



TOXICOLOGICAL SUMMARY REQUIREMENTS

Introduction

The following guidelines respecting the content of a summary of a toxicological study were developed by Health Canada and accepted by a government/industry/labour consensus committee.

Requirements

NOTE: For those studies that did follow OECD, Draize, or other acceptable protocols, less details of methodology would be required.

Was a standard protocol followed?

Concentration, Percentage Purity, Vehicle Dose Levels, Controls?

Species, Number of Animals/Sex/Level

Duration of Exposure

Which observations were made? e.g. : Body weights? Hematology? Biochemistry?

For gross or histopathology, which tissues were examined?

In addition to the above-noted information, the information presented below, if available, would also be required.

ACUTE ORAL (i.e. LD₅₀)

Observation period

Mortality per Dose Level or LD₅₀ value (method of calculation) and 95% Confidence Intervals

Treatment-related Effects: e.g. behavioural, body weights, pathology

ACUTE DERMAL (i.e. DERMAL LD₅₀)

Location and details of application (occlusion?)

Observation Period

Mortality per Dose Level or LD₅₀ value (method of calculation) and 95% Confidence Intervals

Treatment-related Effects: e.g. irritation, behavioural, body weights, pathology

DERMAL IRRITATION

Location and Details of Application (abrasion, occlusion)

Observation Period

Method of Scoring

Scores obtained at each time period, Primary Irritation Index

Observations: erythema, edema, necrosis

EYE IRRITATION

Volume instilled

Controls/Washed?/Unwashed?

Observation Period

Method of Scoring

Score Attained for each time period

Observations (cornea [opacity?], iris, conjunctiva)

DERMAL SENSITIZATION

Induction/Challenge Dose and Method

Positive and Negative Controls?

Observation Period

Method of Scoring

Observations (sensitizing potential?)

SHORT-TERM/SUBCHRONIC STUDIES

Route of Administration

Dosing Schedule

Details of which organs were weighed and which tissues examined.

Results: NO(A) EL, LO(A) EL and basis for establishment

Observations (per dose level): What effects at what dose? mortality, morbidity, body weight, food consumption, clinical analysis, (histo)pathology.

CHRONIC STUDY/CARCINOGENICITY

Route of Administration

If non-dietary route utilized, details of dosing.

Stability of test material in vehicle of administration.

Details of which organs were weighed and which tissues were examined.

Results: NO(A) EL, LO(A) EL and basis for establishment.

Observations (per dose level) : What effects at what dose? mortality, morbidity, body weight, food consumption, clinical analysis, organ weights (histo)pathology.

Neoplastic/Nonneoplastic lesion incidence.

TERATOLOGY

Strain

Method of Pregnancy Determination

Route of Administration, Dosing Period

Observations: Any treatment-related effects with respect to:

Maternal

Body Weight

Food Consumption

Morbidity

Pathology

Reproductive Indices

Fetal

Body Weight

Mortality

Corpora lutea

Resorptions

Sex Ratio

Anomalies: external
visceral
skeletal

REPRODUCTIVE STUDY

Strain, Nulliparous Females?

Route of Administration

Premating dose period for both sexes

Mating and Culling Procedure

Method of Pregnancy Determination

Observations: Any treatment-related effects with respect to:

Reproductive Indices: Fertility, Gestation, Viability, Lactation

Maternal Observations

Gestation Length/Abortions

Body Weight

Stillbirths/Live Births

Fetal Observations

Birth Weight/Post Birth Weight

Survival

Sex Ratio

For those studies looking at male fertility: semen analysis, mating behaviour, testes weights and histopathology, fertility, endocrine measures.

MUTAGENICITY ASSAYS

Was a standard protocol followed?

Dose Levels, Positive, Negative, Vehicle Controls?
Metabolic Activation? S9?
Gene Mutation Endpoint
Overall Result (Positive, weak or strong?)
Cell survival
Mutation Frequency

ACUTE INHALATION LC₅₀

N.B. Additional detail of evaluation criteria are provided here for clarification purposes.

Was a standard protocol followed? If so, which one (EPA, OECD, etc.)?
Percent purity of the Test Material. Was a vehicle used?
Target Exposure Levels for the Study?
Was there a Concurrent Control Group?
Species/Number of Animals per Sex per Exposure Level
Duration of Exposure
Chamber Design: There should be sufficient information on the exposure chamber to allow the reviewer to evaluate the suitability of the chamber used.
Were environmental parameters of chamber monitored during the exposure period? e.g. :
Temperature, Relative Humidity and Airflow Rate.
Physical Form e.g. : dust, mist, fume, vapour
Particle Size Distribution: Particle size determinations need to be made when test atmospheres are generated as aerosols (sprays or dusts)
Actual concentrations achieved at each measurement period or mean concentration and standard deviation. Frequency of measurement.
Type of Exposure (nose-only, whole body)
Length of post-exposure observation period
Mortality per Exposure Level or LC₅₀ (method of calculation) and 95% Confidence Intervals
Treatment-related Effects: behavioural, body weights, pathology (especially respiratory tract)

References: 1) OECD Guidelines, section 403, Acute Inhalation Toxicity 2) Pesticide Assessment Guidelines, Addendum 6 on Acute and Subchronic Inhalation Toxicity Testing. U.S. EPA