE *[#]*.** Microbiological analysis of tissue samples from *[test organism]* challenged by *[dosing method]*

of *[test material]*.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Tissue** | **Negative Control** | **Killed *[test substance]* Control** | ***[test substance]*** | | | |
| ***Dose x1*** | ***Dose x2*** | ***Dose x3*** | ***Dose n*** |
| Blood |  |  |  |  |  |  |

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|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Tissue** | **Negative Control** | **Killed *[test substance]* Control** | ***[test substance]*** | | | |
| ***Dose x1*** | ***Dose x2*** | ***Dose x3*** | ***Dose n*** |
| Brain |  |  |  |  |  |  |
| Lung |  |  |  |  |  |  |
| Liver |  |  |  |  |  |  |
| Spleen |  |  |  |  |  |  |
| Kidney |  |  |  |  |  |  |
| GI tract |  |  |  |  |  |  |
| *[other tissues]* |  |  |  |  |  |  |

###### *[Table suitable for microbial infectivity/pathogenicity (maximum hazard dose) testing. Modify as appropriate to* accommodate differences in experimental design or delete if acute toxicity test is used.]

1. **REPORTED STATISTICS:** *[[If applicable- List the parameters that were analyzed and the statistical tests that were performed.*

***U.S. EPA OCSPP 885.4340*** *LD50 or ID50 in appropriate units with 95% confidence limits, if obtained, methods used, and slope of the dose-* response line, if obtained. From ***U.S. EPA OCSPP 885.0001-*** *Appropriate statistical methods are to be used to summarize experimental data, to* express trends, and to evaluate the significance of differences in data obtained from different test group and methods used shall reflect the current state-of-the art. All data averages or means must be accompanied by standard deviations and the standard errors of the means should also be calculated; however, notations of statistically significant differences accompanied by the confidence level or probability should also be used in place of standard error determinations. Other methods of expressing data dispersion may also be used when appropriate.

***PMRA DIR 2001-02*** *All relevant analyses of results must be provided. NOTE: May attach a copy of the statistical methods from the study with* a statement that the reviewer has no objections to the analyses used.

***Environment Canada EPS 1/RM/44*** *Single concentration test: percent survival and percentage of surviving rodents showing atypical* appearance (necropsy) or behavior at test end, comparing maximum hazard dose to controls; Multiple concentration test: percent survival and percentage of surviving rodents showing atypical appearance (necropsy) or behavior at test end, comparing each test chamber and treatment. Data permitting, calculation of 21-day LD50, 21-day ED50 for atypical appearance and/or behavior, NOED/LOED.

## VERIFICATION OF STATISTICAL RESULTS BY THE REVIEWER:

##### *[If applicable- Report the statistical methods used by the reviewer to verify the applicant’s results; If* values for LD50, LC50, LT50, NOEL, NOEC are greater than the MHD level, use ***<*** *symbol.]*

*Statistical Method:*

|  |  |  |
| --- | --- | --- |
|  | LD50: NOEL: | 95% C.I.: |
| **III.** | Probit Slope:  **CONCLUSION:** | 95% C.I.: |
| **A.** | **REVIEWER’S CONCLUSIONS:** | *[Provide additional comments that do not appear under other* |

*sections of the template. Indicate if the study is acceptable/unacceptable/supplementary. Provide the major conclusions, e.g., values for LD50 (95% confidence interval), NOEL, Probit slope (95% confidence interval), and sublethal effects.]*

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1. **STUDY AUTHOR CONCLUSION:** *[Summarize the study author’s conclusions- Provide the major conclusions e.g., values were [****=, > or <****] LD50 were [****=, > or <****][insert value in appropriate units] (95% confidence interval), NOEL was [****=, > or <****][insert value in appropriate units], Probit slope (95% confidence interval), and sublethal effects.]*
2. **REVIEWER’S COMMENTS:** The reviewer agrees *[does not agree]* with the study author’s conclusion. *[Provide additional comments that do not appear under other sections of the template. Discuss the specific methods/ results/findings that may affect the validity of the study and overall acceptability of the study.]* The study was *[not]* conducted in accordance with the guideline recommendations for a *[contact, oral or dietary]* toxicity and pathogenicity study for wild mammal testing OCSPP 885.4150; PMRA: M9.3and OECD: IIM 8.10, IIIM 10.7) in the *[species]*.

##### **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no* data can be provided to satisfy the deficiency.]

***U.S. EPA OCSPP 885.4150*** *No specific validity criteria.*

***PMRA DIR 2001-02*** *No specific validity criteria.*

***Environment Canada EPS 1/RM/44*** *The test is invalid if <90% survival in negative control at test end.*

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

##### **IV. 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.”].***

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# *(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)***

**EXECUTIVE SUMMARY *[FOR EXAMPLE]:*** *[Applicant]* is submitting a justification for a data waiver wild mammal toxicity and pathogenicity studies (OCSPP 885.4150). The waiver request is based on the rationale that *[name of active ingredient]* is a naturally-occurring *[soil/water/plant-surface. etc.]* colonizer, whose level in the environment will not significantly increase with the use of *[product name]* and that an extensive literature search yielded no *[or no significant]* reports of adverse effects on wild mammal species. In addition, human health data performed on rodent species showed no detrimental effects.

The proposed uses of *[product name]* on *[identify use sites/crops]* is not expected to result in increased exposure or adverse effects to wild mammal species. *[If environmental concentration will show a substantial increase, give the rate of environmental reduction to background levels in days/weeks/months].* Therefore, additional testing is not considered necessary to assess the risks of the *[product name]* to wild mammals. The *[applicant]* requests a waiver of wild mammal testing.

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

##### **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.]

The waiver request is based on the following rationales:

* 1. **Increased environmental exposure to *[name of active ingredient]*, due to use of the end-use product *[product name]*, will be minimal to wild mammals.** *[Applicant should provide further elaboration: Describe the natural habitat of the MPCA. Is it an obligate parasite/epiphyte? Is it ubiquitous in nature (give geographical distribution)? Has the MPCA, and/or phylogenetically close species/strains, been isolated from soil/streams/ponds/lakes and a variety of plant surfaces including (identify names) crops/vegetables/fruits? Provide the known natural concentration of the MPCA in CFU/(weight-volume-surface area) in these environmental niches.]*

Use of *[product name]* will be limited to *[soil, seed, foliar, greenhouse, etc.]* applications *[by spray, dip, soil incorporation, aerial, etc.]* on *[name crops/use sites]*, thus minimizing direct exposure to **wild mammals**. *[Does timing of application preclude direct exposure to insects/arthropods? Discuss crop*

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*use sites and application methods and its effects on limiting runoff, if applicable. Provide the rate in environmental reduction of the MPCA to background levels in days/weeks/months, if available. Include any other factors that would limit exposure to* wild mammal species.*. Would any of the MPCA that reaches the soil/water behave as it would in the wild?]*

* 1. **No evidence of adverse effects.** A literature search of the *[e.g., AGRICOLA, TOXLINE, BIOLOGICAL ABSTRACTS, CHEMTOX, PUBMED, HAZARDOUS AND REGULATED CHEMICALS DATABASE or OTHER]* databases for the period *[year range]* was conducted. In this literature search, *[name of MPCA]* and other phylogenetically close species/strains in the *[family/genus/species-group, etc., as appropriate]*, as well as synonyms *[name of synonyms of MPCA, if any]* were used as the search words. The searches were also used to ascertain the known production of *[genotoxic, carcinogenic, allergenic, mutagenic, toxic]* metabolites, antibiotics, mycotoxins, mycocins, pathogenicity, environmental fate and interactions with wild mammals. *[Include the metabolites found to be produced - does the MPCA strain also produce these or other metabolites? Have natural populations of the MPCA or its metabolites been associated with adverse effects in wild mammal species?]*

##### *[Discuss whether runoff or overspray would result in effects not seen from the naturally occurring MPCA* levels. Discuss whether the MPCA does/does not grow at mammalian body temperatures. Does the MPCA appear on any authoritative list of mammalian pathogens? Provide the lists examined. Have any adverse effects to wild mammals been reported due to naturally occurring populations of the MPCA?]

*[Provide a summary of the mammalian toxicity/infectivity data obtained from human health and safety assessment, including the dose levels in CFU and results obtained (oral, intraperitoneal/intravenous injection, pulmonary, dermal toxicity/infectivity and dermal and ocular, if submitted, irritation studies.]*

**[*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.]*

##### **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data* can be provided to satisfy the deficiency.]

1. **CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]**

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##### **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.]***

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

1. **PURPOSE:** *[Indicate the purpose of the study]*

##### **METHOD:** *[Describe the experimental procedure]*

1. **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.]*

##### **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data* can be provided to satisfy the deficiency.]

1. **CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]**
2. **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.*]**

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

##### **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 in Canada to examine the effects of this MPCA on non-target mammals. These include acute toxicity testing, acute infectivity testing, and subchronic toxicity testing.*

* 1. *.,* ***A. ACUTE TOXICITY TESTING:***
     1. ***Article 1:*** *(summarize and report findings)*
     2. ***Article 2:*** *(summarize and report findings)*
  2. ***ACUTE INFECTIVITY TESTING:***
     1. ***Article 1:*** *(summarize and report findings)*
     2. ***Article 2:*** *(summarize and report findings)*

### *SUBCHRONIC TOXICITY TESTING:*

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

***2 Article 2:*** *(summarize and report findings)]*

1. **CONCLUSION**
2. **LITERATURE REVIEW CONCLUSION:** *[Summarize the study author’s conclusions]*
3. **REVIEWER’S COMMENTS:** *[Note if in agreement with study authors.]*

##### **DEFICIENCIES:** *[List each deficiency with the required data to resolve the deficiency or if no data* can be provided to satisfy the deficiency.]

1. **CLASSIFICATION: [ACCEPTABLE / UNACCEPTABLE / SUPPLEMENTAL, but UPGRADEABLE]**
2. **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.*]**

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